MSHP Pharmascript

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Third Quarter

What's Inside This Issue?

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Welcome Message from the President – 2018

The summer months provide an excellent opportunity to take some well-deserved time to celebrate successes and to take advantage of the backdrop of calming, warm summer weather to focus on planning for the months ahead. The leadership of MSHP has done exactly that as we recently held a strategic planning session to examine the work of the society.

Over the past year, MSHP has made significant progress on several fronts. One of the most active areas of focus has been on the role of the pharmacy technician. MSHP's task force looking at the practice of "tech-check-tech" has been very active this past year and was able to present their findings on this practice to the Maryland Board of Pharmacy who is actively considering how this practice might be implemented in the state of Maryland. Another task force focused on pharmacy technician training has worked to bring together key stakeholders throughout the state of Maryland for discussions at a state-wide Pharmacy Technician Consensus Conference which was held this past June. We expect to see ongoing progress and change in these areas as this coming year unfolds. We have also expanded our membership through the use of "institutional" memberships where we provide opportunities for hospitals to sponsor MSHP membership for all of their employees. MSHP continues to hold successful events for members, our largest being our fall and spring seminars where we saw record number of attendees this past year.

Looking forward as an organization we hope to build on the successes we saw over the past year and

continue our efforts in advancing the role of the pharmacy technician, broadening our reach throughout the state of Maryland, and providing our members with continuous opportunities for engagement.

We also hope to continue to leverage the broad range of expertise of MSHP members to provide guidance as a Society on the wide range of challenges we face in practice on a daily basis. From drug shortages to the opioid crisis, our members are coming up with innovative ways to tackle these issues at their institutions. We hope to enhance our efforts to share these ideas so all members can benefit and learn from each other when it comes to best practices in handling these difficult practice issues.

If you are looking for ways to engage with MSHP, in addition to attending MSHP events, getting involved in committee work is another excellent way to contribute and push forward the work of MSHP. Please review the Committee section of the website (http://www.mshp.org/committees/) for more information about each group and the contact information for committee leadership.

We not only welcome your participation in our committees and events, we would also love to hear from you directly with your thoughts and suggestions on the work of MSHP. Please reach out to me via email at ecpherson@jhmi.edu at any time.

We are looking forward to a great year ahead for MSHP and wish you a safe and relaxing summer!

Emily Pherson, PharmD, BCPS
President, Maryland Society of Health-System Pharmacy

Call for Speakers

The Maryland Society of Health-System Pharmacy (MSHP) is seeking pharmacists, pharmacy technicians, and other healthcare providers to provide timely, relevant, and high-quality presentations for our bi-annual professional development seminars.
Interested Pharmacists and Residents should follow the link below and submit the form!
APPLY HERE

Call for Editors

The editors of *Pharmascript* are seeking content reviewers for upcoming editions. Interested Pharmacists, Residents and Students should contact Vicki Leiman (victorialeiman@umm.edu) or Wesley Oliver (woliver@umm.edu). Reviewers should note specific areas of expertise or interest in their communications.

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Medical Cannabis & Maryland

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Since the establishment of the federal Controlled Substance Act of 1970, marijuana has been classified as a Schedule I substance. Drugs placed into this category have historically proven to have a high potential for abuse, no accepted medical use in treatment, or a lack of accepted safety while used under medical supervision. [1] Although federal law designates marijuana, also known as cannabis, as a Schedule I drug, twenty-nine states and Washington, DC have instituted legislation eliminating criminal penalties with regard to cannabis for medicinal purposes, including our own state of Maryland. Additionally, as time has passed medical experts have begun reviewing the therapeutics of medical cannabis and found evidence to support use for indications such as chronic pain. [2,3] This has led to healthcare organizations to support standardization of cannabis, advocate for regulatory changes to facilitate research, and encourage pharmacist participation in optimizing therapy when scientific data supports medical use.[4,5] As the legal landscape continues to evolve around the use, possession, and/or cultivation of marijuana for medicinal purposes, pharmacists should stay abreast on legislative requirements and consider the implications of medical cannabis on patient care and safety.

