An award-winning, bimonthly, electronic, student-operated newsletter publication by the St. John’s University College of Pharmacy and Health Sciences Rho Chi Beta Delta chapter

THE RHO Chi SOCIETY

Chapter Project Proposal

✦ ♦ AWARD ✦

RHO CHI BETA DELTA CHAPTER FOR THE Rho Chi Post
2014

THE RHO Chi SOCIETY

Chapter Achievement

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recognizing the full scope of chapter activities as documented in the Annual Report

RHO CHI BETA DELTA CHAPTER
2014
A MESSAGE FROM OUR EDITOR-IN-CHEIF

“It is with great pride that I share with you our latest publication. These 5 ensuing articles are a culmination of the hard work and dedication exemplified by all 7 authors, as well as the entire editorial team, over these past few months. These authors have made the voluntary effort to advance the pharmacy profession through the dissemination of scholarly knowledge, and their efforts should be commended. I strongly urge all readers to consider getting involved with our newsletter, whether that be as a writer or an editor. We are always looking to work with talented and motivated individuals. Below are a few frequently asked questions we receive from students, faculty, and preceptors.

Have a happy, safe, and healthy New Year!”

Frequently Asked Questions:

Q: How often does the Rho Chi Post accept draft articles?
A: The Rho Chi Post accepts articles on a daily basis. Whenever you have a draft ready, feel free to upload for our review!

Q: Does the Rho Chi Post determine the article topics or can students choose?
A: The Rho Chi Post does not dictate article topics. Students are free to choose an article topic of their choice. Should a student need help selecting a topic, we would be more than happy to help pitch ideas.

Q: What happens after I upload my draft article on the Rho Chi Post website?
A: Our Editor-In-Chief (EIC) will either edit the article directly, or assign the article to a staff editor, who will evaluate it. If any revisions by the author are needed, the editor will make comments/suggestions and upload the article back to the portal. The author will get notified via email, and should log back into the portal to download the edited article. Once the author makes the necessary revisions, they should upload the article back to the portal, where it will be re-evaluated. Once the staff editor deems the article ready for final review, our EIC will evaluate the article. If further revisions are needed, the EIC will notify the author. If no revisions are needed, the article will be accepted for publication, and will be reviewed by faculty advisor Elsen C. Jacob PharmD, MS, BCPS, BCGP as the final step.

Q: Is there a deadline for authors to send in their revisions?
A: The length of the editing process varies depending on the article, so it is in the authors best interest to submit their revisions as soon as possible. Articles are NOT published in the order of when the draft was first submitted. Articles are published based on whether they have been completely edited, revised, and are deemed ready for publication by both the EIC and faculty advisor.

If you have any other questions or encounter any issues, please email: RhoChiPost@gmail.com
THE RHO CHI SOCIETY

The Rho Chi Society encourages and recognizes excellence in intellectual achievement and advocates critical inquiry in all aspects of Pharmacy.

The Society further encourages high standards of conduct and character and fosters fellowship among its members.

The Society seeks universal recognition of its members as lifelong intellectual leaders in Pharmacy, and as a community of scholars, to instill the desire to pursue intellectual excellence and critical inquiry to advance the profession.

Have something interesting to say?
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Remember, Rho Chi Honor Society membership is NOT a requirement for submitting articles to the Rho Chi Post!

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**QUOTE OF THE MONTH**

Science is telling us that we can do phenomenal things if we put our minds and our resources to it.

