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Authors

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Abstract Title

Flolan® and Veletri® Medication Use and Cost Analysis Audit at an Academic Medical Center

Purpose

The objective of this audit was to evaluate the usage and associated costs of Flolan® (epoprostenol) versus Veletri® (epoprostenol).

Background

In 2012, The Ohio State University Wexner Medical Center (OSUWMC) began an initiative called “Create the Future Now” which aimed to adapt the organization to the rapidly changing health care environment. This endeavor allowed the health-system to become more value-driven while maintaining optimal patient outcomes. One of the pillars of this initiative is financial innovation to reduce health care expenditures in favor of using the most cost-effective therapeutic modalities while maintaining efficacy for the patient.

Prior to the Create the Future Now initiative, OSUWMC only had Flolan® on formulary. The yearly cost to the pharmacy department to carry the medication and diluent products was ~\$250,000.

Veletri® was added to the formulary at OSUWMC on June 4, 2013. It was added with the agreement that all new epoprostenol starts would be on Veletri®. Flolan® was kept on formulary for use only by patients currently maintained on this therapy.

Methodology

This retrospective utilization and cost analysis review evaluated all Flolan® orders from July 1, 2011 through June 30, 2012 (FY12) and July 1, 2015 through June 30, 2016 (FY16) as well as all Veletri® orders from FY16 for any patient admitted to OSUWMC. The data utilized from these

reports included quantity of drug in milliliters (mL) and dose in milligrams (mg) to determine the amount of drug used. The number of patients receiving epoprostenol (either brand) was also obtained.

Results

The estimated cost associated with the use of Flolan® in FY12 was ~\$250,000 for 654 bags of medication and a total of 5467 mg of drug. In FY16, the cost associated with the use of Flolan® was reduced to ~\$70,000 which was associated with 126 bags and 1680 mg of drug, and the cost of Veletri® was ~\$100,000 which was comprised of 390 bags and a total of 2586 mg of drug. The combined cost of both brands in FY16 was ~\$170,000 with a total of 516 bags and 4266 mg of epoprostenol product.

Conclusion

The data demonstrates a cost savings of ~\$80,000 with the addition of Veletri® to the formulary however it must be noted that there were 138 fewer bags and a total of 1201 fewer milligrams of drug dispensed. It is notable that, in FY12, there were five more patients receiving an epoprostenol product than in FY16. Furthermore, the patient population is small and inpatient length of admission may be variable based on severity of disease. Despite the limitations, the results confirm the benefit of having Veletri® on formulary in addition to Flolan®. Although this analysis provides an estimate rather than an exact amount, the cost-savings is significant. This data, we believe, is useful and informative with regards to the success of a pharmacy-based cost-savings initiative.

Authors

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Abstract Title

Transition from Parenteral Prostacyclin Therapy to Oral Selexipag in Pulmonary Arterial Hypertension: a Single Center, Case Series

Purpose

Review all patients with PAH on IV or SC therapy that were transition to selexipag in our institution.

Methods

We reviewed all patients with PAH on IV or SC therapy that transitioned to selexipag therapy in our institution. Rationale for transition was highly individualized and included patient preference, history of complications related to ongoing IV or SC treatment and hemodynamic/clinical profile. NYHA function class (FC) was assessed before and after transition to selexipag; 8 patients in the cohort had follow-up hemodynamics by the time of presentation.

Results

Nine (64%) patients were on IV epoprostenol and five patients on SC treprostinil prior to transition. Duration of parenteral therapy prior to transition ranged from 9-62 months (mean 30.1 ± 18.3 months).

The majority of patients were female (86%) and over the age of 50 (mean 55.6 ± 11 years).

All patients were on background PAH therapy. Eight on combined ERA/NO-pathway medications. Five patients on

NO-pathway alone and one patient on ERA alone.

Average time between transitioning to selexipag and functional class assessment was 6.6 months.

Eleven (79%) of the 14 patients maintained their NYHA FC after transitioning to selexipag.

Two patients had worsening of FC after transitioning. One of these patients required re-initiation of parenteral therapy.

One patient with scleroderma and clinical features of PVOD transitioned to selexipag for difficulty maintaining IV therapy without option of lung transplantation. She was functional class IV prior to transition – and had clinical worsening due to right heart failure and died under hospice care.

Conclusion

The transition from chronic parenteral prostacyclin therapy to oral selexipag is feasible but requires careful individualized consideration with close monitoring during and after the transition period.

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Abstract Title

Specialty Pharmacy Prepared Veletri® Cassette Program

Full Abstract

Purpose

Purpose: Veletri® is administered as a 24 hour continuous IV infusion via central line. Reconstitution and dilution are required before use, and are typically performed by the patient or caregiver. The Veletri® Ready Sette Go Program (RSGP) was undertaken to provide premixed cassettes as a way to improve patient convenience and satisfaction.

Background

Room temperature stable epoprostenol (Veletri®) is a synthetic prostacyclin indicated to improve exercise capacity in patients with pulmonary arterial hypertension (PAH). Epoprostenol remains the recommended treatment for patients with advanced disease and is the only medication that has demonstrated a survival benefit in idiopathic PAH.¹ Despite recommendations, these patients often do not receive intravenous (IV) prostacyclins; this may be due, in part, to issues related to the complex mixing and delivery systems.²

Methodology

The RSGP represents a partnership between practitioners, specialty pharmacy (SP) (Accredo Health Group, Inc.), patients, and industry. On a weekly basis, patients are shipped Veletri® cassettes that have been prepared by pharmacists adhering to USP 797 guidelines. Other processes to ensure

patient and product safety include defined patient inclusion criteria, strict shipment procedures, pharmacist training, SP site audits, and emergency protocols. Referrals are limited to PAH centers with experience using IV prostacyclins. This program is offered at no additional cost to patients or payers.

Findings

The RSGP was piloted in 14 PAH centers between 2014 and 2015. Two expansions were implemented to include 34 additional centers. As of Nov 2016, 233 patients had been referred to the program, with 141 currently active. Limitations to patient enrollment include limited contracting with only one SP, patient decision, and payor restrictions.

Implications

IV prostacyclins are underused in severe PAH, possibly due in part to the complicated administration regimens. The Veletri® RSGP was initiated to improve patient convenience by providing SP-prepared premixed cassettes. Additionally, mixing under sterile conditions may reduce the risk of infection. The program has since been expanded twice due to patient and practitioner interest, and now includes 48 PAH centers across the US. Future analyses will aim to evaluate patient satisfaction and other measures to gauge success of the program.

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Abstract Title

Transition from intravenous epoprostenol to oral treprostinil in a patient with pulmonary arterial hypertension.

Purpose

To describe an experience of transitioning an epoprostenol patient to oral treprostinil in the ICU setting.

Background

Epoprostenol has improved outcomes including survival in patients with World Health Organization functional Class III and IV pulmonary arterial hypertension (PAH)[1]. However, its short half- life and need for strict monitoring of pump function precludes its use in certain populations. Oral treprostinil monotherapy has been shown to have a modest effect on exercise capacity in patients with WHO functional class II to III symptoms, and there is little experience in patients with more advanced PAH.[2,3]. Although guidelines exist for initiation of oral treprostinil in prostanoid naïve patients, evidence regarding transition from parenteral epoprostenol to oral treprostinil remains limited.

Methods

A 59 year- old female with a long history of idiopathic PAH was electively admitted for management of her PAH medications. She has been treated with intravenous epoprostenol, bosentan and sildenafil for over 10 years with resultant improvement in her functional class and exercise capacity. Prior to this admission, she was diagnosed with Alzheimer's dementia which was found on several occasions to have made major errors in programming her CADD pump and unable to appropriately respond to pump alarms. It became clear that she was no longer able to safely manage her parental PAH therapy, and a decision was made to transition her to oral treprostinil.

On, admission, her epoprostenol was 60 ng/kg/min, and we estimated that her final dose of oral treprostinil would be 12 mg every 8 hours. Her weight was 50 kg on admission. We used a conversion factor of 1.67 between intravenous epoprostenol and intravenous treprostinil and a correction factor of 5 based on bioavailability of oral treprostinil. [4]. Her intravenous epoprostenol was decreased by 1 ng/kg/min every 2 hours to a maximum of 4 ng/kg/min on the first day followed by 6 ng/kg/min on day 2 and 8 ng/kg/min from the third day on. Oral treprostinil was started at 0.25 mg every 8 hours and up titrated cautiously in the first 3 days to 1.5 mg and from day 4 by 2-3 mg daily. She tolerated this titration well until day 7, when she developed a slight headache. The treprostinil dosage was subsequently increased by only 1 mg on day 7 and 8 to avoid further adverse events. By day 9 she was off her IV epoprostenol and on her goal of 12 mg every 8 hours of oral treprostinil.

Results

Four days into her new oral regimen, she underwent repeat right heart catheterization which showed moderate PAH with a PA mean of 35.3 mm HG, pulmonary vascular resistance of 5 woods units and a thermodilution cardiac index of 3.56 l/min/m². She was discharged home the following day and continues to live at home with daily assistance.

Conclusion

Certain patients might be candidates for rapid transition from intravenous to oral prostacyclin. Multicenter clinical trials will help in identifying the optimum patient and protocol for the transition.

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Abstract Title

OPUS registry: Treatment patterns with macitentan in patients with pulmonary arterial hypertension

Purpose

To provide insight into the use of macitentan in the real-world, post-marketing setting.

Background

The OPsumit® USers registry (OPUS; NCT02126943) characterizes the use and safety profile of the endothelin receptor antagonist (ERA) macitentan (Opsumit®) in the real-world setting.

Methods

Started in April 2014, OPUS is an ongoing long-term, prospective, multicenter, observational drug registry of patients newly treated with macitentan in the US. This analysis reports patient characteristics, treatment patterns, and safety of macitentan in patients with pulmonary arterial hypertension (PAH) enrolled in OPUS.

Results

By April 17, 2016, 688 PAH patients who newly initiated macitentan had enrolled in OPUS; follow-up information was available for 590 patients. The follow-up cohort had a median age of 63 years (range, 19–90) at enrollment and was primarily female (74.2%). In total, 47.9% of patients had been diagnosed with PAH within 6 months, and 16.3% had switched from another ERA. WHO functional class at enrollment was assessed in 454 patients; 38.4% were class I/II and 61.6% were class III/IV. The median 6-minute walk distance was 300 m (range, 30.0–750.0 m; n=308). Treatment patterns with respect to PAH-specific medications are shown in Table 1. During follow-up, 401 (68.0%) patients received concomitant treatment with at least one PAH-specific therapy, primarily with phosphodiesterase type 5 inhibitors

(PDE5i). Median exposure time of concomitant medications was as follows: PDE5i 5.5 months (range 0.0–20.6 months); i.v./s.c. prostanoids 3.9 months (0.0–20.6 months); inhaled prostanoids 5.4 months (0.0–19.2 months); oral prostanoids 1.1 months (0.0–7.6 months); and soluble guanylate cyclase-stimulators 4.0 months (0.0–17.0 months). Comparisons between the overall follow-up cohort and the subset of patients who switched from another ERA showed similar median macitentan exposure time (5.6 months [range 0.1–22.1 months] versus 6.6 months [0.1–19.9 months]; similar proportions of patients exposed to macitentan for >1 year (15.9% versus 20.9%); and similar treatment discontinuation rates (22.7% versus 19.8%). Adverse events (AEs) were the most common reason for discontinuation. In the overall follow-up cohort, 338 patients (57.3%) experienced ≥ 1 AE during the exposure period, the most common being dyspnea (12.9%) and peripheral edema (8.0%). Twenty patients (3.4%) experienced ≥ 1 hepatic AE, and 55 (9.3%) experienced ≥ 1 PAH-related hospitalization. The 12-month Kaplan-Meier survival estimate was 93% (95% CI: 0.89, 0.95).

Conclusion

OPUS provides further insights into macitentan use in the real-world, post-marketing setting. Specifically, the majority of patients are treated with combination PAH therapy. Further, the safety profile of macitentan in the real-world setting is consistent with that observed in the clinical trial setting when used as monotherapy, in combination with other PAH treatments, and in those who switched to macitentan from another ERA.

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Abstract Title

RESPITE: Riociguat in pulmonary arterial hypertension patients with an inadequate response to phosphodiesterase type 5 inhibitors (PDE5i)

Purpose

RESPITE investigated the safety, feasibility, and clinical benefit of switching from PDE5i to riociguat in patients with pulmonary arterial hypertension (PAH) who had an inadequate response to PDE5i.

Background

PDE5i are widely used to treat PAH; however, some patients fail to reach or maintain treatment goals

Methods

RESPITE (NCT02007629) was a prospective, multicenter, uncontrolled, open-label, single-arm, Phase IIIb trial. PAH patients in World Health Organization (WHO) functional class (FC) III with 6-minute walking distance (6MWD) 165–440 m, cardiac index <3.0 L/min/m², and pulmonary vascular resistance (PVR) >400 dyn·s·cm⁻⁵, despite receiving PDE5i either alone or with endothelin receptor antagonists (ERAs), were enrolled. Following a 1–3 day PDE5i treatment-free period, riociguat was individually adjusted to a maximum of 2.5 mg tid. Exploratory endpoints were assessed at Week 24 including 6MWD, N-terminal prohormone of brain natriuretic peptide (NT-proBNP), pulmonary hemodynamics, WHO FC, and EuroQol 5-Dimensions questionnaire (EQ-5D) score to assess quality of life. A composite endpoint was also assessed, defined as patients who achieved freedom from clinical worsening, WHO FC I/II, and a ≥30 m increase in 6MWD. Safety assessments and recording of adverse events (AEs) were undertaken during the treatment-free period and during the period following the switch to riociguat. At the end of the study, patients could participate in an extended drug-supply phase for 18 months or until reimbursement. Patients who discontinued the study drug or did not enter the

extension phase underwent a 30-day safety follow-up.

Results

Of 61 patients enrolled, 51 (84%) completed the study. Fifty (82%) were receiving concomitant ERAs. Significant improvements were observed in mean 6MWD, NT-proBNP, cardiac index, PVR, and change in WHO FC from baseline to Week 24 (table). Six patients (10%) experienced clinical worsening, two of whom died (unrelated to the study drug). Sixteen patients (31%) achieved the composite endpoint at Week 24. Clinically meaningful improvements were observed in EQ-5D visual analog scale and utility scores with mean±SD increasing from baseline to Week 24 by +7±19 (n=61) and +0.07±0.28 (n=52), respectively. Switching was generally well tolerated, with 32 patients (52%) experiencing study drug-related AEs, the most frequently reported (>10% of patients) being headache (16%), dyspepsia (15%), hypotension (11%), and dizziness (11%). Ten patients (16%) experienced serious AEs, two (3%) of which were study drug-related (right ventricle failure and asthenia). No serious AEs occurred during the PDE5i treatment-free period. Syncope was not reported in the study and there was one mild case of hemoptysis, which was considered unrelated to the study drug. Four patients (7%) experienced AEs leading to discontinuation of the study drug, including two patients with right ventricular failure, one patient with asthenia, and one patient with symptomatic hypotension.

