Pharmascript

Volume 44, Issue No.3,
Supplement 1
Third Quarter

Supplement: 2020 Pharmacy Resident Research Abstracts

Impact of patisiran use in patients with hereditary transthyretin-mediated amyloidosis within ambulatory care and home infusion services

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Background

Patisiran (Onpattro®) was the first infusion drug approved by the FDA for hereditary transthyretin-mediated amyloidosis (hATTR) polyneuropathy in August 2018. The APOLLO study was the Phase III clinical trial for patisiran, which included Johns Hopkins as a trial site. To promote a smooth transition from clinical trial and facilitate patient access within Johns Hopkins Medicine (JHM), Johns Hopkins Home Care Group (JHHCG) collaborated with stakeholders across JHM in spring 2018 to identify patisiran service needs. Once patisiran gained FDA approval, JHHCG rapidly implemented services to transition all clinical trial patients to commercially available drug as well as accept new referrals.

Objectives

(1) Evaluate the timeframe in which patients were newly initiated on patisiran or transitioned from clinical study to commercial drug after FDA approval; (2) Determine patient persistence to patisiran therapy and reasons for treatment discontinuation; (3) Characterize the current monitoring of clinical outcomes relevant to treatment and describe the outcomes.

Methods

First, five discussion sessions with the clinical care team were performed to determine the current state of operational and clinical monitoring for patients taking patisiran. Next, a retrospective analysis of all patients with

hATTR polyneuropathy who had a referral to JHHCG for patisiran therapy from August 1, 2018, to July 31, 2019 was performed. All patients who were referred during the study time frame were evaluated for insurance coverage determination and if they initiated infusion. Data sources used for this study included JHHCG referral intake records, patisiran referral forms, and the electronic health record. The primary investigator performed manual chart reviews in the electronic health record for each individual patient.

Speed to therapy was defined as the number of days between referral date and date of first patisiran infusion for patients who received at least one infusion. Speed to therapy was further evaluated by assessing the timeframe in which the referral occurred after FDA approval to compare results in the early phase after FDA approval (within the first 3 months) compared to patients referred later (3-6 months after). Persistence to therapy was defined as the number of patients continuing to receive infusion at 42 days, 90 days and 180 days after date of first infusion. Baseline and follow-up values for Neuropathy Impairment Score (NIS) and body mass index (BMI) were collected to characterize clinical monitoring.

Results

From August 2018 through July 2019, 35 patients were referred to JHHCG for patisiran infusion therapy. A total of 30 (86%) patients were approved for therapy by their insurance plan and 5 (14%) patients were denied. All patients had insurance coverage with a commercial or Medicare plan. Of the remaining 32 patients eligible for therapy initiation evaluation, 20 (62.5%) started patisiran therapy while 12 (37.5%) did not start therapy. All 20 patients who started therapy were evaluated for speed to therapy. A total of 5 (25%) patients were initiated on therapy 15 – 30 days after, 9 (45%) patients were initiated 31 – 60 days after, and 6 (30%) were initiated >60 days after. Out of the 20 patients who started patisiran therapy, 18 patients met criteria for persistence evaluation. Sixteen of the 18 (89%) patients remained persistent to patisiran for >180 days.

Out of the 20 patients who started therapy, only three patients met criteria for NIS evaluation due to irregular evaluation and reporting practice. The mean baseline NIS was 59.5 (range 27 to 90.5), and the mean change in NIS was -1.3 (range -11 to +2). Out of the 20 patients who started therapy, 16 patients met criteria for BMI evaluation. The mean baseline BMI was 26.15 (range 17.22 to 32.69) and the mean change in BMI was -0.05 (range -4.52 to +2.99).

Conclusion

A high percentage of referrals for patisiran were approved by insurance (86%), with most patients having coverage under a Medicare-based plan or a commercial payer. Speed to therapy improved for patients referred >3 months after FDA approval, and most patients remained persistent to therapy for at least 180 days. While BMI was recorded with every infusion, NIS was not routinely measured within a standardized timeframe, which led to very few patients meeting inclusion criteria for evaluation of change in NIS.

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Development and implementation of a short duration of antibiotic therapy algorithm for uncomplicated Gram-negative bacteremia

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Background
Recent literature suggests no difference in clinical outcomes between short (7 days) and prolonged course (14 days) antibiotic therapy for the treatment of uncomplicated Gram-negative bacteremia (GNB).