— Anthony S. Fauci —

Back Cover
Combating Chronic Diseases with a Plant-Based Diet

By: Ashely Dao, PharmD Candidate c/o 2024

In early 2021, about 6 in 10 American adults had a chronic disease. Chronic diseases are the leading cause of death and disability in the United States with 1 in 3 deaths caused by cardiovascular diseases (CVD).¹ The Coronavirus disease 2019 (COVID-19) pandemic has emphasized the impact of chronic diseases, considering that individuals with chronic diseases are at an increased risk of developing a severe illness from COVID-19. Chronic diseases are not only a public health burden, but they are also an economic problem. Ninety percent ($3.43 trillion) of the nation’s annual health care costs are related to chronic and mental health conditions.¹ It is highly imperative now more than ever to prioritize chronic disease prevention and care. Pharmacists oftentimes encounter patients who suffer from one or more chronic diseases, many of whom often take various medications to control them. When patients are diagnosed with hypertension, pharmacists counsel them on the benefits of smoking cessation, reduced caffeine intake, and increased exercise as preventative measures to control their blood pressure and prevent the risk of developing other diseases. Have we ever considered recommending a plant-based diet? Adopting a plant-based diet is a preventative measure pharmacists can also suggest, as it not only prevents the progression of chronic diseases, but it can also reverse them.

A healthy plant-based diet is defined as a diet rich in plant foods (whole grains, fruits, vegetables, and nuts) and low in animal products (such as dairy, red meat, poultry, and fish).² Contrarily, a less healthy plant-based diet consists of refined grains, potatoes, sugar-sweetened beverages, and a high frequency of animal products.² In this article, the terms “plant-based diet” and “healthy plant-based diet” will be used interchangeably. A healthy plant-based diet has been linked with a decreased risk for CVD, type II diabetes (T2D), and obesity.² 3, 4

A meta-analysis, conducted by Satija, et al. demonstrated that a plant-based diet provides cardiovascular benefits. Vegetarians had a 24% (95% Confidence Interval [CI]: 6%–38%) lower rate of coronary heart diseases compared to nonvegetarians and a 22% lower stroke mortality rate among men (95% CI: 12%–31%). As a side note, nonvegetarians had a diet containing meat or fish.² The meta-analysis also showed that compared to a nonvegetarian diet, a vegetarian diet significantly lowered blood concentrations of total, LDL, HDL, and non-HDL cholesterol, as well as lowered blood pressure, enhanced weight loss, and improved glycemic control.² High levels of LDL cholesterol are known to increase the risk of heart disease and stroke.

A 16-week randomized trial conducted by Kahleova et al. found that a plant-based diet reduced body weight and insulin resistance. This study looked at otherwise healthy overweight or obese men and women with a BMI between 28 and 40 kg/m² and assigned them to a vegan or control group in a 1:1 ratio. The participants in the control group were instructed to maintain their current diet while the vegan group was told to adopt a low-fat vegan diet. After 16-weeks there was a significant reduction in BMI (P < 0.00), weight (P < 0.001), body fat (P < 0.001), and insulin resistance (P < 0.004) in the vegan group. A decrease in animal protein intake decreased fat mass by 1.45 kg, while an increased intake of plant protein decreased fat mass by 0.88 kg.³

An analysis of three cohort studies by Satija et al. demonstrated that a plant-based diet lowered the risk of T2D. Healthy plant-based foods were associated with a 34% reduction in the risk of T2D, with a lowered risk seen even with a modest lowering in animal food intake. Individuals with or without T2D also saw a positive impact on their body weight, blood pressure, lipid profile, and insulin sensitivity after eating a plant-based diet.⁴

The ability of a healthy plant-based diet to decrease the risk of CVD, T2D, and obesity can be linked in part to its antioxidant properties. Many healthy plant-based foods are rich in polyphenols (PPs), which have antioxidant effects and may also contribute to a reduction of risk in cardiovascular diseases. Polyphenols found in food are comprised of four classes: flavonoids, ligands, phenolic acids, and stilbenes. The flavonoid class of PPs, in particular, have been found to reduce the risk of developing cardiovascular diseases. Foods and beverages rich in flavonoids (green tea, blueberry, dark chocolate, capers)⁶ increased the availability of nitric oxide (NO) and endothelium-derived hyperpolarizing factor (EDHF) to maintain vascular homeostasis and prevent endothelial dysfunction. CVD models also demonstrated improved endothelial functions after consuming flavonoid-rich foods. In a review of 12 cohort studies, an increased intake of flavonoids resulted in a decrease in age-

adjusted coronary heart disease (CHD) mortality. Overall, PPs were found to decrease the inflammatory activity of reactive oxygen species (ROS) and reduce the production of potent LDL oxidant peroxynitrite which is responsible for triggering endothelial injury and inflammation. Additionally, a healthy plant-based diet is correlated with high unsaturated fatty acids and low saturated fats, which have also been shown to have anti-inflammatory effects.