Conclusion

The clinical improvements in 6MWD and WHO FC, as well as in hemodynamic variables, NT-proBNP and EQ-5D scores, suggest that PAH patients with insufficient response to PDE5i may benefit from switching to riociguat.

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Abstract Title

Rationale and design of the REPLACE trial: Riociguat rEplacing Phosphodiesterase 5 inhibitor (PDE5i) therapy evaLUated Against Continued PDE5i thERapy in patients with pulmonary arterial hypertension

Purpose

The REPLACE study (NCT02891850) will investigate the potential efficacy and safety benefits of switching to riociguat versus continued treatment with PDE5i therapy in patients with pulmonary arterial hypertension (PAH).

Background

A significant proportion of patients with PAH fail to achieve or maintain treatment goals with PDE5i therapy. This may indicate impairment of the nitric oxide-soluble guanylate cyclase (sGC) pathway, leading to insufficient endogenous cyclic guanosine monophosphate levels. Data from the single-arm, open-label RESPITE study provided preliminary evidence that these patients may benefit from switching from PDE5i to riociguat, an sGC stimulator.

Methods

REPLACE is a prospective, randomized, international, multicenter, two-arm, 24-week, controlled, open-label study in patients aged 18–75 years with PAH who do not achieve or maintain treatment goals with PDE5i therapy. Insufficient clinical response to PDE5i therapy at screening is determined by: World Health Organization (WHO) functional class (FC) III and 6-minute walking distance (6MWD) 165–440 m, despite stable doses of PDE5i with or without background endothelin receptor antagonists (ERAs). Eligible patients will be randomized to remain on PDE5i treatment (sildenafil 60 mg minimum daily or once-daily tadalafil 20–40 mg) or

switch to riociguat up to a maximum of 2.5 mg tid (dose adjusted from a starting dose of 1.0 mg tid) (figure). Riociguat therapy will be initiated following washout periods of 24 and 48 hours for sildenafil and tadalafil, respectively. ERA treatment will be continued at the stable dose in both arms.

Results

The planned enrollment of REPLACE is 218 patients. The primary efficacy endpoint 'satisfactory clinical response' will be assessed at Week 24 and is defined as a composite fulfillment of 2 of the 3 parameters – $\geq 10\%$ or ≥ 30 m increase from baseline in 6MWD; WHO FC I or II; and $\geq 30\%$ reduction from baseline N-terminal prohormone of brain natriuretic peptide (NT-proBNP) – in the absence of clinical worsening. This will be reviewed and confirmed by an independent clinical endpoint committee. Secondary efficacy outcomes will comprise change from baseline in 6MWD (blinded assessment), NT-proBNP, WHO FC (blinded assessment), and clinical worsening. Exploratory analyses will include quality of life (Living with Pulmonary Hypertension questionnaire), modified REVEAL risk score, and cardiac magnetic resonance imaging of a subset of patients. Safety will be evaluated by adverse events and all-cause mortality.

Conclusion

The REPLACE study will evaluate whether it is clinically beneficial to switch patients with PAH who do not achieve or maintain treatment goals with PDE5i therapy to riociguat.

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Abstract Title

The rationale for a washout period when switching patients from phosphodiesterase type 5 inhibitors (PDE5i) to riociguat

Purpose

To establish the optimal washout period for switching from PDE5i to riociguat in patients with pulmonary arterial hypertension (PAH) who have an inadequate response to PDE5i.

Background

PDE5i and the soluble guanylate cyclase (sGC) stimulator riociguat are treatments for PAH that target the nitric oxide (NO)-sGC-cyclic guanosine monophosphate (cGMP) pathway at separate molecular targets. Patients with PAH exhibit endothelial dysfunction resulting in decreased NO bioavailability and low levels of intracellular cGMP, which may render PDE5i ineffective, and many PAH patients receiving PDE5i do not reach treatment goals. Concomitant administration of PDE5i with riociguat is contraindicated, as an increased risk of side effects over the long term (particularly hypotension) and no evidence of a positive benefit:risk ratio were observed in the PATENT PLUS study (Galiè et al. *Eur Respir J* 2015;45:1314-1322). Riociguat stimulates sGC through an NO-independent mechanism, meaning that its mechanism of action is unaffected by the decreased NO levels characteristic of patients with PAH. Therefore, switching patients with insufficient response to PDE5i to riociguat may optimize signaling in the NO-sGC-cGMP pathway.

Methods

We reviewed published and unpublished data for PDE5i (sildenafil and tadalafil) and riociguat, and data from PATENT PLUS to propose a washout period for patients switching between these agents.

Results

PDE5i are contraindicated with organic nitrates, as this can cause a profound, synergistic drop in blood pressure. As

pharmacodynamic data (blood pressure and heart rate) show no interaction between sildenafil and nitrates after 24 hours' washout (six sildenafil half-lives), a 24-hour sildenafil washout period before starting nitrates is recommended. Interaction studies showed a moderate additive, but not synergistic, effect of riociguat and sildenafil on blood pressure; therefore, a 24-hour washout period should also be appropriate before starting riociguat.

Tadalafil labeling recommends a 48-hour washout before starting nitrates, derived from findings that the hypotensive tadalafil-nitrate interaction is no longer present after 48 hours. There are no available data on concomitant therapy with riociguat and tadalafil; however, based on the available evidence, a 48-hour washout period is proposed for switching from tadalafil to riociguat.

Conclusion

Data from the PDE5i and nitrate interaction studies indicate the effectiveness of a 24-hour (sildenafil) or 48-hour (tadalafil) washout period for reducing the interaction between PDE5i and nitrates. The use of the same washout periods for switching from PDE5i to riociguat represents an appropriate balance between safe transition and minimizing the delay during which patients may be deprived of treatment and at risk of deterioration. In line with American Thoracic Society recommendations (Hill et al. *Ann Am Thorac Soc* 2015;12:269-273) and the US prescribing information for riociguat, in the ongoing REPLACE study, riociguat treatment will be started after a washout period of 24 hours with previous sildenafil therapy and 48 hours with previous tadalafil therapy.

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Abstract Title

Uptravi® (Selexipag): tHe usErs dRug rEgistry (SPHERE) - A US-Based, Prospective Drug Registry of Selexipag in Clinical Practice

Purpose

To describe the design and objectives of the SPHERE registry.

Background

Uptravi® (selexipag) is an oral, selective IP prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to delay disease progression and reduce the risk of hospitalization for PAH. In the Phase III GRIPHON trial of 1,156 patients with PAH, selexipag significantly reduced the risk of occurrence of the primary outcome composite of morbidity or mortality by 40% compared with placebo (Sitbon et al. *N Engl J Med*, 2015). Based on these data, selexipag was approved by the FDA in December of 2015. SPHERE will report data from routine clinical practice including disease characteristics, clinical outcomes, and dosing regimens of patients treated with selexipag.

Methods

SPHERE is a US, multicenter, prospective, real-world observational registry that will enroll approximately 500 patients with PAH (from approximately 75 centers) who initiate selexipag at the time of enrollment or who have been receiving treatment with selexipag and have a documented titration regimen. Patients who have previously been treated with selexipag as part of a clinical trial or who have discontinued selexipag will be excluded from the registry. Patients currently enrolled in a blinded clinical trial or trial

of an unapproved drug will also be excluded. Data will be gathered from electronic medical records from routine clinical practice on a quarterly basis and will be collected for up to 18 months from the date of enrollment.

Results

The main objectives of SPHERE are to describe: (1) disease characteristics; (2) dosing regimens and titration; and (3) the clinical course of patients being treated with selexipag. Adverse events and serious adverse events will also be collected during the observation period. Data analysis will be conducted for all patients as well as separately for patients who newly initiated selexipag treatment, and who had previously initiated selexipag at the time of enrollment. Dosing regimens, including titration and maintenance doses, will be described. Transitions from or to a prostacyclin (intravenous/subcutaneous, oral, or inhaled) will be analyzed. Clinical course will be evaluated by survival time, death related to PAH, change in WHO functional class, 6-minute walk distance, hemodynamic measurements, and vital signs. Analyses will be adjusted for covariates including PAH prognostic factors and prior PAH therapies.

Conclusion

SPHERE will describe disease characteristics, characterize dosing regimens and titration, and the clinical course and outcomes in patients treated with selexipag in a real-world setting.

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Abstract Title

Preliminary Data from the United States CTEPH Registry

Purpose

A U.S. CTEPH Registry was organized to characterize the demographics, evaluation, and clinical course of CTEPH in the United States and to assess short and long term outcomes of surgical and non-surgical therapy of CTEPH in the U.S. health care system.

Background

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare, life-threatening condition that represents the most severe long-term complication of acute pulmonary embolism. Yet the symptoms of CTEPH, which include exercise intolerance, fatigue, and dyspnea, are nonspecific. As such, CTEPH may be underdiagnosed in patients presenting with such symptoms or may be misdiagnosed as pulmonary arterial hypertension due to a lack of disease awareness. CTEPH is the only form of PH that is potentially curable, and only with pulmonary thromboendarterectomy (PTE), so it is critical that it be appropriately diagnosed. The epidemiology and demographics of CTEPH have yet to be adequately described in the U.S. population.

Methods

Multi-center, prospective observational registry of newly diagnosed CTEPH patients. First subjects were enrolled in April 2015 with plans for a total enrollment of 750 subjects over a 3-year period at 30 U.S. sites.

Results

As of May 2017, 588 subjects were submitted for radiologic adjudication and 548 subjects were enrolled in the Registry (6.7% did not meet adjudication criteria). Median age = 56 yrs (range 16-87 yrs), 50.4% male. Caucasians comprise 72% of the population, Blacks/AA 21%, Asians 1.4%. Hispanic

or Latino = 6%. WHO Functional Class: I (2%), II (20%), III (64%), IV (11%). History of DVT reported in 49% and acute PE in 87%. Lupus anticoagulant was the most common thrombophilia identified (13%). Most subjects were anticoagulated with warfarin (50%), with 35% treated with NOACS. Prior to PTE surgery, 54% of subjects were on pulmonary arterial hypertension target medical therapy (PAH therapy), the most common being sGCS (54% of those on PAH therapy, 28% of all subjects) followed by PDE-5 inhibitors (23% on PAH therapy, 12% all subjects), parenteral prostanoids (8% on PAH therapy, 4% all subjects), or ERAs (8% on PAH therapy, 4% all subjects) with 7% of subjects on more than one PAH therapy. 45% of subjects were on supplemental O₂ at enrollment, 57% on diuretics.

Enrollment RHC mean values: RA 10 mmHg, mPAP 45 mmHg, PCWP 12 mmHg, C.O. 4.8 L/min, C.I. 2.5, TPR 10.3 WU. Operability assessments performed on 456 subjects by enrolling centers yielded 87% subjects operable, 10% inoperable and 3% unsure. Of the 440 subjects referred to surgical centers, 92% were deemed operable and 98% of those were referred for surgery. Early post-operative hemodynamics are available from 334 subjects: RA 8.6 mmHg, mPAP 26.3 mmHg, C.O. 5.8 L/min, TPR 4.7 WU. Fifteen subjects have undergone balloon pulmonary angioplasty.

Conclusion

Demographic characteristics of initial patients in the U.S. CTEPH Registry appear to be similar to those previously reported. Despite the vast majority of subjects being deemed operable, medical therapies for CTEPH/PAH are commonly being used. Preliminary data also confirms significant early hemodynamic improvement following PTE surgery.

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Abstract Title

Long Term Results Following the Use of a Novel Educational Program to Enhance Nursing Knowledge of Pediatric Pulmonary Hypertension

Purpose

The aim of this project was to better understand what educational programs best enhance knowledge on a busy inpatient step-down unit, as well as to detail the impact of this educational program on acquired knowledge and confidence levels for its intended audience, up to eighteen months after the initial program.

Background

The nursing care and management of pediatric patients with pulmonary hypertension (PH) is complex, challenging and not widely understood. As the PH program at Children's Healthcare of Atlanta has grown at a rapid pace, the need for an intensive educational program for nurses caring for PH patients was recognized. There is no description in the literature of effective nursing education models in pediatric pulmonary hypertension.

Methods

The unit selected for the educational program was a 27-bed cardiac step-down unit, staffed by more than 60 nurses. This 5-week long voluntary program consisted of several components. First, a test was offered to all nurses to assess knowledge in five content areas: basic PH knowledge, signs and symptoms, treatment, safety considerations, and PH crisis. All nurses were then sent a pre-intervention survey, inquiring about education needs and knowledge gaps, the largest of which was on pulmonary hypertension crisis. Survey results were used to develop educational content. A novel educational approach was used to impart knowledge, including various modes of sharing knowledge and information. Modes used for education included two articles; 3 posters, one of which focused on PH crisis; several short 'lunch and learns' on all nursing shifts; a daily email for 30 days which included a "PH fact of the day"; two games; and several case studies which involved utilizing critical thinking skills. At the end of the educational intervention, a survey was sent to all nurses, inquiring about confidence levels in caring for PH patients and what educational tools were most

impactful and least helpful. A post-test was offered to all nurses four months after the intervention, as well as eighteen months after the intervention.

Results

Of the more than 60 nurses who were asked to participate on a volunteer basis, 20 took both the pre- and post-test and both surveys. The post-test was given four months after the educational intervention. Of the 20 nurses, 17 improved their test score from an average of 58% to 77%. When asked to rate the education mode from most helpful to least helpful, daily emails of PH facts and oral presentation/lectures topped the list, while reading textbooks/articles and the crossword puzzle were at the bottom. Confidence was measured on a scale of 0-3, where 0 is no confidence, 1 is mildly confident, 2 moderately, and 3 is extremely confident. Average scores improved by 18% in the area of confidence to care for a PH patient, increasing from 1.7 to 2. The confidence in recognizing symptoms of PH crisis improved by 60%, increasing from 1 to 1.6, and the confidence in caring for a PH patient in crisis improved by 75%, increasing from 0.8 to 1.4. Finally, of the 20 nurses that completed the pre- and post- tests four months after the intervention, 12 of these nurses completed the same test eighteen months after the intervention. Four of the 12 nurses further improved their scores from the post-intervention test, and all 12 nurses maintained higher scores when compared to their initial, pre-intervention test scores.