Methods
The objectives of the study were to develop and implement a treatment algorithm that identifies patients who are eligible for 7-day therapy for uncomplicated GNB and evaluate its impact on patient outcomes at The Johns Hopkins Hospital (JHH) in Baltimore. The algorithm was developed and implemented at JHH on 11/11/2019. From 11/11/2019 to 3/31/2020, the Infectious Diseases (ID) Pharmacy Resident and ID pharmacists reviewed cases of GNB on weekdays and contacted teams to provide algorithm-compliant treatment recommendations. To quantify the impact of the intervention on clinical outcomes, data from the same time period during the previous year (baseline) were collected and compared to those collected during the intervention. The primary outcome was duration of antibiotic therapy for GNB. Secondary outcomes included: duration of intravenous (IV) antibiotics, length of hospital stay (LOS), and recurrent bacteremia. Patient characteristics and clinical outcomes in the baseline and intervention periods were compared using Chi-square testing for categorical variables and Mann-Whitney *U* test or Student's t-test for continuous variables.

Results
A total of 345 patients with GNB were identified (142 baseline; 203 intervention) of which 59 and 55 patients met criteria for 7-day therapy, respectively. The Pitt bacteremia score (median 1), bacteremia source [urinary (43%), abdominal (23%)], and organisms [E. coli (48%) and Klebsiella spp. (33%)] were similar between the periods. More patients in the intervention period were treated for ≤8 days (60.0% vs. 37.3%; p=0.015), and the median duration of therapy was 2 days shorter (8 vs. 10 days; p=0.04). Median duration of IV antibiotic therapy (4 vs. 7 days; p=0.004) and median LOS (4 vs. 7 days; p=0.029) were also shorter in the intervention period. There were no differences in the rate of 30-day recurrent bacteremia between the periods (3.4% baseline vs. 1.8% intervention; p=0.60).

Conclusion
Our pharmacist-led intervention successfully shortened the duration of therapy, increased conversion from IV to PO therapy, and reduced LOS, without negatively impacting the number of patients with recurrent GNB.

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Investigation of antidepressant use during pregnancy and risk of postpartum hemorrhage: a case-control study

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Purpose

Postpartum hemorrhage (PPH) is a significant cause of maternal morbidity and mortality, and the incidence has been on the rise over the last few decades. Serotonergic antidepressants (ADs) have been linked to increased rates of bleeding disorders, likely through the inhibition of serotonin uptake into platelets, which in turn impairs platelet aggregation and hemostasis. Evidence concerning the relationship between serotonergic ADs and risk of PPH is conflicting, where some studies show an increased risk of bleeding and others show an unclear association or no increased risk. Serotonin may protect against postpartum bleeding through its role in regulating uterine contractions, which has the potential for significant implications, as the majority of PPH cases are due to uterine atony. There are currently no published studies which have hypothesized and explored the possible beneficial effects of ADs on the outcome of PPH. The primary aim of this study was to evaluate whether serotonergic AD use during pregnancy is associated with a decreased risk of PPH.

Methods

This was a multicenter, retrospective, case-control study of pregnant women ≥ 18 years of age admitted for delivery between July 1, 2016 and June 30, 2019 at three hospital sites in Washington, DC and Baltimore, MD. Patients were excluded if they experienced intrauterine fetal demise, were on antithrombotic or thrombolytic therapy prior to or during admission, or had a history of coagulopathy. Cases were defined as women with a discharge diagnosis of PPH, and each case was matched to fourteen controls on the basis of age. Conditional logistic regression was used to estimate the unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for the association between AD use and PPH.

Results

The analysis included 372 cases and 5208 controls. A greater percentage of cases used ADs than the large number of matched controls (12% versus 10%). After adjusting for confounders, all risk estimates related to AD use and the development of PPH were not significant, with 95% CIs crossing 1.0. AD use was found to be associated with a greater risk of PPH, with an overall 23% increased odds independent of other covariates (adjusted OR: 1.234; 95% CI: 0.874-1.743). The AD-specific estimates showed an increased risk of PPH across most AD classes, with selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors (SNRIs), and bupropion retaining non-significant ORs greater than 1.0. The highest odds of PPH were among patients on SNRIs (adjusted OR: 1.898; 95% CI: 0.848-4.247). Tricyclic antidepressants and trazodone did not show an increased risk after adjustment, yet CIs were wide due to low utilization.