Who Can Receive Medical Cannabis?

With the increased prevalence and utilization of medical cannabis, it is crucial for pharmacists to collect and have access to information supporting indications. Currently, Maryland has thirty-four operating dispensaries. In 2013, the Maryland General Assembly created the Maryland Medical Cannabis Commission (MMCC) to develop policies, procedures, and regulations to implement programs that ensure medical cannabis is available to qualifying patients in a safe and effective manner. [5] According to the MMCC, providers may issue certification for, or recommend, medical cannabis use for patients with chronic or debilitating diseases/medical conditions whom: [6]

- Are in palliative care or hospice care
- Are afflicted by symptomology such as cachexia, anorexia, wasting syndrome, severe or chronic pain, severe nausea, seizures, severe or persistent muscle spasms, glaucoma, post-traumatic stress disorder
- Are diagnosed with a chronic medical condition which is severe and for which other treatments have been ineffective

Patients must be registered with the MMCC prior to receipt of provider certification for medical cannabis use. As of October 25, 2017, approximately 17,000 patients and 500 caregivers have registered with MMCC.[6]

Who Can Certify Patients Medical Cannabis?

According to the MMCC, “any provider with an active, unrestricted license in good standing and actively registered to prescribe controlled substances in Maryland” may recommend or certify qualifying patients to be treated with medical cannabis.[7] As of May 2018 providers include dentists, physicians, podiatrists, nurse midwives, and nurse practitioners; however, it does not include pharmacists. Nevertheless, pharmacist participation in furnishing cannabis and its various components is supported when scientific data supports the legitimate medicinal use of the products and delivery mechanisms and federal, state laws permit.[4]

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What is the Current Role of Pharmacists with Regard to Medical Cannabis?

As the medication experts, pharmacists are in a prime position to foster the safe and efficacious use of medical cannabis. Pharmacists should make a conscientious effort to become educated on the clinical and safety information, focusing on the drug interaction profile to optimize therapy, especially as this product is primarily used outpatient.[8] Cannabis contains over 60 types of cannabinoids, including tetrahydrocannabinol (THC), the psychoactive component, and cannabidiol (CBD), the non-psychoactive immune and neurohormone modulator. [8] While THC and CBD are primarily metabolized by CYP3A4; THC is also metabolized by CYP2C9 and CBD by CYP2C19. Additionally, different cannabis strains may contain various amounts of these cannabinoids. Though states may require labeling of the concentrations of cannabinoid components, a study performed in Colorado found discrepancies in edibles ranging from 5-95% between the actual and labeled THC content. [9]Cannabinoid content not only has the potential to affect therapeutics but also clinical efficacy of drug therapy. [8,10] Drug interactions that have been studied include: warfarin, alcohol, theophylline, indinavir, docetaxel, irinotecan, clobazam, benzodiazepines, and antifungals. [8,10] Another consideration is that cannabis products come in various formulations and can be administered via various routes which can affect onset of action or drug effect.[8] The most notable being the difference between inhaled and ingested products. [11] Pharmacists well versed on laws and regulations regarding medical cannabis, as well as therapeutics, will be equipped to take leadership roles in developing guidelines and policies concerning this patient population.

References:

1. United States Department of Justice. Title 21 Unites States Code (USC) Controlled Substance Act. Available: https://www.deadiversion.usdoj.gov/21cfr/21usc/812.htm. Accessed May 11, 2018.
2. Hoffmann DE, Weber E. Medical marijuana and the law. N Engl J Med. 2010;362(16):1453-7.
3. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA. 2015;313(24):2456-73.
4. American Pharmacists Association. 2014–2015 APhA Policy Committee Report: Role of the pharmacist in the care of patients using cannabis. https://www.pharmacist.com/sites/default/files/files/Role%20of%20the%20Pharmacist%20in%20the%20Care%20of%20Patients%20Using%20Cannabis%20.pdf. Accessed May 12, 2018
5. Borgelt, Laura M., and Kari L. Franson. “Considerations for Hospital Policies Regarding Medical Cannabis Use.” *Hospital Pharmacy* 52.2 (2017): 89–90.
6. Maryland Medical Cannabis Commission. Maryland Medical Cannabis Law. Title 13, Subtitle 33. Available: http://mmcc.maryland.gov/Documents/Subtitle%2033_Sept2015_Corrected.pdf. Accessed. May 11, 2018.
7. Maryland Medical Cannabis Commission. Provider FAQ. Available at: http://mmcc.maryland.gov/Pages/physicians_faq.aspx. Accessed May 11, 2018
8. Drug Topics. No Matter the Law, Pharmacists Need to Know About Cannabis. Available at: http://www.drugtopics.com/drug-topics/news/no-matter-law-pharmacists-need-know-about-cannabis. Accessed May 11, 2018.
9. Baca, R. “Tests show THC content in marijuana edibles is inconsistent”. *The Denver Post.* 2014, March 8. Available at: https://www.denverpost.com/2014/03/08/tests-show-thc-content-in-marijuana-edibles-is-inconsistent/. Accessed June 4, 2018.
10. Medical Cannabis: Adverse Effects and Drug Interactions. Government of The District of Columbia Department of Health. Available at:

https://doh.dc.gov/sites/default/files/dc/sites/doh/publication/attachments/Medical%20Cannabis%20Adverse%20Effects%20and%20Drug%20Interactions_0.pdf. Accessed May 17. 2018
11. Barrus DG, Capogrossi KL. Cates SC, et al. Tasty THC: Promises and Challenges of Cannabis Edibles. Methods report (RTI Press). 2016;2016: 10 3768/rtipress.2015.op.0035.1611

Evaluation of Albumin Use in Adult Medicine Patients

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Introduction: Albumin is commonly used in clinical practice for a variety of indications, some with more robust evidence than others. However, it is a limited resource that can add significant expense to a hospital stay when administered inappropriately. Globally, 40 – 90% of albumin use is off-label for indications not proven to be beneficial, including nutritional interventions and correcting hypoalbuminemia not associated with hypovolemia.[1] In non-critically ill patients, albumin has been shown to reduce mortality in cirrhosis patients with spontaneous bacterial peritonitis (SBP), receiving large volume paracentesis greater than five liters, or those with hepato-renal syndrome (HRS). Additionally, patients with refractory diuresis, not responding to furosemide 100 mg, may also benefit from albumin administration.

The University of Maryland Medical Center (UMMC) has developed guidelines for albumin use based on evidence based indications to assist healthcare providers in ordering albumin appropriately with regards to indication, product, dose and duration. For non-critically ill, adult medicine patients, albumin 25% is indicated for SBP (1.5 g/kg on day 1 and 1 g/kg on day 3), large volume paracentesis when >5 liters is removed (6-8 g/L removed), HRS (25 g every 6-8 hours for 2-3 days) and refractory diuresis (12.5 g every 6 hours for 24 hours with high dose furosemide).[2,3]

The primary objective of this study was to characterize the use of albumin for patients admitted to general medicine at UMMC with respect to indication, product, dose and duration. As a secondary objective, we compared the appropriateness of albumin orders based on UMMC guidelines before and after requiring providers to include an indication on the albumin order.

Methods: This was a retrospective, single center analysis evaluating adult patients who received at least one dose of albumin while admitted to a general medicine service at UMMC. Electronic medical records were reviewed during a six month period prior to and after requiring providers to include the albumin indication on the order (January 1, 2016 to June 30, 2016 and January 1, 2017 to June 30, 2017, respectively).

Data collection included patient demographics, baseline characteristics, albumin order details, and, if applicable, total volume removed during paracentesis. Appropriateness of albumin was determined by adherence to current UMMC guidelines. Total cost of the orders identified as inappropriate was also collected.