Conclusion

Based on findings, certain educational components will be left out in future educational endeavors, and the length of time will be shorter in duration. More hands-on activities and training videos will be used in the future, and more PH education will be included in new hire orientation lectures and orientation manuals. Limiting factors to the intervention included nurses' time required on a busy unit with a high turnover rate despite the 24/7 access to information and incentives.

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Abstract Title

Get with the guidelines - turning a heart failure nurse into a pulmonary hypertension coordinator.

Purpose

The guidelines for management of the pulmonary arterial hypertension (PAH) population are relatively new and less well-established, with a much fewer number of providers, as compared to the heart failure population. The objective was to review heart failure guidelines and apply appropriate nursing measures in PAH to increase comfort in providing cost-effective, evidence-based care for this resource intensive population.

Background

Heart failure is a well-researched area of medicine, and nurse involvement in the outpatient setting is extremely important in managing patients' symptoms and issues, and the application of these concepts of heart failure education can be applied to the PAH patient. Pulmonary hypertension patients, like heart failure patients, are complex and often have multiple health issues and a strong nurse presence helps manage the patient in an outpatient setting and improve outcomes. The management of PAH can be overwhelming for a nurse new to the field. It is important to build upon knowledge and experience to help bridge this gap while also learning new aspects of the role in a continually evolving discipline. To achieve optimal outcomes, the ACCF/AHA Heart Failure guidelines give a class 1 recommendation for patient education to facilitate self-care. Similarly, the ACCF/AHA PH consensus

supports educating the PH patient on symptom management, low sodium diet, medication adherence and side effects, remaining active, and encouraging regular contact with the nurse coordinator to allow a shared sense of responsibility.

Methods

Reviews of the 2013 ACCF/AHA Guideline for the Management of Heart Failure and the 2009 ACCF/AHA PH Consensus were completed. The basic tenets and principles of these guidelines were modified to cater toward a PAH specific population.

Results

Guideline based order sets and protocols were developed to streamline efficiency in the multidisciplinary management of these patients and standardize care in the inpatient and outpatient settings.

Conclusion

Nurse involvement in the care of CHF and PAH patient is invaluable. There is considerable overlap in the nursing role as outlined by the ACCF/AHA guidelines for Heart Failure and Pulmonary Hypertension. Highlighting the similarity in nurse education allows for easier transition into the PAH coordinator position.

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Abstract Title

Transitioning Patients with Pulmonary Hypertension from Tadalafil to Riociguat: Single-Center Experience

Purpose

To study the effects of transitioning patients with pulmonary hypertension from tadalafil to riociguat therapy.

Background

Pulmonary Arterial Hypertension (PAH) is a devastating disease with increasing options for therapy. If a patient is not responding to a particular therapy, other options can be tried. Riociguat is an option to treat patients diagnosed with CTEPH (WHO Group 4) and PAH (WHO Group 1). We report our single center experience transitioning patients with CTEPH and PAH from tadalafil to riociguat.

Methods

We retrospectively reviewed the charts of patients transitioning from tadalafil to riociguat from November 2013 through March 2017.

Results

A total of 19 patients (average age 60.9 + 18 years; 11 females) with PAH (5 idiopathic, 6 congenital heart disease, and 4 collagen vascular disease) and CTEPH (n=4) transitioned from tadalafil to riociguat. The reasons for transition included attempting to augment PAH therapy (n=14), simplifying the medication regimen (2 therapies to 1; n=2), and the

underlying etiology was CTEPH (n=4). Concomitant therapies were ERAs (n=5), prostacyclins (n=5), ERA + prostacyclin (n=2), and none (n=5). Compared to tadalafil, after 5.9 + 1.7 months on riociguat, 19 (of 19) patients' average BP decreased (121/68 to 112/63), 6 min walk increased (462 m to 503 m), NYHA class decreased (3 to 2), PASP decreased (76mmHg to 74mmHg), and RAP, TAPSE, and RV size/function were unchanged. None of the changes were statistically significant (Table 1). Compared to tadalafil, after 12.5 + 1.4 months on riociguat, 11 (of 19) patients' average BP decreased (121/68 to 111 /61), 6 min walk decreased (462 m to 414 m), PASP decreased (76mmHg to 73mmHg), RAP decreased (12 to 11), TAPSE decreased (18 to 17), and NYHA and RV size/function were unchanged. None of the changes were statistically significant (Table 1).

Conclusion

No statistically significant changes in BP, 6 min walk distance, NYHA class, or echo parameters were observed in our patient population transitioned from tadalafil to riociguat. Limitations to the study were small sample size and selection bias. Further and larger study is required to determine if there is any benefit in transitioning specific patient populations from tadalafil to riociguat.

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Abstract Title

Transitioning Patients with Pulmonary Arterial Hypertension from Subcutaneous Treprostinil to Intravenous Treprostinil: Single-Center Experience

Purpose

Evaluation of our patients transitioned from subcutaneous (SQ) treprostinil to intravenous (IV) treprostinil.

Background

Pulmonary Arterial Hypertension (PAH) is a devastating disease with multiple therapy options. Several prostacyclin therapy options are available depending on the patient's PAH etiology, disease severity, and preference. We report our single-center experience transitioning patients with PAH from subcutaneous (SQ) treprostinil to intravenous (IV) treprostinil.

Methods

We retrospectively reviewed charts of patients transitioned from SQ treprostinil to IV treprostinil from April 2010 through September 2015.

Results

A total of 4 patients (mean age 44 years [range 32-56], 4 females) with PAH (1 idiopathic, 1 collagen vascular disease, 1 congenital heart disease, 1 portal hypertension) transitioned from SQ treprostinil to IV treprostinil. Of the 4 patients

transitioned, 3 were due to site pain and 1 due to need for higher prostacyclin dosing because of declining status. Average dose of SQ treprostinil before transition was 49.3 ng [range 15-100 ng] and average dose of IV treprostinil after transition was 37 ng [range 8-78 ng]. After transition, the site pain resolved in 3 patients experiencing it. The one patient transitioned due to declining status has improved to an NYHA class II on IV treprostinil.

Conclusion

In this small case series we were able to demonstrate that patients can safely transition from SQ treprostinil to IV treprostinil. IV treprostinil can be an alternative parenteral prostacyclin therapy if patients are experiencing site pain from SQ treprostinil. The one patient with a declining functional status improved once transitioned to IV treprostinil. IV treprostinil can be a safe and beneficial alternative to SQ treprostinil. It provided relief from site pain in multiple patients and provided higher prostacyclin dosing to improve the functional status of one patient. Further study is required to validate these benefits in larger populations.

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Abstract Title

Prevalence of Right Ventricular Non-compaction: Single-Center Experience

Purpose

Determine prevalence of RV non-compaction in our clinic population.

Background

Non-compaction of the left ventricle, characterized by prominent trabeculae with deep intertrabecular recesses in the ventricle, is well documented. The existence and prevalence of non-compaction of the right ventricle is documented but considered rare. However, in our clinical experience, with frequent detailed echo imaging of the right ventricle along with 3D imaging, RV non-compaction seems more prevalent than originally thought.

Methods

We prospectively reviewed echoes of patients evaluated in the pulmonary hypertension (PH) clinic from May 2014 through March 2017.

Results

A total of 75 patients (mean age 65 [range 27-91]; 63 females (84.0%)) were found to have non-compaction of the right

ventricle using 3D echo imaging. Sixteen of the 75 patients (21.3%) had biventricular non-compaction. Fifty three of 75 patients (71.0%) had WHO group I PAH, 1 patient (1.3%) had CTEPH, 17 patients (22.7%) had WHO group II PH (5 systolic dysfunction; 12 diastolic dysfunction), 1 patient (1.3%) had WHO group III PH (sleep disordered breathing), and 3 patients had no PH.

Conclusion

Based on our observations, RV non-compaction is more prevalent than originally thought. In our experience, careful assessment of the RV with 3D echo imaging has been the most useful tool to detect RV non-compaction. 3D echo imaging allows detection of increased trabeculae in the RV and differentiation from RV hypertrophy or the normal RV anatomy in patients. The significance of RV non-compaction in patient symptomatology and prognosis is unknown. Identifying RV non-compaction is important in the treatment of PAH patients as it may be mistaken for RVH resulting in over treatment with PAH vasodilator therapies.

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Abstract Title

Oral Treprostinil (Orenitram) Overdose in a Patient with Pulmonary Arterial Hypertension: A Case Report

Purpose

To present a case report of oral treprostinil (Orenitram) overdose, reason for overdose, and prevention strategy

Background

Oral treprostinil (Orenitram) is a prostacyclin vasodilator that was approved by FDA in December 2013 for treatment of Pulmonary Arterial Hypertension (PAH) (WHO Group I) to improve exercise capacity. There have been few case reports of treprostinil overdose though no published case report of Orenitram overdose. Here we present a case of Orenitram overdose, reason for overdose, and necessary precautions to prevent it.

Methods

A 57-year-old African American male with a history of Pulmonary Arterial Hypertension (PAH), Chronic Thromboembolic Pulmonary Hypertension (CTEPH) s/p pulmonary endarterectomy and Chronic Obstructive Pulmonary Disease (COPD) on 4litres oxygen was admitted to outside hospital for altered mental status. He was diagnosed with and treated for community-acquired pneumonia. Course was complicated with hemorrhagic shock due to GI bleed requiring hepatic artery embolization and multiple blood transfusions. The patient was transferred to our hospital for management of acute decompensated heart failure and pulmonary hypertension.

Patient was on Tadalafil 10mg daily, Macitentan 10mg daily and Orenitram 6.25mg TID at home. On the day of admission all his PAH meds were started including Orenitram (6.25mg TID). Within few hours of Orenitram administration he developed flushing, hypoxic respiratory failure, and shock. He was intubated and started on pressors and ionotropes.

Results

Review of records from ACCREDO (specialty pharmacy) showed that the patient last filled his Orenitram two months ago, and had not taken it for more than a month. Also, reviewing records from outside hospital showed that he was not started on Orenitram at their facility. The occurrence of adverse events within few hours of drug administration correlate with the drug's pharmacokinetics (Orenitram has dose-proportional systemic exposure and peak dose effect is seen within 4 to 6 hours). All the above data led to the conclusion that the patient had hemodynamic collapse due to resuming high dose of Orenitram after not taking it for several weeks.

He was eventually started on inhaled flolan and IV remodulin. Over a period of 5 days, he was weaned of pressors, extubated, discontinued inhaled flolan and continued IV treprostinil(remodulin). The patient was transitioned from IV remodulin to Orenitram after 10 days. Patient responded well to the transition process and was slowly uptitrated to his home dose.

Conclusion

Orenitram has dose-proportional systemic exposure. Suddenly stopping or starting drug will mimic turning on/off IV treprostinil pump and this may lead to fatal consequences. So Orenitram should be administered under guidance of Pulmonary Arterial Hypertension experts. Also prior to resuming Orenitram on admission we should confirm the patient's home dose and date last filled with the specialty pharmacy to ensure proper compliance

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Abstract Title

Safety and Efficacy of Rapid Transition From Parenteral to Oral Treprostinil

Purpose

To determine safety and efficacy of rapid transition from parenteral to oral treprostinil.

Background

Prostanoid therapy is the most efficacious treatment for pulmonary arterial hypertension (PAH) however the frequently used parenteral delivery systems are inconvenient and require central venous access or subcutaneous infusion catheters that are complex to use and are associated with important complications. The recently approved oral prostanoid, oral treprostinil, represents a potential alternative to parenteral therapy and it may be appropriate in some patients to convert from parenteral to oral treprostinil. Safe transition from parenteral to oral treprostinil has been reported but conversion required 5 days of inpatient observation. We have developed a rapid transition protocol to safely convert patients during a 48-72-hour hospitalization.

Methods

We reviewed medical records to identify patients who had undergone conversion from parenteral to oral therapy and extracted information about adverse effects and hemodynamics before and after conversion.

Results

A total of 6 patients with idiopathic PAH were transitioned from intravenous to oral treprostinil. All of the patients were females aged 26 to 64 years old. Pre-conversion parenteral treprostinil dose was between 15 to 52 ng/kg/min. Conversion required 24hrs in 1 patient and 48 hours in 5 patients. Post conversion oral treprostinil dose ranged from 3.25 to 8.625 mg TID. There were no significant changes in vital signs or hemodynamics following conversion and no patients required readmission. No patient experienced significant adverse effects during the conversion period other than headaches and diarrhea which resolved with oral treprostinil dose adjustment.

Conclusion

Rapid transition from parenteral to oral treprostinil is safe and reduces the length of the required hospitalization reducing the cost of the transition as well as the total time patients are exposed to potential complications of hospitalization.

Authors

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Abstract Title

Navigating Transitions: IV Epoprostenol to oral Treprostinil

Purpose

At one time IV therapies were the only treatment option indicated for the pulmonary hypertension (PH) patient, today there are alternative medications and routes to choose from. While IV prostacyclins have been proven to be effective in the treatment of severe PH, the central line itself carries risks for infection, line fractures, and are associated with lower quality of life scores due to common side effects including: flushing, sinus congestion, GI discomfort, generalized edema and headaches. This case study details the transition from an IV Epoprostenol to oral Treprostinil over a seven-week period.

Background

Although there have been significant advances in therapies for the treatment of PH, there is a lack of clinical trials to support the transition from IV to oral therapies. The lack of scientific evidence makes transitioning patients from IV drug therapy to oral challenging for most practitioners.

Methods

When establishing the transition, table used in this case study, multiple disciplines were consulted in order to create a safe and comprehensive plan of care including cardiology, pulmonology, pharmacy, nursing, and the pharmaceutical company. Once the oral medication was identified, the clinical pharmacist assembled the transition schedule. Weekly transitions were closely monitored by the cardiologist and the Outpatient Pulmonary Hypertension Clinic staff. The patient's mental and physical wellbeing was evaluated and documented during the seven week period.