Animal foods have been associated with an increased risk of CVD due to the abundance of heme iron. Processed meats also consist of sodium, nitrites, and nitrates that may increase blood pressure, impair insulin response, and lead to endothelial dysfunction. Animal proteins contain essential amino acids such as threonine, leucine, lysine, methionine, and tyrosine. While protein is a staple in our diets, a high intake of branched-chain amino acids (BCAA) is correlated with an increase in inflammation and CVD by triggering ROS production. Plant protein consists of non-essential amino acids. When individuals swap animal protein for plant proteins there is a decrease in leucine intake which was associated with positive changes in BMI and energy intake. Plant protein intake also decreased histidine intake which was associated with decreased insulin resistance.

Utilizing this information, pharmacists and other health care providers can better assist patients by encouraging them to implement a plant-based diet to prevent the development of chronic diseases or at the very least minimize their progression. Transitioning to a plant-based diet can be an intimidating process for many, but with the proper guidance and encouragement, it can be made simpler and less stressful. A healthy plant-based diet can be customizable to each patient based on accessibility, affordability, and personal preference. This can lead to increased adherence with a consequent decrease in associated health care costs. For patients that are not yet ready to make such a big change, they can start by gradually increasing their intake of plant-based foods before reducing their intake of animal foods. For example, patients can start by adding an additional serving of fruits and vegetables to their breakfast, then gradually replacing the meat with healthy plant-based breakfast. Once they are comfortable with one meal change, they can apply the same strategy to their other meals.

Some hospitals are already implementing a healthy plant-based diet into their treatment plans, such as Montefiore’s Cardiac Wellness Program and UC Davis’s Integrative Medicine. Montefiore’s Cardiac Wellness program is working with patients who have been diagnosed with chronic diseases and are implementing a healthy plant-based diet with the aim to lower their cholesterol and blood pressure, and even reverse their T2D and CVD. Patients enrolled in the program are educated about the impact of a healthy plant-based diet and are taught how to prepare budget-friendly plant-based meals. UC Davis’s Integrative Medicine also has a free “Good Food is Good Medicine” blog accessible on their website; it consists of recipes and guides such as video tutorials on how to make tofu tacos as well as tips on how to make a healthy meal plan on a budget.

While this transition is highly beneficial, every patient does not have access to resources like Montefiore’s Cardiac Wellness program. Data shows that 10.5% of US households were food insecure at some point in the 2020 calendar year, and the pandemic has only exacerbated these numbers. Pharmacists are the most accessible health care professionals and as such should understand the scientific benefits of a plant-based diet and how a plant-based diet can be implemented in their communities. By working with community leaders and nutritionists, pharmacists can make healthy plant-based foods more accessible and teach communities how to prepare budget-friendly meals, just like Montefiore and UC Davis. Every patient deserves the opportunity to utilize a healthy plant-based diet to prevent or even reverse chronic diseases, and pharmacists have the ability to ensure that this happens.
Combating Chronic Diseases with a Plant-Based Diet

By: Ashely Dao, PharmD Candidate c/o 2024

References:


Depression is a terrible beast of an illness to battle with, and there are nearly 14 million individuals at any given moment fighting it. Only around 50% of patients struggling with depression will get some form of treatment. Sixty to seventy percent of patients who do get treatment will show an adequate response, with 10-30% of patients showing an inadequate response. The latter group of patients are said to have treatment resistant depression. This is more accurately defined as experiencing a poor or unsatisfactory response to two trials of two different classes of antidepressants at optimal dosing and duration. This failure in treatment, just like that seen with untreated depression, can greatly affect the patient and lead to functional impairment, poor quality of life, suicide ideation and attempts, and self-injurious behavior. For this reason, any “weapons”, so to speak, that we can develop and use against treatment resistant depression would be a great victory.