Conclusion

The findings of this case-control study suggest a trend towards increased PPH risk with AD use, although this effect was not significant. These results do not support the hypothesis that serotonergic ADs have a beneficial effect on the outcome of PPH. It is likely the effect of ADs on PPH, if truly present, is small, and would require a larger sample size to uncover a statistically significant signal.

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Evaluation of anti-asthmatic monoclonal antibodies in the prevention of asthma exacerbations

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Background
Severe asthma is a highly prevalent and economically burdensome disease. Patients who have persistent symptoms, despite maximally optimized therapy, may be started on biologics. While randomized controlled trials have compared these agents to placebo, no studies have conducted head-to-head comparison.

Objectives
The primary objective was to compare the incidence of emergency department (ED) visits and admissions related to asthma exacerbations (AEs) among patients on these different agents (Figure 1). The secondary objective was to characterize the oral corticosteroid sparing effect (OCSE), if any (Figure 2).

Methods
Patients who received either omalizumab, mepolizumab, benralizumab, and reslizumab between October 2016 and September 2019 were included. Patients were excluded if they received any of these biologic agents for indications other than severe asthma. Descriptive statistics were used to analyze data.

Results
This study included 129 patients. Of those, 87 patients received mepolizumab, 25 received omalizumab and 17 received benralizumab. No patients received reslizumab. Mepolizumab was associated with the highest number of AEs at 0.91 ED visits and 0.42 hospitalizations per patient. Omalizumab followed with 0.45 and 0.21 ED visits and hospitalizations, respectively. Benralizumab was associated with the lowest rate of AEs with 0.29 ED visits and 0.12 hospitalization per patient. Conversely, benralizumab displayed the smallest OCSE (4mg mean difference; 16% reduction) in prednisone-equivalents. Mepolizumab had a moderate effect at a 12mg or 42% reduction, and omalizumab had the largest effect with about a 20mg or 54% difference.

Conclusion
Overall, patients in the benralizumab group had the lowest incidence of AE despite having the smallest OCSE.

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Figure 1. Incidence of Acute Asthma Exacerbations per Patient

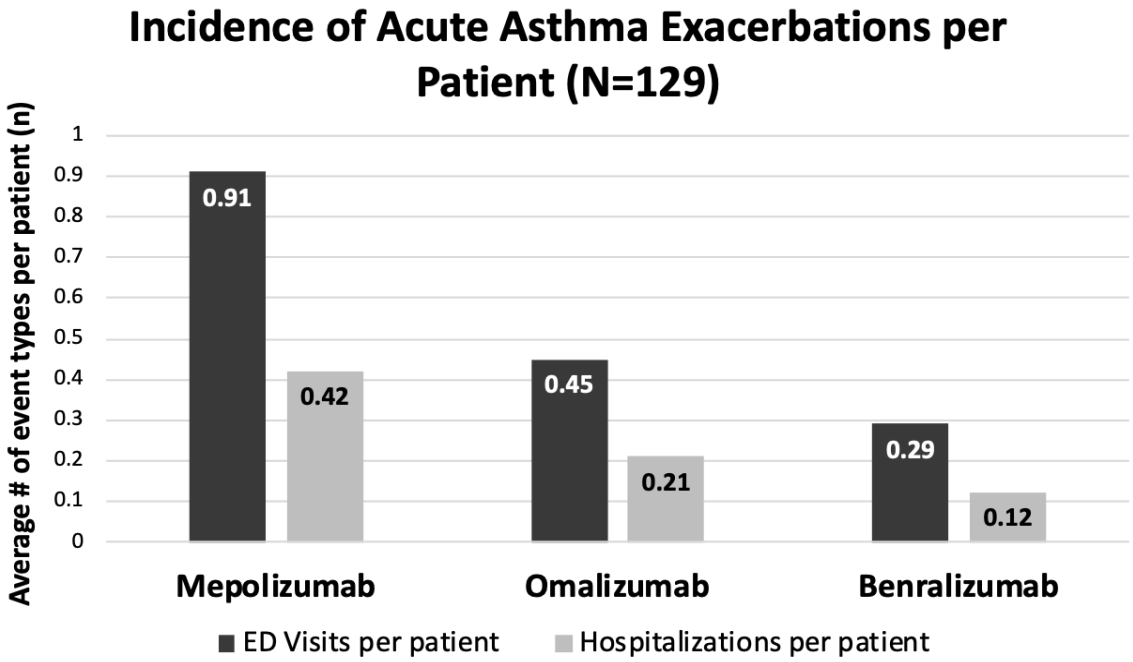

Figure 2. Oral Corticosteroid Sparing Effect