Medication: prostacyclin Total epoprostenol

Week 1

Dose: 0.125mg po TID (use 1 tab of 0.125mg tabs TID)
0.375mg/day 18ng/kg/min

Week 2 Dose: 0.5mg po TID

(use 2 tablets of 0.25mg tab TID for total of 6 tabs / day)
1.5mg/day 14 ng/kg/min

Week 3

Dose : 1mg po TID

(use 4 tablets of 0.25mg tabs TID for total 12 pills /day)
3mg/day 10ng/kg/min

Week 4

Dose: 2mg po TID

(use 2 tablets of 1mg TID for total of 6 pills/ day) 6mg/day
6ng/kg/min

Week 5

Dose:

morning 3.5mg (use 2.5mg tab + 1mg tab)

noon 3.0mg (use 2.5mg tab + 0.5mg tab)

evening 3.5mg (use 2.5mg + 1mg tab) 10mg/day 3 ng/kg/
min

Week 6

Dose:

Morning 4mg (use 2.5mg tab +1mg tab +0.25tab +0.25tab)

noon 4mg (use 2.5mg tab +1mg tab +0.25tab +0.25tab)

evening 4.5mg (use 2.5mg tab+ 2 tabs of 1mg tabs) 12.5mg/
day 1.5ng/kg/min

Week 7

Dose:

morning 4mg (use: 2.5mg tab + 1mg tab +2 tablets of .25mg
tab)

noon 5mg (use: 2 tabs of 2.5mg)

evening 5mg (use: 2 tabs of 2.5mg) 14mg/day Stop infusion

Results

The patient was successfully transitioned from IV to oral therapy with no adverse events or decline in functional class. The patient reported having an improved quality of life and was able to resume swimming and other hobbies that had been contraindicated when IV therapy was initiated.

Conclusion

This case study demonstrates that patients meeting certain criteria can safely be transitioned from IV prostacyclins.

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Abstract Title

New Insights into Inpatient Symptom Burden in Pulmonary Arterial Hypertension

Purpose

To present insights into the inpatient symptom burden in pulmonary arterial hypertension, and identify whether palliative care can play an important role in this patient population.

Background

Pulmonary arterial hypertension (PAH) is a progressive illness resulting from various conditions, which can lead to a high symptom burden and mortality. Severity of functional impairment has been compared to patients with spinal cord injuries or with cancer unresponsive to chemotherapy. Nearly half of PAH patients note profound deficiency in overall quality of life (QOL) and emotional well-being. Palliative Care is transdisciplinary care that aims to prevent or relieve suffering in patients with a serious progressive illness like PAH. Despite expert opinion encouraging Palliative Care consultation for patients with PAH, little data guides this clinical intervention.

Methods

A retrospective chart review was performed on all PAH patients receiving inpatient Palliative Care consultation from January 2015 to December 2015. Data was collected from Palliative Care assessments and included relevant clinical issues, reason for consultation, prognosis, disposition, and symptom burden at baseline and 48 hours (recorded using Edmonton Symptom Assessment Scale). Types of Palliative Care interventions included such things as advanced care planning, spiritual counseling, disease state education, medical proxy determination, and intimacy counseling. Also

categorized were details about the hospitalizations, such as length of stay and time to consultation.

Results

Palliative care inpatient consults were performed on 11 PAH patients (median hospital length-of-stay 6 days). Two patients developed PAH secondary to scleroderma, one patient developed PAH secondary to systemic sclerosis, and the rest of the cohort had idiopathic PAH. Predominant reasons for consultation were to establish goals of care and for pain control. The retrospective analysis shows that forty-eight hours following consultation, there was an overall improvement in patient-reported pain, dyspnea, and depression scores. Importantly, the Palliative Care team's transdisciplinary interventions were diverse, including advance care planning, spiritual care, psychosocial counseling, and introducing hospice services. Of the patients seen by Palliative Care, 55% were discharged home, 18% to Nursing Home, 18% to Nursing home with outpatient palliative care, and 9% were Lost-to-follow up. By introducing Palliative Care services as part of best PAH care at our institution, patients readily accepted these interventions.

Conclusion

This case series suggests that inpatient Palliative Care consultation is not only effective for managing important disease-related symptoms, but also important to providing holistic support in the shape of clarifying medical decision-making and advance care planning, as well as introducing concepts relevant to end-of-life care.

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Abstract Title

A Proof of Concept Study of LTB₄ Inhibition in Patients with Pulmonary Arterial Hypertension (WHO Group 1) (LIBERTY)

Purpose

To conduct a clinical proof of concept study to test the role of inhibition of leukotriene B₄ (LTB₄) in patients with pulmonary arterial hypertension (PAH) WHO Group 1.

Background

Pulmonary Arterial Hypertension is a progressive and life-threatening disease characterized by increased pulmonary vascular resistance, heart failure, and premature death. Although management of PAH has improved significantly with the development of multiple drugs targeted on 3 pathways, the mortality rate remains high, with a life expectancy of 7 years after diagnosis (McGoon 2014). Thus, new approaches are needed, and approaches which may modify disease progression.

Ubenimex is an oral, small molecule inhibitor of both leukotriene A₄ hydrolase (LTA₄H) and aminopeptidase. Animal models demonstrate that inhibition of LTB₄ ameliorates multiple manifestations of pulmonary vascular disease (Tian et al, 2013). A prominent pathological feature of PAH is accumulation of macrophages near the arterioles of the lung. In both rat models of PAH and human PAH lung tissue, accumulated macrophages expressed high levels of LTA₄H, the enzyme that converts leukotriene A₄

(LTA₄) to leukotriene B₄ (LTB₄). In addition, elevated levels of LTB₄ are seen in some patients with PAH. These data suggest that LTB₄ may be important in patients with WHO Group 1 PAH, and inhibition of LTB₄ may be a novel therapeutic approach to treatment of PAH.

Methods

We designed a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group study in patients with PAH (WHO Group 1). The study was conducted at multiple sites in North America. Patients were randomized in a 2:1 ratio to receive 150 mg TID of ubenimex or matching placebo, administered orally for a total of 24 weeks. All approved PAH specific drugs were allowed as background therapy, and at least one background drug was required. Patients who complete the randomized, double-blind study may be eligible to enroll in an open-label extension study.

Results

We describe the key eligibility criteria and enrollment of a proof of concept study enrolled entirely in North America.

Conclusion

Sixty-one PAH patients were enrolled in a 10-month period across 45 clinical sites in the United States and Canada.

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Abstract Title

Unit Based Approach to Caring for Pulmonary Hypertension Patients

Purpose

Through a collaborative approach, the Transitional Medical Unit (TMU) has developed and implemented a streamlined process for the care of pulmonary hypertension patient receiving intravenous or inhaled prostacyclins.

Background

To reduce patient harm and improve quality care, all pulmonary hypertension patients on intravenous or inhaled medications are admitted to TMU. Nurses on TMU specialize in the administration of pulmonary hypertension medications and are well versed in the disease process.

Methods

TMU has developed a strategic approach to caring for the pulmonary hypertension patient. TMU nurses receive extensive training on the pathology of PAH, pharmacodynamic/kinetics of intravenous/inhaled medications, and administration/monitoring of PAH therapies. All nurses are required to pass hands on bi-annual competency testing. Through an electronic medical alert system all patients on intravenous or inhaled prostacyclins are recognized immediately once they enter our health care system. This alert message is sent via page to the TMU charge nurse and the PAH on call team. TMU partnered with the emergency department to develop a process to communicate

all PAH line and drug infusion issues to the TMU charge nurse in the moment. This process includes bringing TMU PAH trained RN down to the emergency department to directly troubleshoot central line or infusion complications. A Clinical Management Guideline (CMG) available on the system portal provides guidance and promotes patient safety during initiation, titration and monitoring of these complex patients. In addition, members of the PAH team work closely with the TMU staff and order entry for these medications are restricted to the PAH team providers.

Results

Cohorting patients to the TMU and training of specialized staff have resulted in a decrease in patient harm. In addition, patients are familiar to the staff and patient hand offs are minimized.

Conclusion

TMU has successfully set a standard of care for the PH patient. By recognizing the specific needs of the PH patient and closely monitoring their care, TMU has implemented safety standards to optimize patient outcomes. TMU continues to increase the awareness about the specialized management of the PH patient and PH standards of care.

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Abstract Title

Optimizing Pharmacotherapy in Pulmonary Arterial Hypertension with a Specialty Pharmacy Clinical Care Management Program

Purpose

The application of a Clinical Care Management program at the specialty pharmacy (SP) level can prolong positive outcomes of oral therapy and alert prescribers to potential clinical worsening which may necessitate advancement through the evidence-based treatment algorithm.

Background

Pulmonary arterial hypertension (PAH) is a rapidly progressive disease; early detection and management of clinical worsening is paramount to optimizing long-term outcomes.

Methods

Claims data was retrospectively reviewed to evaluate the impact of the SP clinical model. Patients were included if they: carried a diagnosis of PAH, were newly diagnosed (no prior claims for a PAH medication), had a prescription for an endothelin receptor antagonist (ETRA) or a phosphodiesterase type 5 (PDE-5) inhibitor and were continuously eligible with uninterrupted admission to the SP through the review period. Patients were divided into groups by pharmacotherapy: ETRA or PDE-5 inhibitor. Patients in the ETRA group were evaluated via the Clinical Assessment and Risk Evaluation (CARE) protocol; monthly screening for potential clinical worsening during routine reorder placement. On identification of a potential clinical worsening event, the patient was triaged to a PAH specialist nurse for assessment. As opportunities were identified, intervention strategies to optimize therapy were offered and the prescriber engaged as warranted.

The primary endpoint was the rate of and time to prostanoid combination therapy; the secondary endpoint was adherence to the index therapy. An exploratory endpoint included review of interventions offered by the specialist nurse.

Results

6551 patients met the inclusion criteria; 3506 on an ETRA and assessed per the CARE protocol (intervention group) and 3045 on a PDE-5 inhibitor (control). The rate of progression to prostanoid combination therapy was significantly higher in the intervention group (9.4% vs. 7.0%; $p=0.0043$). The average time to prostanoid combination therapy also differed between the two groups, with a trend toward a longer duration of oral monotherapy in patients on the ETRA and assessed per CARE (140.2 days intervention group vs. 112.7 days' control).

Adherence to pharmacotherapy, as measured by average adjusted prescriptions, was significantly higher in the intervention group referred to a PAH specialist nurse for potential clinical worsening (14 vs. 13.5; $p=0.0004$).

166 (4.7%) patients in the intervention group were identified as having a potential clinical worsening event on routine monthly reorder triggering assessment by a PAH specialist nurse. 207 interventions were performed to address root cause of clinical worsening. See Figure 1 for intervention by type:

Conclusion

Our data show that the application of an evidence-based protocol to detect potential clinical worsening will drive appropriate escalation to prostanoid combination therapy while management of the root cause may delay the time to that progression – an average of 27.5 days in this sample. The Clinical Care Management program also significantly increases adherence to pharmacotherapy.

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Abstract Title

Reducing Rates of Readmission and Development of an Outpatient Management Plan in Pulmonary Hypertension: Lessons from Congestive Heart Failure Management

Purpose

The aim of the abstract to review individual studies and comprehensive meta-analyses to identify effective interventions with Congestive Heart Failure that can be used to develop similar disease management programs in Pulmonary Hypertension and ultimately reduce hospital readmissions.

Background

Pulmonary Hypertension currently has minimal guidelines for outpatient disease management. Heart failure is the most common cause for readmission for patients with both Pulmonary Hypertension and Congestive Heart Failure. CHF studies have shown that disease management plans are effective in reducing CHF readmissions.

Methods

A comprehensive review of literature performed from 1993 to 2009, including original trials and meta-analysis and reviews. We reviewed the topics of outpatient CHF interventions to decrease CHF mortality and readmission and patient management strategies in CHF.

Results

The most studied interventions included case management (CM-specialist nurse driven, education pre/post discharge, specialist nurse home visits, scheduled telephone calls for symptom management, when to seek help), multidisciplinary Intervention (MI-coordinated interventions and

communications; specialist nurse driven, patient-caregiver education regarding disease, medication and diet, nurse clinic visits, regular telephone calls, individualized follow-up plan, access to physician, nurse, dietician, pharmacist, social worker), remote monitoring programs consisting of structured telephone strategy (STS-monitoring collected data via human-human or human-machine interactive response system) or tele-monitoring (TM-physiologic data transmission of EKG, blood pressure, weight, respiratory rate digitally). Clinic visits did not have a significant effect on CHF readmission or mortality. CM showed decreased all-cause mortality (ACM) at 12 months, all-cause re admission (ACR) at 12 months and CHF readmission at 6 and 12 months. MI resulted in decreased ACR and CHF readmission. There was some discrepancy on effectiveness of TM programs alone in individual studies, however large meta-analysis suggests TM provided a reduction in ACM and risk of CHF hospitalization. STS had similar results to TM including decreased risk of CHF hospitalization, without an effect on mortality.

Conclusion

Extrapolating from CHF data, it seems that strategies to improve the health of PH patients and the development of comprehensive care programs should include structured telephone strategy and/ or tele-monitoring, case management strategies and multi-disciplinary interventions

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Abstract Title

Transition from Oral Selexipag to Subcutaneous Treprostinil in a patient with Scleroderma-related Pulmonary Arterial Hypertension (PAH)

Purpose

Medications targeting the prostacyclin pathway in PAH (prostacyclin, prostacyclin analogues, and prostacyclin receptor agonist) are available in various delivery routes including oral, intravenous, subcutaneous (SQ), and inhaled. Transition between medications in this class may be indicated due to progression of PAH, side effects (SEs), and/or patient preference. The lack of established protocols guiding transition is problematic, especially in the absence of comparative pharmacokinetic data. We present here our experience with a single patient with scleroderma-related PAH transitioning from selexipag to subcutaneous treprostinil.

Background

Our patient is a 69 y/o male with scleroderma-associated PAH treated with selexipag, tadalafil and sitaxsentan. Despite triple therapy for one year, his disease progressed as indicated by worsening symptoms and right heart catheterization findings. His maximum dose of selexipag achieved was 800 mcg twice daily with dose escalation limited by intolerable lower extremity (LE) pain. His weight on transition day was 73 kg.

Methods

We estimated the dose conversion of selexipag 200 mcg BID=treprostinil 10 ng/kg/min based on discussions with PAH providers with transition experience in the opposite direction (treprostinil to selexipag). Using this “best estimate” we calculated the treprostinil target dose at 40 ng/kg/min. Due to the severity of our patient’s SEs from the selexipag, we aired conservatively and modified the target dose to 20 ng/kg/min during hospitalization, with up-titration as an outpatient in the subsequent 2-4 weeks. The transition occurred in the

intensive care unit to provide close monitoring.

The planned inpatient titration schedule is outlined in Table 1. Columns A and B. The actual titration schedule is columns C and D.

Results

The planned schedule in columns A and B in table above was modified by early cessation of selexipag* after the 12-hour dose in response to the patient experiencing intense side effects of flushing and headache at 16 hours (columns C and D). The inpatient transition was complete at 36 hours and the patient was discharged to home at 48 hours. A dose increase to 22 ng/kg/min was attempted 3 days’ post discharge with de-escalation to 20 ng/kg/min due to intolerable LE pain despite best practice symptom management. He was readmitted for 24 hours at 5 days’ post hospitalization for evaluation and treatment of a greater than usual injection site reaction. The remodulin dose was decreased to 18 ng/kg/min at 4 weeks’ post discharge due to ongoing severe leg pain. The patient reports improved shortness of breath and exercise tolerance on 18 ng/kg/min compared to pre-transition.