Data were analyzed using descriptive statistics for frequencies and ranges. To compare differences between pre and post intervention, t-test for continuous variables and chi-square test or Fisher's exact test for categorical variables were performed. Chi-square test was used for comparison in primary outcome (followed guidelines, y/n) between pre and post-intervention. Odds ratio and 95% confidence intervals (CI) were

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calculated for measures of association between followed guidelines and pre/post intervention. For comparison in hospital cost pre- to post- intervention, Wilcoxon rank-sum test was performed. Analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC).

Results: A total of 69 albumin orders were identified from a generated report of albumin that was dispensed. Thirty-seven orders (133 doses) were included pre-intervention and 32 orders were included post-intervention (157 doses). Fourteen patients had albumin orders for multiple indications during their hospital stay. The majority of patients were Caucasian with a mean age of 58 years and a primary liver disease etiology of either alcoholic cirrhosis, nonalcoholic steatohepatitis (NASH) or hepatitis. There were no significant differences in baseline demographics between the 2016 pre- and 2017 post-intervention groups (Table 1). Paracentesis, HRS, and SBP were the most common indications listed on the albumin orders (Table 2).

Table 1. Distribution of characteristics across pre and post intervention

Characteristics	Intervention		p value
	2016 (n=37)	2017 (n=32)	
Age, years	56.9(8.2)	58.9(12.6)	0.52
Gender			
Male	15(48.4)	17(70.8)	0.09
Actual body weight, kg	87.5(28.2)	89.9(26.4)	0.75
Ethnicity			0.35
White	19(61.3)	15(62.5)	
Black	9(29.0)	9(37.5)	
Hispanic	3(9.7)	0(0)	
Baseline albumin	2.6(0.5)	2.6(0.5)	0.84
Serum creatinine	2.2(1.6)	2.7(1.9)	0.28
Etiology of liver disease			0.59
Alcoholic cirrhosis	7(22.6)	3(12.5)	
Nonalcoholic steatohepatitis	4(12.9)	4(16.7)	
Hepatitis	13(41.9)	8(33.3)	
Cryptogenic	3(9.7)	2(8.3)	
No liver disease	2(6.5)	2(8.3)	
Primary biliary cirrhosis	1(3.2)	0(0)	
Cholangiocarcinoma	1(3.2)	0(0)	
Alcohol and Hepatitis cirrhosis	0(0)	2(8.3)	
Primary sclerosing cholangitis	0(0)	1(4.2)	
Acute liver failure	0(0)	1(4.2)	
Cirrhosis secondary to iron overload	0(0)	1(4.2)	
Volume removed, L			0.22
<5	10(76.9)	5(50.0)	
≥5	3(23.1)	5(50.0)	

Note: data were presented as mean (SD) for continuous and number (column %) for categorical variables.

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Table 2. Comparison of indication between pre and post intervention

Outcome	Intervention (n, %)			
Indication	2016 (n=37)	2017 (n=32)	Total	p value
SBP[a]	10(27.0)	4(12.5)	14(20.3)	0.36
Volume/albumin repletion	0(0)	3(9.4)	3(4.4)	
Paracentesis	11(29.7)	10(31.3)	21(30.4)	
Refractory diuresis	1(2.7)	1(3.1)	2(2.9)	
HRS[b]	13(35.1)	12(37.5)	25(36.2)	
Unknown	2(5.4)	1(3.1)	3(4.4)	
Nonhemorrhagic shock	0(0)	1(3.1)	1(1.5)	

[a] spontaneous bacterial peritonitis; [b] hepato-renal syndrome

Overall, only 40.6% of albumin orders were appropriate per UMMC guidelines [35.1% pre-intervention and 46.9% post-intervention; 95% CI 1.6 (0.6, 4.3), p=0.32]. The most common reasons for nonadherence to the UMMC guidelines in the pre-intervention group was indication (41.7%), followed by dose (25%) and frequency (16.7%). In the post-intervention group, indication (42.9%), product selected (28.6%), and frequency (14.3%) were the most common reasons for nonadherence to UMMC guidelines (Table 3). In 2016, 56.8% of albumin orders included an indication. After requiring indication on albumin orders, 90.6% of orders included an indication in 2017 (p=0.0025). There were no significant differences in the hospital costs for inappropriate albumin orders (p=0.34).