Treatment resistant depression is managed by either changing, increasing, or adding antidepressant regimens. Currently, there are few options targeted for treatment resistant depression. Ketamine and esketamine, schedule III analgesics, are two such examples. Ketamine has been shown to be effective, off-label, in treating severe resistant depression. It is administered initially as a single intravenous injection of 0.5 mg/kg over 40 minutes or can also be given as a course of repeated infusions administered 2 to 3 times per week for a total of 4 to 8 infusions. It should not be used in patients with substance use disorders, due to its high risk for abuse. Ketamine can additionally cause profound sedation and respiratory depression. Esketamine (Spravato®) has Food and Drug Administration (FDA) approval for treatment for resistant depression, and is given as a series of intranasal doses. More specifically, it is given as an adjunct to an oral antidepressant and is given as a loading dose of 56 mg intranasally on day 1 followed by 56 or 84 mg twice weekly for 4 weeks. As maintenance therapy, it is dosed as 56 or 84 mg once weekly during weeks 5 through 8, then 56 or 84 mg every 2 weeks or once weekly starting week 9 and onward. Esketamine is contraindicated in patients with a history of intracerebral hemorrhages or aneurysmal vascular disease. Like ketamine, esketamine has potential for abuse and respiratory depression. It is important to note that because of the above-mentioned safety concerns, patients cannot simply pick up a month supply of this medication from their neighborhood pharmacy. Esketamine is subject to REMS program requirements, and must be administered in a physician’s office by a healthcare provider enrolled in the REMS program. After receiving a dose, the patient must be monitored for 2 hours for emergence of adverse effects.

Recent studies have showed the potential for another treatment option for treatment resistant depression. AXS-05 is an investigational drug combination of dextromethorphan and bupropion, developed by Axsome Therapeutics. Dextromethorphan acts as an NMDA receptor antagonist, an ionotropic glutamate receptor, and a sigma-1 receptor agonist. Bupropion, which is a norepinephrine and dopamine reuptake inhibitor, serves primarily to increase the bioavailability of dextromethorphan. The MERIT (Mechanistic Evaluation of Response in TRD) trial was a randomized, double-blind, placebo-controlled multicenter study in the United States. This study included 44 adults recruited from a long-term open label phase 3 trial for AXS-05, who were stable for at least 12 months after treatment and were randomly assigned to a placebo group or the AXS-05 group (45 mg dextromethorphan/105 mg bupropion twice daily). Stable remission was defined as 2 or more consecutive Montgomery-Åsberg Depression Rating Scale (MADRS) scores of ≤12, separated by at least 4 weeks. The participants were tracked for at least 26 weeks or until a relapse of symptoms occurred.

AXS-05 met its primary endpoint of significantly delaying time to depression relapse by up to at least 6 months (p = 0.002), with no relapses observed over at least 6 months of double-blind treatment. AXS-05 also met its secondary endpoint of preventing depression relapses (0.0% of AXS-05 patients, 36.4% of patients switched from AXS-05 to placebo, p=0.004). Furthermore, the medication was well tolerated, with no treatment related adverse events recorded in more than one participant in the AXS-05 group, according to the company. One patient had experienced gout and bacteremia, but this was deemed unrelated to the study medication. Currently, AXS-05 has breakthrough therapy designation for the treatment of major depression disorder. This is a process created to expedite the development of medications that are intended to treat serious conditions, and is based on preliminary clinical evidence that
shows substantial benefit over currently available options. Based on these positive results, Axsome Therapeutics has submitted a New Drug Application (NDA) to the FDA. Despite all this positive news, according to Axsome, the FDA has found "deficiencies that preclude labeling discussions at this time." The FDA informed Axsome of "two deficiencies related to analytical methods in the Chemistry, Manufacturing, and Controls (CMC) section of the NDA". The CEO of Axsome, Herriot Tabuteau, MD, has noted that this may lead to a delay in the potential approval of AXS-05. While it may take some time for all the details to be worked out, AXS-05 seems to be a promising potential addition to the armory of medications for treatment resistant depression.