Conclusion

This case is a successful transition from selexipag to subcutaneous treprostinil in 36 hours without apparent physiologically significant SEs. The estimated equivalent selexipag to treprostinil dose in our patient is 200 mcg BID=5 ng/kg/min.

Table 1.

Planned			Actual	
Time (hr)	A Selexipag mcg (% dose)	B Treprostinil ng/kg/min (% dose)	C Selexipag mcg (% dose)	D Treprostinil ng/kg/min (% dose)
0	600 (75)	5 (25)	600 (75)	5.00 (25)
12	400 (50)	10 (50)	400 (50)	10.00 (50)
24	200 (25)	15 (75)	0*	15.00 (75)
36	0	20 (100)	0	20.00 (100)

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Abstract Title

Mixed PH in the Real World- An Ill-defined Phenotype

Purpose

Mixed PH in the Real World – An Ill-defined Phenotype
Patricia Gresham, Vijay Balasubramanian
Pulmonary Arterial Hypertension (PAH) is a devastating condition that leads to premature death if left undiagnosed or untreated. The Evian Classification and more recent revisions (J Am Coll Cardiol 2013;62(25 Suppl): D34-41) reclassified PH into 5 subgroups based upon etio-pathogenesis. Group I PH (Pulmonary Arterial Hypertension, PAH) represents a growing list of entities, and outcomes are different for various phenotypes. In the “real world”, clinical characterization can often pose a challenge when there are mixed etiologies for PH in the same patient often referred to as “Mixed PH”. Proving primary Pulmonary vascular disease and initiation of pulmonary vasodilator therapy can be a very difficult decision. We wish to present a patient with “Mixed PH” in the real world, who demonstrated an impressive clinical response to Pulmonary vasodilator therapy despite very atypical hemodynamic characteristics.

Background

A 62-year-old HF presented to the hospital with a background of multiple hospitalizations for Dyspnea and recurrent edema. She had a history of CAD – Prior myocardial infarction along with 2 vessel disease, Valvular heart disease – Mitral regurgitation, Pacemaker insertion for Complete Heart Block. In addition, Pulmonary history included severe restrictive Lung disease (TLC 46%, DLCO 19%) & Prior large Right pleural effusion. Clinical and Hemodynamic Characteristics are summarized in the table below.

Methods

2012 Before TX 2015 Following
Left atrial Dim 4.5 4.5
LVEF 68% 65%
MR Mod to Sev Mild to Mod
mRAP 25 15
PAP 105/45 118/32
mPAP 65 60
PCWP 20 25
LVEDP 20
CO/CI 6.03/3.22 6.2/3.52
PVR 7.5 5.6
TPG/DPG 45/25 35/7
BNP 450 20
6MWT 207M 345M
Hospital Admissions
3 in 15 months 0
WHO FC IV II

Results

Pt had 3 hospitalizations prior to and none since initiation of Pulmonary vasodilator therapy.

Conclusion

This real world “Phenotype” is still not well-characterized by the available recognized tools and clearly may need to be studied further. Although, TPG & DPG are useful in clinical delineation, other biomarkers and clinical characteristics are needed to enable better definition of these unique phenotypes.

Authors

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Abstract Title

Filter change on inpatient administered epoprostenol infusion associated with improved safety and consistency of dose delivery

Purpose

To describe a change in practice guidelines regarding add-on filters for inpatient intravenous (IV) epoprostenol administration for management of pulmonary arterial hypertension (PAH).

Background

Intravenous epoprostenol is used for treatment of PAH in both ambulatory and inpatient settings. Filter and tubing types for delivery of IV epoprostenol with inpatient infusion pumps are not specified, however, manufacturers advise a 0.2 micron in-line filter for administration with ambulatory infusion systems. Based on this recommendation, University of Maryland Medical Center (UMMC) guidelines require use of a 0.2-micron add-on filter with CareFusion SmartSite tubing 2420-0007 for inpatient IV epoprostenol delivery via CareFusion Alaris 8100 infusion pumps. The filter used for this purpose at UMMC was ICU-B9061 by ICU Medical.

Methods

This case describes a 61-year-old female patient admitted to the Cardiac Care Unit (CCU) for management of severe PAH and administration of IV epoprostenol (Veletri). While in the CCU, the patient had repeated episodes of systemic hypotension, acutely altered mental status and respiratory decompensation. Clinical changes were not responsive to dose adjustments and the patient required intubation on two occasions. Nursing assessment noted blood reflux into the IV tubing through which epoprostenol was infusing. The patient care team initially attributed the back-siphoning to a defect with the patient's central venous access, however, the problem persisted despite placement of two subsequent central venous access sites. A nurse priming a new IV set observed air to enter

the tubing distal to the filter and dependent on its position relative to the medication bag. Unit nurses conducted a literature search to investigate best practices and determine if the 0.2-micron filter might be associated with back-siphoning and inconsistent delivery. A single article was found describing both back-siphoning and bolusing effects seen with 0.2 micron filters secondary to filter position. The article indicated that a 0.2-micron model with a smaller priming volume might be utilized to mitigate this effect. A Vygon AMS-427 0.2-micron add-on filter with a 0.52 ml priming volume was obtained as a substitute for the ICU-B9061 (priming volume 4.6ml) and epoprostenol therapy was continued with this product.

Results

After the filter change, the patient experienced rapid and marked improvement in PAH symptoms with no further hemodynamic instability or alteration in mental status. She was later discharged on home prostacyclin infusion therapy. Following discussions with nursing, the medical team, product manufacturers and other institutions, UMMC revised practice guidelines to require the use of the AMS-427 0.2-micron filter for inpatient IV epoprostenol administered via the Alaris 8100. No further incidences of back-siphoning or bolusing have been observed since switching to the AMS-427.

Conclusion

Consideration of filter dynamics as a potential source of unexplained and inconsistent symptoms in patients with PAH receiving IV epoprostenol through hospital infusion pumps may be warranted. Filters with smaller priming volumes may deter back-siphoning and bolusing.

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Abstract Title

Compatibility of Treprostinil and Dopamine during Y-site Administration

Purpose

The primary objective of this study was to evaluate the physical and chemical compatibilities of treprostinil and dopamine via simulated Y-site administration. The secondary objective was to identify any reports of line associated events in patients that necessitated Y-site administration of these medications due to limited IV access and acute clinical requirements.

Background

Intravenous treprostinil is a synthetic prostacyclin analog used to treat pulmonary hypertension (PH). During acute exacerbations of PH dopamine may also be required for cardiac support. In patients with limited intravenous access, it may be necessary to infuse these medications via Y-site. However, there is a lack of compatibility information available for treprostinil and dopamine, thus making it difficult for pharmacists to safely provide recommendations regarding administration.

Methods

Sterile preparations of treprostinil (4000 ng/ml, 76000 ng/mL, and 500000 ng/mL) were mixed in equal parts with dopamine (0.6 mg/mL, 3.2 mg/mL, 6 mg/mL, and 40 mg/mL) to simulate Y-site administration. Samples were withdrawn from the resulting mixtures at time 0, 1 hour, 2 hours, and 4 hours and subjected to physical compatibility and chemical stability testing. The physical stability of the admixtures was assessed in triplicate for each sample by visual examination (particulate matter, haze, and color change), turbidity measurements (nephelometry), and pH measurements. Drug concentration in all samples was also assessed by liquid chromatography mass spectrophotometry (LCMS) for treprostinil and high performance liquid chromatography (HPLC) for dopamine. Chemical stability tests were conducted on 2 separate days with 2 samples assessed each day. To assess for line associated events (infiltrates, loss of line, inability to flush +\ the use of medications to restore patency) a retrospective review of existing medical records of patients that received treprostinil and dopamine via Y-site from January 2011 until October 2015 was completed.

Results

The results are listed in table 1 and were consistent at all time periods studied.

Drug		Physical Compatibility	Chemical Stability	
Treprostinil	Dopamine	Treprostinil:Dopamine	Treprostinil	Dopamine
4000 ng/mL	0.6 mg/mL	No precipitation, cloudiness, pH or color change	Retains > 90% of initial concentration	Retains > 90% of initial concentration
	3.2 mg/mL			
	6 mg/mL			
	40 mg/mL			
76000 ng/mL	0.6 mg/mL			
	3.2 mg/mL			
	6 mg/mL			
	40 mg/mL			
500000 ng/mL	0.6 mg/mL	No precipitation, cloudiness, pH or color change	Retains > 90% of initial concentration	Retains > 90% of initial concentration
	3.2 mg/mL	Precipitation occurred	N/A	N/A

Complete data was available from 12 patients who received treprostinil and dopamine via Y-site. One patient, receiving treprostinil 4000 ng/mL and dopamine 6 mg/mL, experienced a transient inability to flush the line but no change in therapy or clinical status occurred.

Conclusion

Data confirms that treprostinil 4000 ng/mL and 76000 ng/mL in normal saline are stable for 4 hours when administered via simulated Y-site with dopamine 0.6 mg/mL, 3.2 mg/mL, 6 mg/mL, and 40 mg/mL. Only dopamine at 0.6 mg/mL is stable with treprostinil of 500000 ng/ml. These findings will enable pharmacists to provide precise information to the health-care team regarding the Y-site compatibility of these commonly co-administered medications.

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Abstract Title

Safety of sildenafil in hemodynamically unstable children

Purpose

To determine if current empiric sildenafil dosing recommendations are appropriate for hemodynamically unstable children receiving concurrent vasoactive infusions.

Background

Sildenafil is a first-line agent used to treat pulmonary hypertension in pediatric patients. While it is utilized in children receiving continuous infusion inotropic or vasopressor medications, it is unknown whether the administration of sildenafil worsens hemodynamic instability in this patient population. We hypothesized that hemodynamic instability occurs frequently in children receiving concurrent enteral sildenafil and vasoactive infusion administration.

Methods

This retrospective chart review included children younger than 2 years of age admitted to Riley Hospital for Children at Indiana University Health between January 1, 2010 and September 30, 2016 who received enteral sildenafil and concurrent inotropic or vasopressor medications. Patients were excluded if they received mechanical circulatory support 24 hours prior to sildenafil administration, or if they received renal replacement therapy or had suspected septic shock at any point during the study period. Data collection included demographic information, sildenafil dose and frequency, medications with known drug interactions with sildenafil, history of sildenafil exposure prior to initiation of vasoactive support, mean arterial pressures (MAP), and vasoactive infusion dosing. The primary outcome was a composite endpoint of the frequency of sildenafil discontinuation, increased vasoactive support, epinephrine intravenous push administration, or need for initiation of mechanical circulatory support within 24 hours of the first sildenafil

administration with concurrent vasoactive support.

Results

A total of 130 patients were included. The median age was 4.6 (0.3-7.7) months, and 26 (20%) had a diagnosis of Trisomy 21. The median initial sildenafil dose for all patients was 1.5 (1.0-2.5) mg/kg/day, with a median vasoactive inotrope score (VIS) of 5.0 (3.0-7.5) at the beginning of the study period. Thirty-two patients (25%) met the primary composite endpoint. Twenty-five patients (19%) required increased inotropic support and one patient required sildenafil discontinuation during the study period. Five patients (4%) required both increased inotropic support and sildenafil discontinuation. One patient required increased inotropic support and epinephrine intravenous push administration. No one required initiation of mechanical circulatory support during the study period. Patients with Trisomy 21 appeared to have a lower frequency of hemodynamic instability than patients without Trisomy 21 (15% versus 36%). Patients who met the primary composite endpoint (n=32) were younger [2.0 (0-8.0) months versus 5.0 (1.0-7.5) months], with a lower median initial sildenafil dose [1.3 (0.6-2.0) mg/kg/day versus 1.6 (1.1-2.6) mg/kg/day] and median VIS score during the study period [4.2 (3.0-7.1) versus 5.0 (3.0-7.5)].

Conclusion

Children receiving vasoactive infusions may be at risk for further hemodynamic instability if treated with sildenafil. Empiric sildenafil dosing recommendations may need to be decreased for this patient population. Patients with Trisomy 21 were not at increased risk of hemodynamic instability compared to those patients without Trisomy 21. Further studies are warranted to define optimal sildenafil dosing strategies for pulmonary hypertension in children receiving concomitant vasoactive infusions.

Authors

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Abstract Title

Best Practice Advisory (BPA) Trigger Alerts using Electronic Health Record System to facilitate safe management of Pulmonary Arterial Hypertension patients with Continuous Infusion of Prostaglandins

Purpose

To develop and implement best practice advisory (BPA) alerts within Electronic Health Record (EHR) system to facilitate communication and improve patient safety for patients with pulmonary arterial hypertension (PAH) using continuous infusion of Prostaglandins (PG).

Background

Safe management of continuous infusion of PG for PAH patients requires training of hospital staff. In a large hospital network (HN), training on safe infusion of PG is often limited to hospital staff on select hospital units. Adverse outcomes and serious errors can occur during hospital encounters outside of these specialty units. Some current EHR systems have capacity to build BPA alerts to alert providers of special safety information on these patients. We hypothesize that using a BPA alert for infused PG patients would decrease medication related errors and provide better provider communication.

Methods

Key triggers for PAH were identified and a BPA was developed for the EHR system at a single hospital within a large HS consisting of five hospital facilities. The key triggers for alert included epoprostenol or treprostinil infusion on the home medication list at any time. The alert read, "Patient is receiving a continuous infusion of PG through a CADD pump. Do not disconnect the pump for any reason. Do not stop the infusion during a "code blue." Call the PAH team for further information," and specific contact phone numbers for PAH team were provided. The BPA alerted

users including emergency room (ER) physicians, nurses, and paramedics. Simultaneously, an alert is generated for the PAH clinic notifying PAH staff that a patient on PG infusion has presented to our HS, providing patient's location. A Reporting Workbench report allows us to track BPA usage and the actions the staff took in response to the warning.

Results

From April 2015 to November 2016, we had 19 encounters of PAH with 1 near miss at ER of a non-PAH trained facility. From December 2016 to May 2017 after implementation of BPA alert for PAH patients on infusion PG, alert occurred for total of 18 patients. Interestingly, 2 PAH patients from outside facilities were also identified with the BPA alert at ER of these non-PAH trained facilities. No serious errors involving PAH patients have been encountered at non-PAH trained units since the BPA was implemented. Physicians and nursing staff from non-PAH trained units have reported increased confidence in providing safer care for PAH patients because important safety information and contact resources are given to them at the point of service.