Table 3. Comparison of reasons between pre and post intervention if not followed guidelines

Outcome	Intervention			
Reason	2016 (n=24)	2017 (n=14)	Total	p value
Indication	10(41.7)	6(42.9)	16(42.1)	0.042
Product[a]	0(0)	4(28.6)	4(10.5)	
Dose	6(25.0)	1(7.1)	7(18.4)	
Frequency	4(16.7)	2(14.3)	6(15.8)	
Duration	0(0)	1(7.1)	1(2.6)	
Indication and product[a]	2(8.3)	0(0)	2(5.3)	
Dose and frequency	2(8.3)	0(0)	2(5.3)	

[a]Albumin 5%

Discussion

While albumin is of great benefit when used appropriately, it is a limited resource that can add significant expense to the patient and to the hospital. Based on the results of this study, the majority of albumin orders are inappropriate per UMMC guidelines, specifically with regards to dose, frequency, and product selected.

Therapeutic paracentesis is a first line treatment for patients with tense and refractory ascites, but is associated with post-paracentesis circulatory dysfunction (PCD). This may lead to recurrent ascites, HRS, hyponatremia and increased mortality.[4] Administration of albumin has been shown to reduce PCD by 61%, hyponatremia by 80%, and mortality by 36% when volume removed exceeds 5L.[5] In our study 65% (n=15) of

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patients who received paracentesis had less than 5L removed. However, to date, there is a lack of evidence to support albumin infusion following paracentesis of <5L. Therefore, post-paracentesis albumin may not be necessary in these patients to reduce adverse effects and improve outcomes.[3]

SBP is a severe complication in patients with cirrhosis and ascites, resulting in increased mortality.[3] Development of renal impairment despite non-nephrotoxic antibiotics in these patients is thought to be secondary to reduced blood volume in the setting of infection.[3,6] Sort et al demonstrated significantly reduced renal impairment and mortality when albumin was given for volume expansion (on day 1 and day 3) in addition to cefotaxime compared to patients who only received cefotaxime (renal impairment: 10% vs. 33%; p=0.002; mortality: 10% vs. 29%; p=0.01, respectively).[7] In our study, inappropriate albumin orders for SBP were primarily due to incorrect dose and frequency (i.e. only day 1 dose given or given multiple times a day). Although alternative dosing is not supported by the literature. There is an ongoing randomized controlled trial to determine if low dose albumin on day 1 (1 g/kg) and day 3 (0.5 g/kg) leads to similar outcomes.[8]

In patients with cirrhosis and ascites, about 20% will develop HRS after 1 year and 40% at 5 years.[3,9] HRS may develop spontaneously or following a precipitating event (infection, gastrointestinal hemorrhage or paracentesis). In addition to poor renal circulation, other factors, including splanchnic vasodilation, decreased cardiac output, increased intrahepatic pressure and increased stimulation of the renin-angiotensin aldosterone system, lead to renal failure. Current guidelines recommend dosing albumin 1 g/kg/day (max 100 g/day) for HRS.[3] Treatment of HRS per UMMC guidelines is albumin 25 g every 6-8 hours for 2-3 days.[2] In our study, duration (administered for <48 hours) and frequency of albumin were the most common reasons orders were deemed inappropriate for patients with HRS.

As expected, there was a significant increase in the inclusion of albumin indication on orders after this became mandatory. However, inclusion of indication on orders did not significantly improve adherence to UMMC guidelines nor decrease hospital and patient costs associated with inappropriate albumin orders.

Limitations to this study include the retrospective study design and the small sample size. Subjective information with regards to liver disease etiology and rationale for albumin was not always documented in the patient's medical records.