References:
Aspirin belongs to a class of medications called nonsteroidal anti-inflammatory drugs (NSAIDS). Known by many for its analgesic and anti-inflammatory properties, as well as its association with gastrointestinal (GI) bleeding, aspirin plays an essential role in stroke prevention. As such, it has a crucial role in the lives of many living with cardiovascular conditions. As of October 2021, however, there has been a change in guidance regarding its use for prophylaxis.

The leading cause of death in the United States is heart disease. Approximately 659,000 people die annually from cardiovascular events including heart attacks, stroke, and coronary artery disease. Heart disease is an umbrella term that refers to several types of heart conditions including but not limited to arrhythmias and coronary artery disease, which affect blood flow to the heart. These conditions can increase the risk of a heart attack or stroke. Other risk factors for heart disease include high blood pressure, high cholesterol, diabetes, as well as lifestyle habits (unhealthy diet and physical inactivity).

Aspirin is an irreversible cyclo-oxygenase (COX)-1 and COX-2 enzyme inhibitor. Unlike other NSAIDS, aspirin has a higher propensity for the COX-1 variant at a dose of <100mg/day which leads to decreased production of thromboxane A2. For reference, thromboxane is a type of eicosanoid similar to prostaglandins, that promotes platelet aggregation and vasoconstriction, resulting in clotting activity. COX-1 is also an enzyme responsible for producing some prostaglandins which are associated with GI protection. The COX-2 activity remains intact at low doses of aspirin, which still allows prostaglandin I2 to be produced. Prostaglandin I2 acts as a vasodilator and platelet inhibitor which aids in the anticoagulation properties. By decreasing thromboxane and continuing prostaglandin I2 production, aspirin can reduce thrombosis and prevent cardiovascular events. However, in doing so, aspirin can also alter the GI mucosa protection through its inhibition on the COX-1 enzyme. This results in reduced production of protective GI prostaglandins, which predisposes patients to GI bleed.

In 2016, the United States Preventive Services Task Force (USPSTF) announced a universal recommendation in support of initiating aspirin for the first time in high-risk patients 50-59 years old, as long as their risk of bleeding was low. Risk is based on the score calculated using the atherosclerotic cardiovascular disease (ASCVD) Risk Calculator, which measures the patient’s chances of having a cardiovascular event in the next 10 years. High risk (ASCVD score > 10%) adults 60 and older were recommended to consult their doctors prior to making a decision. However, as of October 2021, the USPSTF has retreated from their recommendation and is strongly discouraging anyone 60 years of age and older from starting a low-dose aspirin regimen, citing concerns of age-related heightened risk for life-threatening bleeding. High risk adults (>10%), between ages 40 to 59 years old, are now recommended to talk with their doctors and make a personal, individualized choice on whether to initiate a low-dose aspirin daily regimen.

This change in aspirin recommendations comes years after advice against its general use from several other medical organizations and federal agencies. In 2014, the FDA conducted a review of aspirin that concluded in discouraging its use for primary prevention of heart disease, noting the side effects related to bleeding. The FDA stated, “there are serious risks associated with the use of aspirin, including increased risk of bleeding in the stomach and brain, in situations where the benefit of aspirin for primary prevention has not been established”. In 2019, the American College of Cardiology and American Heart Association came together to narrowly recommend that low-dose aspirin might be considered for primary prevention of ASCVD in select high risk adults aged 40-70 years who are not at increased bleeding risk. They advised against the use of low-dose aspirin in patients >70 years old for primary prevention of ASCVD, with the goal to prevent further increased risk of bleeding.