Conclusion

The process improvement using EHR BPA alerts for PAH patients resulted in increased knowledge and awareness of continuous infusion PG amongst bedside clinicians within the Hospital system. We believe that implementation of treatment-specific BPA trigger alerts can reduce errors and improve safety of continuous infusion of PG amongst PAH patients.

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Abstract Title

A review of high risk OB patients with PAH

Purpose

To describe a single center experience in the pregnant patient with pulmonary arterial hypertension.

Background

Pulmonary hypertension (PH) remains a contraindication to pregnancy. However, with the increased number of proven treatment options, outcomes have improved. Despite these improvements in the pregnant patient, Kiely et al (2013) report maternal mortality between 12% to 33%. It is recognized that the right ventricle (RV) is the Achilles heel in PH. Due to progressive narrowing in the pulmonary arterial vasculature, right ventricular afterload increases leading to right heart failure and even death. In pregnancy, the normal physiology changes significantly in relation to several factors. Oxygen consumption increases by 30% and blood volume can increase by 40-50% by 32-36 weeks' gestation (Weiss 2000 and Bonica 1995). These changes result in higher cardiac output. Accordingly, this strain on the RV can produce symptoms of failure; shortness of breath and edema. However, it has been shown that fluid shifts in the immediate post-partum period place the patient at the greatest risk of mortality and morbidity (Weiss, 1998). In addition, it has been postulated that hormonal changes during pregnancy can be protective in their "vasodilatory" properties which is reduced immediately after delivery. Lastly, the "procoagulant effect may cause obstruction of the vasculature by thrombosis". (Kiely 2013). This is thought to further compromise the narrowed vasculature in the pulmonary artery.

Methods

Retrospective review of our center's pregnant patients between 2006-2017. The following variables were identified: WHO

group, treatment, age, race, management during pregnancy and in the post-partum period, maternal outcomes, and number of pregnancies

Results

This descriptive review from 2006-2017 reveals severity of disease, age at time of pregnancy, management strategies during and after pregnancy using a multi-disciplinary approach. The cohort consists of 8 women with 20 pregnancies among them. All of them were WHO Group 1: {2- idiopathic, 3- Congenital heart disease, 2- mixed connective tissue disease and 1- CTEPH}. Demographics revealed: RACE- 2/8 Caucasians, 5/8 African American. 1/8 Asian. AGE range at time of pregnancy :19-33 years old. There was one maternal death post-partum (5%). All but one patient had multiple pregnancies. 50% of pts presented to an OSH during their pregnancy. 10/20 (50%) were managed at this center during their entire pregnancy.

Conclusion

PH remains a contraindication to pregnancy. However, it has been demonstrated in one center's experience, that with a multi-disciplinary approach, early treatment, vigilant monitoring during pregnancy and post-partum, successful outcomes can occur. PH patients who became pregnant tended to have multiple pregnancies. For those pts known to our practice prior to pregnancy, they were routinely and repeatedly counseled regarding the risks of pregnancy. Pts with financial and social resources tended to weigh the risk of pregnancy making a more informed decision to become pregnant and follow up with recommended monitoring. Further study is needed to determine if pregnancy is more likely among socially and financially disadvantaged PH patients.

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Abstract Title

Utilization of Electronic Health Record Alerts for Early Identification and Appropriate Treatment of Pulmonary Arterial Hypertension Patients

Purpose

To employ immediately visible Best Practice Alerts (BPAs) within the Epic Electronic Health Record (EHR) to identify patients with Pulmonary Arterial Hypertension and their specialized medication regimens upon presentation to the emergency room, or other clinical locations within the Lifespan health care organization that may be otherwise unfamiliar with the consequences associated with interruption of PAH therapies.

Background

Despite advances in care for PAH patients and the emergence of PH Care Centers in the United States, knowledge gaps remain in appropriate management of PAH patients outside of PAH-centric units and clinics. This can present several risks, particularly for patients receiving continuous prostacyclin therapies. Infused prostacyclins continue to play a vital role in treatment regimens for patients with PAH. PAH patients who present to the emergency room with pump malfunctions or central line complications face risks in receiving appropriate medical care, as interruptions to these infusions or inadvertently administering a prostacyclin bolus could result in life-threatening complications. There is minimal literature to address strategies for utilizing functionality with EHRs to improve the care of high-risk patients. Efforts should be made to easily identify PAH patients with complex treatment regimens, especially if the patient is unable to meaningfully contribute to their care due to illness or injury. As the level of sophistication in EHR functionality improves, many systems now possess the capability to create patient-specific flags with information that is vital to providing appropriate patient care. These flags would be useful to clinicians in areas such as the emergency department where PAH patients may be considered low-volume but high-risk patients for complications.

Methods

Lifespan, a compressive academic health care organization affiliated with The Warren Alpert Medical School of Brown University implemented the Epic EHR in early 2015. Since this implementation, there are ongoing initiatives to improve system functionality. In September of 2016, a team of 45 employees (including the Program Coordinator for the RI Hospital Pulmonary Hypertension Center) formed a committee to develop a process for creating high-risk patient alerts within the Epic system. PAH patients were identified as a high-risk population and plans were made to 1) identify patients on intravenous or subcutaneous prostacyclin who are treated at the RI Hospital Pulmonary Hypertension Center (RIHPHC) via EHR query 2) build a “Smart Phrase” that would be entered individually into each patient’s electronic record via a Care Coordination Note (CCN) to identify PAH patients on a prostacyclin infusions and information about where the patient should be admitted if necessary as well as the PH

clinician on call cell phone number, and 3) upon saving the “Smart Phrase” documentation, a Best Practice Advisory (BPA) is triggered for any new user who accesses the patient’s clinical data. The user is unable to bypass the BPA without acknowledging that they have reviewed the information. Thirty-seven patients were identified as receiving IV or SC prostacyclin infusions in the Lifespan organization and CCNs were created by the RIHPHC nurse practitioner and two registered nurses from the Respiratory ICU/PH inpatient unit. The functionality was tested to ensure that BPAs were generated after entering this information.

A face-to-face educational in-service was provided for all clinical staff on the PH-centric inpatient units about this functionality and how to edit or add/remove a patient BPA when applicable. A specialized educational in-service was also offered to the emergency room charge nurses and critical care team at their monthly meeting. Reinforcement training and skills assessment was also required via the Net Learning educational module within the organization.

Results

PAH patients require specialized plans of care that are initiated at the time of presentation to the emergency department or other care area to ensure that any risks or delays to appropriate care are mitigated. Upon entry to the emergency department, the BPA alert is generated upon entering the patient’s record with information specific to their PAH management. The clinician acknowledges the alert and an audit trail is generated in Epic. The resource nurse in the emergency department contacts the resource nurse on the PH-specialized critical care unit to determine the best course of assignment and seek additional assistance if warranted. The resource nurse can then contact the provider to expedite the admission process and notify pharmacy of any specialty medications that must be mixed or ordered. Quality measures are currently being developed to monitor the improvement to quality of care that PAH patients receive in the emergency department.

Conclusion

While the PAH patient population within this organization is small in comparison to the population served at large, PAH patients, particularly those receiving infused prostacyclins require specialized care delivered in an expeditious fashion, particularly during an emergent or unexpected hospitalization. The introduction of the BPA alert and detailed CCN, along with education tailored to specific care areas is intended to decrease the risk of adverse events with PAH patients. Ongoing monitoring of the use of these BPAs and CCNs is required to assess their efficacy. The selective nature of this initial program may provide the framework for adoption of this functionality at other PH Centers or to identify needs for other patient populations with a need for delineation and education.

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Abstract Title

Hemodynamic improvement and prognostic impact of intravenous iloprost in patients with systemic sclerosis

Purpose

Our aim was to determine if vasodilator treatment with intravenous (i.v.) iloprost for treatment and/or prevention of Raynaud's phenomenon and digital ulcers could impact on prognosis and hemodynamic features of pulmonary circulation in patients with systemic sclerosis (SSc).

Background

Pulmonary arterial hypertension is a late, well known complication of (SSc), which significantly impacts on prognosis and quality of life. Vasodilator treatment with i.v. prostanoids have been approved for the management of Raynaud's phenomenon and digital ulcers. Moreover, they contribute to attenuate vascular remodeling on pulmonary circulation in patients with connective tissue disease.

Methods

From January 2007 until September 2012, 28 SSc patients (18 with limited cutaneous form, 7 with diffuse cutaneous form and 3 with 'Overlap' syndromes) underwent right heart catheterization on the basis of high clinical and echocardiographic suspicion of pulmonary hypertension. All the patients fulfilled the diagnostic criteria for SSc proposed by the American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR). Thirteen SSc patients were in treatment with monthly cycles of i.v. iloprost (0,5-2 ng/kg/min/6 hours/cycle) for the management of Raynaud's phenomenon and/or digital ulcers, while the other 15 did not receive any i.v. prostanoids.

Results

Both groups of SSc patients were comparable in terms of sex, age and anthropometric features. Patients treated with i.v. iloprost showed a low mean value of pulmonary vascular resistances ($4.7 \text{ W.U.} \pm 4.0$ vs $6.9 \text{ W.U.} \pm 4.61$; $p=0.07$) and mean pulmonary arterial pressure ($33.3 \text{ mmHg} \pm 12.4$ vs $37.6 \text{ mmHg} \pm 9.1$ $p=0.4$), although statistically nonsignificant, and a significant increase of cardiac index ($3.1 \text{ l/min/m}^2 \pm 0.6$ vs $2.5 \text{ l/min/m}^2 \pm 0.7$; $p=0.03$) than those untreated with i.v. prostanoids. Moreover, survival in patients treated with i.v. iloprost at 5 and 7 years from SSc diagnosis was 97.4% and 96.8% respectively, whereas untreated patients had a worse survival rate at 5 and 7 years (86.3% and 72.4% respectively). Vasodilator treatment with i.v. iloprost was associated with the greatest survival advantage both at 5 (OR 6.18; $p=0.042$) and 7 years (OR 7.14; $p=0.036$) from SSc diagnosis.

Conclusion

Our data suggest how vasodilator therapy with i.v. iloprost for the management of Raynaud's phenomenon and/or digital ulcers may impact on hemodynamic profile and survival, suggesting a potential protective role on pulmonary circulation in patients with SSc.

Authors

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Abstract Title

The Stability of Remodulin® (treprostinil) Injection Combined with Intravenous Medications in Normal Saline

Purpose

To evaluate the chemical stability of treprostinil individually mixed with twelve intravenous (IV) medications in normal saline.

Background

Treprostinil is a prostacyclin analogue approved in the United States for the treatment of World Health Organization Group 1 pulmonary arterial hypertension (PAH). Patients with PAH and patients in clinical trials (e.g., neonates with persistent pulmonary hypertension of the newborn) treated with IV treprostinil in the hospital setting may be acutely ill or experience additional comorbidities requiring concomitant utilization of other IV medications. Lack of data demonstrating the chemical stability of treprostinil with other IV medications complicates the ability of health care teams to make decisions regarding co-administration.

Methods

Treprostinil and twelve IV medications (i.e., dexmedetomidine, dobutamine, dopamine, epinephrine, fentanyl, furosemide, heparin, midazolam, milrinone, morphine, norepinephrine, and vasopressin) were diluted with normal saline to low and high concentrations (unless otherwise noted) and combined. Combined medication solutions were stored at ambient conditions (20 to 23 C) and

concentrations were analyzed at t=0, t=18, and t=24 hours (and t=52 hours with heparin). Stability was defined as not less than 90% and not more than 110% of initial medication concentrations and no visible precipitation or color change.

Results

Chemical stability results of tested solutions are outlined in Table 1.

Conclusion

This study demonstrated the chemical stability of treprostinil individually mixed at low and high concentrations (unless otherwise noted) with: dopamine (low concentrations) at 18 hours; dexmedetomidine, dobutamine, fentanyl, furosemide, midazolam, milrinone, morphine, norepinephrine, and vasopressin (one concentration tested) at 24 hours; and heparin (one concentration tested) at 52 hours. A variety of diluents may be utilized when preparing treprostinil for IV infusion (e.g., Sterile Diluent for Remodulin, Sterile Diluent for Flolan, sterile water for injection, and 0.9% Sodium Chloride for injection). This study utilized normal saline as a diluent and samples were stored at ambient conditions. Additional studies should be considered to determine the chemical stability of treprostinil and these medications when mixed with other diluents and stored at higher temperatures.

Table 1. Stability Results of Tested Solutions

Solutions	Medications	Low Concentrations	High Concentrations
<i>Not stable</i>			
A ¹	Dopamine		40.0 mg/mL
	Treprostinil		1.0 mg/mL
B ²	Epinephrine	8.0 µg/mL	90.0 µg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
<i>Stable at 18 hours</i>			
C ³	Dopamine	1.6 mg/mL	
	Treprostinil	0.4 mg/mL	
<i>Stable at 24 hours</i>			
D	Dexmedetomidine	4.0 µg/mL	4.0 µg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
E	Dobutamine	1.0 mg/mL	8.0 mg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
F	Fentanyl	10.0 µg/mL	50.0 µg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
G	Furosemide	1.5 mg/mL	10.0 mg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
H	Midazolam	0.1 mg/mL	5.0 mg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
I	Milrinone	0.2 mg/mL	1.0 mg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
J	Morphine	5.0 mg/mL	5.0 mg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
K	Norepinephrine	16.0 µg/mL	80.0 µg/mL
	Treprostinil	0.4 mg/mL	1.0 mg/mL
L	Vasopressin	2.0 units/mL	Not performed
	Treprostinil	8.0 mg/mL	Not performed
<i>Stable at 52 hours</i>			
M	Heparin	20.0 units/mL	Not performed
	Treprostinil	8.0 mg/mL	Not performed

¹Deemed not stable as solution did not meet the acceptance criteria for concentration assay or appearance at 18 or 24 hours.

²Deemed not stable as epinephrine did not pass system suitability standards due to epinephrine peak degradation during analysis.

³Deemed stable at 18 hours as precipitate formed at subsequent 24-hour time point.

Authors

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Abstract Title

Sexual Function and Health-Related Quality of Life in Pulmonary Arterial Hypertension

Purpose

To establish whether patients with pulmonary arterial hypertension (PAH) experience deficits in sexual health-related quality of life (SHRQoL) and whether there is a relationship between SHRQoL and established measures of general health-related quality of life (HRQoL) in PAH.