Following the conclusion of this study, order panels consisting of the correct albumin product, dose, and frequency per indication have been marked and strategically placed at the top of the albumin order preference list in the electronic medical record. Furthermore, prescribers and pharmacist verifying orders, may benefit from education regarding evidence based indications for albumin in medicine patients, and the availability of guidelines and order sets to assist with ordering. It is clear that additional interventions are necessary to improve the appropriate use of albumin in medicine patients.

References

1. Caraceni P, Domenicali M, Tovoli A, Napoli L, et al. Clinical indications for albumin use: still a controversial issue. *Eur J Intern Med* 2013; 24:721-728.
2. University of Maryland Medical Center Guidelines for Use of Albumin in Adult Patients. Last updated July 2015.
3. AASLD. Management of adult patients with ascites due to cirrhosis: update 2012. https://www.aasld.org/sites/default/files/guideline_documents/141020_Guideline_Ascites_4UFb_2015.pdf

4. Gines P, Tito Llucia, Arroyo V, Planas Ramon et al. Randomized comparative study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. *Gastroenterology* 1988; 94: 1493-1502.
5. Bernardi M, Caraceni P, Navickis RJ and Wilkes MM. Albumin infusion in patients undergoing large-volume paracentesis: a meta-analysis of randomized trials. *Hepatology* 2012; 55: 1172-1181.
6. Narula N, Tsoi K, and Marshall JK. Should albumin be used in all patients with spontaneous bacterial peritonitis? *Can J Gastroenterol* 2011; 25(7):373-376.
7. Sort P, Navasa M, Arroyo V, Aldeguer X, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *NEJM* 1999; 341(6): 403-409.
8. Araujo A, Rossi G, Lopes A, Ness S, et al. Effect of intravenous albumin (standard vs dose reduced regimen) on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis: A double blind randomized clinical trial – interim analysis of the alternate study. The Liver Meeting; Boston, Massachusetts. October 2009.
9. Lenz K, Buder R, Kapun L, and Voglmayr M. Treatment and management of ascites and hepatorenal syndrome: an update. *Therap Adv Gastroenterol* 2016; 8(2):83-100.

Use of N-Acetylcysteine for Gastric Lactobezoars in a Three Month Old

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Introduction: Gastric lactobezoars (GLB) are a result of the inability to digest milk and mucous. Risk factors for GLBs include both formula specific or endogenous sources. Formulas with high casein concentrations, medium triglyceride oils, or high caloric density can increase the risk of GLBs. N-acetylcysteine (NAC) is a mucolytic agent used to clear secretions and is hypothesized to be effective in the treatment of GLBs due to the cleavage of disulfide bonds in mucoproteins.

Case Report: The patient was a 1 month old male (4.5 kg ex 40 week old) who was transferred to the pediatrics floor for continued poor oral feeding after a one month NICU stay. His hospital stay was complicated by respiratory failure secondary to meconium aspiration syndrome with pulmonary hypertension requiring nitric oxide support, suspected sepsis, and completion of cooling protocol. An upper GI series identified a persistent filling defect in the distal body which was suggestive of a milk bezoar. Pharmacy was consulted to review the use of NAC for the management of the patient's milk bezoar. A dose of 45mg (10mg/kg) of 10% NAC diluted in 50mL of normal saline was recommended every 6 hours was recommended via NG tube followed by clamping of the NG tube for 2 hours. Aspirating the stomach contents at 3 hours and 6 house post NAC administration was discussed. A total of 4 doses were administered every 6 hours with total aspirate volumes of 8mL, 5mL, 5mL, and less than 1 mL. Treatment was stopped when aspirates were a clear mucus consistency.

Summary: This is a patient case where 10 mg/kg/dose of 10% NAC in 50mL NS given every 6 hours for at least 4 doses was successful in the treatment of gastric lactobezoar

Deadlines for Pharmascript Submission

Submit articles for publication in the Fall edition of the Pharmascript by September 15th, 2018
Submit articles for publication in the Winter edition of Pharmascript by November 15th, 2018