Background

Sexual health and function is an important component of general HRQoL. There are no data that elucidate SHRQoL and its role as an important unmet need for patients, their partners and caregivers, and their care team. Studies in other chronic cardiopulmonary diseases suggest that patients have high rates of sexual dysfunction due to fear of dyspnea during sexual activities. Sexual dysfunction may be even more prevalent in PAH, which has the added challenges of parenteral therapies and fears of pregnancy since more than 80% of prevalent PAH patients are women. Phosphodiesterase type-5 inhibitors are commonly used to treat PAH, but are also approved for erectile dysfunction and may also directly affect sexual function. Several tools have been developed to assess general HRQoL in PAH, but no validated measures exist for evaluating SHRQoL in PAH. We hypothesized that there would be at least a moderate correlation between SHRQoL and established HRQoL measures in PAH, and that patients on parenteral therapies would have greater deficits in SHRQoL as compared to patients on oral therapies only.

Methods

We conducted a cross-sectional study in the Research Room at the 2016 Pulmonary Hypertension Association's (PHA) International Pulmonary Hypertension Conference in Dallas, Texas. Subjects were recruited to participate if they had a self-reported history of World Health Organization (WHO) Group 1 PAH. Four surveys (the Arizona Sexual Experience Scale [ASEX], the Female Sexual Distress Scale-Revised [FSDS-R], the Short Form [SF]-36 Health Survey, and the emPHasis-10) were administered to each participant via electronic tablets. The validated SHRQoL questionnaires

(ASEX and FSDS-R) addressed a myriad of measures including sexual drive, arousal, ability to reach orgasm, and distress related to sexual function. These were then correlated with established general (SF-36) and PAH-specific (emPHasis-10) HRQoL surveys and common PAH surrogates such as functional class. The PHA Conference's Research Room Leadership Committee and local Institutional Review Board (#408516) approved this study.

Results

A total of 34 women with self-reported WHO Group I PAH completed quantitative surveys. The median age was 46 years (range 31 – 72); 69% (n=22) of the women who answered the question about race identified themselves as white. 48% of 29 women with complete data reported treatment with prostacyclin analogue therapies via intravenous or subcutaneous pumps. The FSDS-R and ASEX scales demonstrated excellent reliability (Cronbach's $\alpha = 0.97$ and 0.89 , respectively). There were significant positive correlations between the FSDS-R total score and emPHasis-10 (Pearson's $r = 0.64$, $p < 0.01$) and significant negative correlations between six of eight SF-36 domains (Pearson's $r = -0.36$ to -0.64 , $p < 0.05$ for all). There were no significant correlations between ASEX scores and emPHasis-10 nor SF-36 scores. Total FSDS-R scores show a trend toward discriminating patients who were treated with parenteral prostacyclin analogues (ANOVA $F = 3.22$, $p = 0.084$) in this sample, while ASEX, emPHasis-10 and SF-36 subscales did not.

Conclusion

Validated SHRQoL surveys perform well psychometrically in women with PAH. The FSDS-R, a tool designed to capture anxiety and distress related to impaired sexual health and function in women, was moderately correlated to general and established HRQoL measures in PAH and may have greater fidelity to detect impaired SHRQoL related to parenteral therapies than general HRQoL surveys. Future research should further elucidate SHRQoL assessment and intervention as gaps in PAH care to facilitate discussions between patients and their providers on this important but sensitive topic.

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Abstract Title

Feasibility and Acceptability of Integrative Therapy for the Management of Symptom in Persons with Pulmonary Hypertension

Purpose

To describe research study plan testing feasibility, acceptability and preliminary efficacy of an integrative program for symptom management in persons with pulmonary hypertension (PH). Evaluating preliminary efficacy of a multi-modal behavioral intervention, Urban Zen Integrative Therapy (UZIT), requires documentation of the intervention fidelity. Consistent delivery of the intervention dose is essential to the integrity of any research design, but of particular concern in research study testing integrative therapy intervention. Proper description and delineation of intervention fidelity assessment is necessary to ensure consistent treatment delivery. This poster will present plans for measuring study's feasibility, acceptability, and intervention fidelity.

Background

Pulmonary Hypertension (PH) is a progressive and debilitating chronic cardiopulmonary condition and serves as an excellent model for symptom management intervention development and testing. Elevated pulmonary pressure and associated high symptom burden can impair patients' ability to manage and adhere to medical treatments leading to reduced quality of life. Integrative approaches to symptom management are urgently needed. Many integrative approaches have shown benefit in symptom alleviation in chronic conditions such as cancer and heart disease, and may have therapeutic benefits in PH. A patient-centered, pragmatic integrative approach to symptom treatment can provide holistic management without added side effects. The purpose of this mixed-methods pilot study is to determine the feasibility, acceptability, and preliminary efficacy of a 6-week integrative therapy program, UZIT among community-dwelling adults with PH.

Methods

Feasibility will be determined by 1) Recruitment rate (>40% recruited from those approached), 2) Enrollment rate (>2 /

month), 3) Home practice (> 1/week), and 4) retention rate (>70% of participants remain). Acceptability will be determined by 1) Participants' evaluation of the UZIT program (composite mean System Usability Scale score > 5, scale 1-7), 2) Session completion rate (83% attendance by the participants retained at the study end). UZIT intervention fidelity will focus on consistency of intervention delivery and intervention dose which will address: 1) research intervention protocol, 2) interventionists' competency training, 3) quality audit, and 4) research process evaluation.

We will enroll a single cohort of 20 PH participants at an academic medical center. UZIT intervention will include four integrative modalities: essential oil, gentle body movement/restorative pose, body-awareness meditation, and Reiki. Trained UZIT therapists will provide treatments tailored to patients' symptoms and physical capability, however, within the bounds of the research protocol. Study field notes, semi-structured interviews, and daily symptom diaries will provide qualitative description of symptoms and UZIT acceptability and constant comparison. Intervention sessions will be remotely video recorded and examined for fidelity.

Results

TBD

Conclusion

Implementation of behavioral intervention research is challenged by many threats to study's internal validity. Mind-body integrative therapy with multi-modal components adds further complexity to the scientific testing standards. With the goal of establishing study feasibility and acceptability, consistent intervention delivery is paramount to optimize scientific rigor. Future efficacy testing of UZIT for symptom management in PH will rely on this scientific standard. If feasible and acceptable to PH patients, this intervention has the potential to mitigate the bothersome symptoms inherent in PH and improve patients' quality of life.

Authors

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Abstract Title

Journey to High Reliability Pulmonary Hypertension Nursing practice

Purpose

Design an Inpatient Nursing practice using High Reliability principles to create a zero-defect environment.

Background

Hospital admissions for Pulmonary Hypertension (PH) patients can be dangerous. The smallest of medication errors could mean serious injury or death. Developing a nursing care program that keeps PH patients safe from harm is not an easy task. High Reliability principles when applied to health care result in stunning improvement in quality, safety and outcomes. High Reliability health care has been described as a "passionate commitment to excellence" that permeates the daily actions of health care workers, producing a culture so effective that nearly perfect safety procedures are the norm.

Methods

High Reliability principles were applied in the development of:

1. PH nursing policies and procedures with yearly reviews to continuously improve processes and performance
2. PH nursing education and training at three levels of competence
 - a. Orientation- Competent Level
 - 8 hour class containing 4.5 hours of Lecture, 1.5 hours of skill stations and 1.5 hours of simulation
 - b. Proficient Level (Level 2)
 - 8 hour class 4.5 hours of Lecture, 1.5 hours of skill stations and 1.5 hours of simulation
 - c. Expert Level (Level 3)
 - Prerequisite pretest using online or printed material
 - 4 hour class: 1.5 hours of skill stations and 2.5 hours of simulation
 - Requirement to assist in teaching Orientation or Level 2 class or precept new hires in the care of PH patients

c. Expert Level (Level 3)

- Prerequisite pretest using online or printed material
- 4 hour class: 1.5 hours of skill stations and 2.5 hours of simulation
- Requirement to assist in teaching Orientation or Level 2 class or precept new hires in the care of PH patients

Results

Elimination of prostacyclin emergencies and medication errors related to nursing practice in the two core PH nursing units where patients are admitted within the first 12 months of program launch. The program is in the third calendar year with only one minor error occurring on the PH nursing units. A significant increase in near-miss (where error never reaches the patient) reporting through nursing and pharmacy channels.

Conclusion

High Reliability Pulmonary Hypertension Nursing practice is possible when leadership, Medical staff, Pharmacy staff and Nursing staff share the culture and practice where all members of the PH team are acutely aware that even small failures in safety protocols or processes are unacceptable where ZERO is the goal. Maintaining excellence is as difficult as attaining excellence. High Reliability principles provide the tools and guidance to successfully maintain excellence if ZERO defines the attitude of the organization.

Authors

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Abstract Title

Oral Treprostinil in 2 Pediatric patients with IPAH

Purpose

Describe the experience of oral treprostinil in 2 children with IPAH.

Background

IV, SQ and inhaled treprostinil use had been described in children and can improve PH symptoms and quality of life. Oral treprostinil is simpler and less risky to deliver. In adults, side effects can limit dosing. No reports on oral treprostinil have been published.

Methods

Patient 1

10 year old girl with severe idiopathic pulmonary hypertension on triple therapy (IV treprostinil, tadalafil and bosentan) underwent Potts shunt. Eleven months later, she was transitioned from IV to oral.

Time	Change	Treprostinil dose	6MWD	Fxnl class	Side effects	Possible cause
	Post Ports downtitration	110 ng/kg/min	531	I-II		
	Transition dose (assumed 5:1)	75 ng/kg/min to 5 mg TID	480	III		
	Uptitrated due to PH symptoms	8.625 mg TID	445	III	Daily headaches, nausea and occasional vomiting	Peak/trough phenomenon
9 months	Divided into QID	6.5 mg QID	470	III	Nighttime headaches and nausea	Associated with evening tadalafil dose
	Divided tadalafil into BID				Middle of the night severe headaches and vomiting, worse after hot or active day	Dehydration
	Increased fluids daily and especially evening				Significantly improved headaches and vomiting	
11 months	Increased nighttime dose due to PH symptoms and morning fatigue and "fogginess"	7 mg TID and 8 mg HS	592	II		
18 months	Uptitrated due to PH symptoms	8 mg QID			Rare headaches at night when fluid intake is low	

Patient 2

10 year old boy with IPAH on tadalafil and ambrisentan

Time	Change	Treprostinil dose	6MWD	Fxnl class	Side effects	Possible cause
		0	333	III		
	Initiation and uptitration 3 times a week	0.125 mg TID				
3 months	Slowed uptitration to weekly	2.635 mg TID		II	Severe headaches	
6 months	Slowed uptitration to every other week	4 mg TID		II	Moderate evening headaches	
9 months	Divided into QID	4.75 mg TID	495	II	Middle of the night headaches and vomiting	Dehydration
	Increase fluids with 8 ounces in evening				Increase fluids with 8 ounces in evening	
12 months		5 mg TID	557	I	Mild daytime headaches and nausea	
	Divided tadalafil BID				Rare headaches	

Results

Both patients experienced improvement in 6 min walk distance and functional class. Both patients experienced severe headaches, which improved by improving hydration and dividing tadalafil. In addition, one patient's headaches improved by changing to QID dosing and the other needed to slow up titration. Both families report good quality of life.

Conclusion

Children with IPAH can tolerate and experience improvement in PH on oral treprostinil. Side effects of headaches can be due to many reasons and requires dedication to treat effectively

Authors

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Abstract Title

Implementation of Epoprostenol Protocol in Outpatient Infusion Center

Purpose

The purpose of this protocol implementation was to safely utilize epoprostenol in the outpatient setting to improve blood flow for scleroderma (SSc) patients with severe Raynaud's phenomenon and critical digital ischemia, thereby improving digital ulcers and reducing incidence of digit loss.

Background

Much of the available literature for outpatient IV prostacyclin use in this patient population has been from Europe, where IV Iloprost is routinely prescribed in SSc subjects to manage vascular as well as fibrotic manifestations. In the US, where IV Iloprost is not available, short term use of IV epoprostenol (Flolan or Veletri) to treat critical digital ischemia has been proposed. Some inpatient experience with use of epoprostenol for this indication has been reported by other institutions. Therefore, we elected to develop and implement our own protocol at UCSF.

Methods

Our Scleroderma team partnered with the Pulmonary Hypertension Nurse Coordinator for this project. A low-dose epoprostenol protocol was created for patients with severe Raynaud's phenomenon with several safety considerations in place such as: pre-screening of patients to ensure they do not have significant pulmonary hypertension or heart failure and review of recent echo, creating a specific order set in the electronic medical record to ensure standard ordering practices, creation of a SOP (Standard Operating Procedure) for the Infusion Center for this therapy, limiting staff who would care for these patients to a small group, setting

pumps with hard stop max dosing to prevent accidental miss-programming of the pump, obtaining approval by several committees including Medication Safety Committee, Pharmacy & Therapeutics Committee, and Patient Safety Committee. Prior to implementing the protocol, hands-on training was completed for a core group of nurses and pharmacists in the Outpatient Infusion Center, and our team was readily available to staff during first few patient infusions for any questions or concerns. In our first 6+ months of infusions, we have had 4 patients receive epoprostenol treatment (2 of the 5 patients have received the treatment twice).

Results

Five patients received treatment in the first 6 months of using the protocol. Overall, the administration of epoprostenol per the UCSF protocol has been tolerated extremely well. No severe adverse event has been recorded. Findings also include improvement of existing ulcers, shortened healing time (in conjunction with current therapies), and decreased pain.

Conclusion

With appropriate safety measures and implementation of a well-defined infusion protocol, low-dose epoprostenol can be safely administered in the outpatient setting to SSc patients suffering from severe Raynaud's phenomenon and critical digital ischemia. Our findings to date suggest that this approach is clinically effective and can prevent substantial morbidity from severe peripheral vascular disease in this patient population.

Authors

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Abstract Title

Case Report: Transition from oral treprostinil to selexipag in a pediatric patient with pulmonary arterial hypertension

Purpose

The use and transition to selexipag in a female patient with WHO Group I pulmonary arterial hypertension (PAH) will be described.

Background

Selexipag is an agonist of the prostacyclin receptor, and has gained wider use in the adult PH population. Pediatric use is limited. The patient was an 18-year-old with a history of ventricular septal defect, initially banded, and with delayed complete repair at 8 years of age. She had documented progression of her PAH, with progressive therapy culminating in oral treprostinil as her third drug. However, debilitating symptoms of headache and facial flushing, despite dose adjustment prompted the transition. This report summarizes the development and implementation of a standardized approach to transition from oral treprostinil therapy to selexipag.

Methods

Consideration for this decision was prompted by ongoing side effects on oral treprostinil that remained unresolved after 6 months of attempts at symptom alleviation, and with growing concern for deterioration in medical compliance. Literature and industry also reported a lesser side effect profile with similar efficacy with selexipag in treating PAH. The model for the transition plan was developed within our multidisciplinary PH service and with input from our adult colleagues, since no data for transitioning between these two therapies exists. At the commencement of the transition, her oral treprostinil dose was 6mg QID (approximately equivalent to an infused prostacyclin dose of 45-50ng/kg/min). The calculated initial goal dose of selexipag was 800-1000mcg, an

equivalent to intra-venous treprostinil dose of 40-50ng/kg/min. Upon admission, her oral treprostinil dose was reduced to 6mg TID to ease the transition. Selexipag was started on the same day with a dose of 200mcg Q12 hours scheduled with a simultaneous decrease in oral treprostinil dose by 2mg. In the subsequent days, doses were adjusted with increases in selexipag by 200 mcg and decreases in oral treprostinil by 2mg with every dose. By day 3, oral treprostinil was discontinued, and the selexipag dose was 600mcg. On day 4, the final increase to 800mcg selexipag was completed shortly before discharge.

Results

During the hospital stay, the patient was prophylactically treated with scheduled ondansetron, with acetaminophen and ibuprofen available as needed for headache. She had no emesis or abdominal discomfort. Vital signs were monitored consistently during the admission and remained stable at patient baseline. Post discharge follow-up consisted of daily phone calls for the first week with self-reporting of only minor headaches. One week after discharge, she tolerated the final increase to 1000mcg of selexipag with no further side effects reported. Further follow up is pending.

Conclusion

We have shown that with multidisciplinary team planning, a transition from oral treprostinil to selexipag can be completed safely and with minimal side effects in the pediatric population. This model of comprehensive and collaborative pediatric medical care has resulted in improved patient outcomes and quality of life, which we hope will contribute to improved compliance.

Authors

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Abstract Title

Oral treprostinil Use in the Management of a Pediatric Pulmonary Hypertension: A Case Report

Purpose

The use of oral treprostinil in the management of four pediatric WHO Group I pulmonary arterial hypertension (PAH) patients will be described.

Background

Symptoms and hemodynamics measured by repeated right heart catheterization indicated the need for prostacyclin therapy in all 4, and all had been treated with other routes of prostacyclin therapy. Although limited data is available to define the role of oral treprostinil in pediatric PH patients, it was selected as the most appropriate prostacyclin formulation in these patients. This abstract will discuss the method of titration and the initial response to oral treprostinil.

Methods

The model for initiation of oral treprostinil was developed within our PH service using a review of available clinical trials, our current practice, input from the manufacturer, and discussion with the families. The goal was a safe and tolerable commencement of oral prostacyclin therapy in an intensive care setting, with achievement of comparative dose administration. The patients were 4-15 years old, weighing 19-70kg. Two patients were simultaneously transitioned off SQ therapy, 1 off IV and 1 patient a new start having previously failed SQ therapy. A detailed titration plan (considering oral versus parenteral dose equivalency) was derived for each patient. Oral treprostinil was started at

0.125-0.5mg and increased at 0.125-0.25mg increments with goal doses of 1.5-6.5mg TID. Simultaneously, the parenteral administration in those three patients on SQ and IV therapy was accordingly down-titrated. The transitions were completed in 6-13-days.

Results

Three of the 4 patients had minimal to no side effects, with 1 patient experiencing GI symptoms. That patient had their oral up-titration slowed, with alleviation of symptoms, but with the ultimate dose attained prior to discharge. We believe the experience gained with the commencement of this therapy will further expand the utility for oral prostacyclin use in other pediatric patients. Based on the clinical responses and family reports, the oral treprostinil has provided the clinical benefit of parenteral therapy, but without infection risk, impact on quality of life and a diminution in the risk of medication errors.

Conclusion

Oral treprostinil was relatively well tolerated in this patient group. These cases illustrate various clinical scenarios in which oral treprostinil provided an opportunity to maximize medical therapy and deliver prostacyclin treatment in a broad range of pediatric patients. Additionally, this report emphasizes that institution of all prostacyclin agents requires close collaboration with the health care team and family members to ensure safe and effective administration.

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Abstract Title

Safety and pharmacokinetics of ralinepag (APD811) in healthy adult subjects

Purpose

To study the safety, tolerability, and pharmacokinetics (PK) of ralinepag in two Phase 1 placebo-controlled clinical studies.

Background

Ralinepag is a novel, next-generation, oral, selective, and potent prostacyclin receptor agonist in development for the treatment of pulmonary arterial hypertension, that has demonstrated potent activity on human vascular smooth muscle cells and platelets. The safety, tolerability and PK needs to be determined in clinical studies.

Methods

In a single-dose escalation study, four cohorts (n=8/cohort; 6 on ralinepag; 2 on placebo) of healthy adults received ralinepag 0.03, 0.05, 0.1 or 0.2 mg in a fasted state. In a multiple ascending dose study in healthy volunteers, Cohort A (ralinepag n=20; placebo n=10) received ralinepag 0.05 mg once-daily (q.d.), increasing every sixth day to 0.1, 0.2, 0.3 and 0.4 mg for up to 27 days. Cohort B (ralinepag n=20; placebo n=5) received ralinepag 0.01 mg twice-daily (b.i.d.), increasing every sixth day to 0.03, 0.04, 0.05 and 0.07 b.i.d for up to 30 days.

Results

In the single-dose study, all 32 subjects completed. Ralinepag was tolerated at 0.03, 0.05 and 0.1 mg. Dose escalation was discontinued at 0.2 mg due to treatment-emergent adverse events (AEs), most commonly vomiting, headache and nausea (6/6, 5/6 and 3/6, respectively); nausea and vomiting were

moderate-to-severe. AEs were similar for male and female subjects. There were no clear dose-dependent changes in blood pressure and no clinically significant changes in ECG or laboratory tests. There were increases in mean heart rate from 0.05 mg upwards, most evident at 0.2 mg. In the PK analysis, the median t_{max} (time to maximum plasma levels) and estimated mean terminal half-life across dose groups were approximately 1.25 hrs. and 23 hours, respectively.

In the multiple ascending dose study, 26/30 subjects in Cohort A and 24/25 subjects in Cohort B completed the study. Most subjects on ralinepag reported moderate AEs, most commonly headache, nausea and jaw pain. Most common AEs with placebo were constipation and headache. Four subjects withdrew due to AEs (0.05 mg q.d., vomiting, headache; 0.1 mg q.d., nausea, headache, palpitations; 0.05 mg q.d., atrial fibrillation; 0.01 mg b.i.d., ECG wave changes). The highest tolerated doses were 0.3 mg q.d. and 0.07 mg b.i.d. Exposure of ralinepag was dose proportional, independent of q.d. or b.i.d. administration, and there was no appreciable accumulation of ralinepag after multiple dosing.

Conclusion

The tolerability of ralinepag in healthy adults varied across doses, with the observed AEs being consistent with prostacyclin agonists. AEs were generally dose-related, but not associated with plasma concentration. Individual dose titration is needed to determine the optimal individual dose level. These results support progress into clinical studies evaluating ralinepag in patients with pulmonary arterial hypertension.

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Abstract Title

Pulmonary Hypertension Comprehensive Care Center - Spreading the Word

Purpose

Evaluate the referrals received at our center to identify the changing trends among our patient population since our accreditation as a Comprehensive Care Center including time to referral, time to treatment, functional class and diagnosis at referral.

Background

It is well known in the PH community, oftentimes, by the time patients are referred to a PH center, they are often late into the disease process. By evaluating our referrals over the past three years (1-year prior (2014), the year of (2015), and the year since (2016) accreditation) we hope to identify positive trends, as well as those gaps that could potentially be addressed by education of our current patients with the importance of follow up, education within the surrounding communities including those physicians who are encountering these patients; about what the disease is, how to treat, when to refer etc. We have tracked patients by their age, diagnosis, who group status, functional status at referral, if they were started on PAH specific therapy, as well as their functional class over the past 12 months.

Methods

We have over 500 patients within our center to utilize in this historical review of data. This information is being gathered to be compared as a conglomerate data source to identify trends over the past three years individually and collectively to better

serve our patients and our associate physician with whom we collaborate for patient care.

Results

We anticipate seeing important trends over the past year as compared to two years ago, These trends will identify appropriate referrals for those with disease at an earlier functional class 2-3 more often so that appropriate treatment can be started. We also hope to see an improvement in functional class for those established patients over the past 12 months since those patients are being identified appropriately and treated in a timelier manner. Negative trends in any of the evaluated categories will be areas that can be utilized to tailor educational campaigns.

Conclusion

It is hypothesized that by becoming a pulmonary hypertension comprehensive care center, this is going to have a positive impact on both our center and our community. By advertising this new achievement and sharing our mission as such a center, this will bring improved awareness of the disease process as well as educate both our current patients, future patients, and community physicians of why early detection is so important to long-term survival. These trends will also help us to tailor our education within our own center to ensure general understanding among all units who may encounter this patient population and how to best customize their plans of care while receiving care within our health system.

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Abstract Title

Transition between SQ, PO, and IV treprostinil: A Case Report

Purpose

This case study describes the clinical reasoning and titration schedule utilized in transitioning a PAH patient from SQ to PO treprostinil, with eventual transition to IV treprostinil.

Background

A 73 year old female with PAH WHO Group 1, NYHA Functional Class III symptoms was initiated on SQ treprostinil after 6 months of limited improvement on combination therapy with a PDE-5 Inhibitor and ERA. Twenty months after initiating therapy, severe site pain prompted a discussion about newly-available oral prostacyclin therapy options as an alternative to parenteral therapy. Ultimately, the provider and patient agreed to transition to PO treprostinil.

Methods

With limited amounts of published transition guidelines and clinical experience with SQ to PO transitions, collaboration with pharmacists and PAH providers was required, along with a detailed review of the manufacturer's recommendations and clinical trial data. The transition plan began with decreasing the treprostinil dose at home by 4-5 ng/kg/min every 3 days from 60 ng/kg/min to 35 ng/kg/min without adverse clinical effects. Then, PO treprostinil was initiated and titrated as shown in Fig. 1.

Fig. 1 – In-home titration schedule

Day	Orenitramdose (TID)	Remodulin ng/kg/min	Pump rate
17	2.5 mg	35	0.016
20	2 mg	30	0.014
23	3	26	0.012
25	3.5	22	0.010
28	4	17	0.008
31	5	13	0.006
34	6	8	0.004
37	7	4	0.002
40	7	OFF	OFF
43	8	OFF	OFF
46	9	OFF	OFF
49	10	OFF	OFF

This transition was accomplished at home with minor prostacyclin side effects of dizziness, nausea and headache. The SQ pump was removed on day 40. Four days later, with the patient on 8 mg TID of PO treprostinil, she developed severe nausea which worsened with increasing doses. On day 51, acute bronchitis complicated her course; she also developed worsening PAH symptoms. Eventually, she experienced dose-limiting side effects of nausea, hypotension and dizziness and was admitted to the hospital. She was transitioned to 30 ng/kg/min IV treprostinil while simultaneously decreasing her PO dose over the course of 2.5 days. Further IV titration was completed at home up to 40 ng/kg/min with improvement in her symptoms and functional capacity back to her baseline values.

Results

The in-home transition from SQ to PO treprostinil was initially successful and tolerated well. Dose-related intolerance of PO treprostinil, combined with acute bronchitis, limited the successful titration and confounded the origin of the patient's symptoms. The eventual transition from PO to IV treprostinil was rapid and tolerated well by the patient with resolution of all prostacyclin-related side effects.

Conclusion

This case study leads to questions regarding the tolerance of PO treprostinil at high doses, especially considering the quantity of tablets required per day. Decreasing the SQ dose of treprostinil as much as possible prior to the PO transition is an important step to consider if the patient is on a relatively high dose of infused prostacyclin. This theoretically decreases the goal dose of PO treprostinil and the likelihood of PO prostacyclin-related side effects.

Clear documentation of symptoms and frequent communication during the transition is imperative to successful titration, especially if completed in the patient's home. Patient education and clinical documentation should emphasize the difference between prostacyclin-related complaints versus signs and symptoms of worsening PAH and/or other underlying disease processes.

Lastly, there is a need for continued research and trials contributing to the development of transition guidelines and/or protocols for such transitions in this era of emerging oral prostacyclin therapies.

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Abstract Title

Beyond the Basics: Development and Implementation of a Pulmonary Arterial Hypertension (PAH) Nurse-Patient Communications Pilot Program

Purpose

The 2017 Beyond the Basics pilot program includes a series of interactive educational workshops in which pulmonary arterial hypertension (PAH) nurses and social workers discuss means to enhance care through enriched nurse-patient communications.

Background

While PAH-specific communications and counseling strategies to address patients' psychosocial and emotional needs are beneficial, training and techniques are not widely available and only a few centers have access to a social worker. In this program, PAH nurses and social workers share communication strategies and approaches to conversations with patients about the impact of their disease beyond clinical fundamentals. The PAH social workers also share best practices to address quality of life (QoL) issues.

Methods

An advisory committee comprising expert PAH nurses and social workers was convened in 2016 to develop an educational PAH nurse-patient communications program. The resulting pilot consists of small group, interactive 2-hour workshops, sponsored by Actelion Pharmaceuticals. The curriculum consists of case-based presentations on psychosocial and emotional needs of patients with PAH, and communications and counseling strategies to address them. Participants learn about and discuss means to tailor communications to the individual patient, to assess health literacy and comprehension, to address PAH-specific sensitive issues such as depression/anxiety and the dangers of pregnancy, and to coach patients on self-care and "ownership" of PAH management. Ten nurse and social worker faculty are trained to present the content and moderate discussions. Each workshop features a 3-member faculty team: 2 nurse moderators and 1 social worker. The workshops are attended by 5 to 10 PAH nurses and other care team members from the local area. Evaluation forms allow attendees to opt in for future programming.

Results

Seven of 10 pilot program workshops were completed in cities across the country, and were attended by 52 nurses, nurse practitioners, and other PAH care team members as of June 2017. In response to the question, "What information did you find most important, interesting, or impactful?" participants stated they valued the social worker presentation, the open dialogue, and techniques on making sure the patient fully understands their diagnosis. Key insights from the regional workshops were:

- Nurses want opportunities to collaborate and share best practices with peers
- Strategies to address difficult conversations are needed/valued
- Nurses rarely have access to social workers but highly value their services
- Limitations in access to and knowledge of PAH support services overburden nurses and compromise care delivery
- Nurses do not have enough time to discuss patients' reduced QoL
- PAH care team communications enrichment is an area of need

Conclusion

Implementation of a program that educates PAH nurses on communications and counseling strategies may help address psychosocial and emotional needs of patients with PAH. Social workers offer valuable insights, techniques, and feedback on access to support services and communications-based means to enrich PAH patient care. Further education and resources are warranted to improve patient communications and access to support services. Peer sharing of best practices is critical to fully address the real world patient communications needs of nurses and other PAH care team members.