The call for change in recommendation of aspirin comes from mounting evidence in support of non-superiority. One such example is the Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE) trial. This was a randomized, double-blind, multicentered, placebo-controlled study of more than 12,000 participants. The study population included men aged ≥55 years and women aged ≥60 years with a 10-year risk of major adverse cardiovascular events (MACE) who were randomized to take 100mg of Aspirin (81-100mg is considered low dose) or a placebo, in addition to antihypertensives and statins, for a period of 5 years. Over a median 60-month follow-up, there was no significant difference in efficacy between both groups in
preventing MACE, with a recorded hazard ratio (HR) of 0.96 and a 95% confidence interval (CI) of 0.81–1.13 (p = 0.604). Similarly, the incidence of mortality rates were not significantly different. With respect to safety, GI bleeding events were more frequent in the aspirin groups than in the placebo groups (HR = 2.11, 95% CI = 1.36–3.28; p<0.001). The overall net balance of benefit to harm is non-superior, which is why the USPSTF has decided to revise their previous recommendations.

As pharmacists and aspiring clinicians, it is imperative that we stay abreast of these recommendation updates, so we can continue to provide the best care for our patients. Fortunately, aspirin is not the only therapeutic option for preventing heart disease. Patients should, as always, be encouraged to maintain a healthy diet, engage in physical activity where possible, and adhere to their medications regimens so they can manage any comorbidities (hypertension, hyperlipidemia, etc).

References:
An Overview of Ketamine Cystitis

By: Pallak Sharma, PharmD Candidate c/o 2022 and Mia Cord-Cruz, PharmD Candidate c/o 2022

Ketamine (Ketalar®) is currently approved by the Food and Drug Administration (FDA) for use as a general anesthetic, with additional indications listed within its package insert. Ketamine is a highly abused “street drug”, especially in China. To demonstrate, in Hong Kong it has remained atop the list for most commonly abused psychotropic drugs since 2001. Between the years 2004 and 2013, ketamine was the most abused psychotropic drug with a peak of over 5000 abusers in 2009, according to the Hong Kong Central Registry of Drug Abuse Sixty-third Report. A small-scale survey conducted by a psychotropic substance rehabilitation center in Hong Kong reported that lower urinary tract symptoms (LUTS) were experienced in approximately 30% of ketamine abusers. Prior to these small-scale surveys, cystitis induced from ketamine was a less commonly known adverse event, being that most patients who abuse ketamine also abuse other substances, and may not seek medical care until severe symptoms are present.

The onset of ketamine cystitis results from ketamine abuse and it is rarely associated with the medically prescribed use of ketamine. The onset of LUTS can occur within a few days to a few years after ketamine use, and it is unclear if this is a dose-dependent adverse event. Researchers from Hong Kong have concluded that the exact prevalence of ketamine cystitis is difficult to quantify being that most patients who abuse ketamine allow symptoms to become more severe before seeking care.

Ketamine is produced as a racemic mixture of the (R) and (S) enantiomers. A pharmacologic review explains that the (S) enantiomer of ketamine (esketamine) is more potent than the (R) enantiomer. When ketamine is used as a street drug, it is generally crushed in order to snort the drug for faster onset of its effects. According to studies conducted on the ketamine metabolites, (S)-ketamine contributes to illusions and alterations in hearing, vision, and proprioception whereas (R)-ketamine experienced in approximately 30% of ketamine abusers. (S) enantiomer of ketamine (esketamine) is more potent than the (R) enantiomer, especially, caused acute psychotic reactions whereas the (R)-enantiomer did not. When ketamine is abused, the most common route of administration is nasal insufflation. This route provides an onset of feeling “high” ranging between 5 and 10 minutes and lasting between 40 and 75 minutes. It is reported that ketamine induces a highly dissociative experience marked by an altered state of consciousness and sensory detachment at peak levels of intake. Some users describe this as being comparable to a near-death experience.

Racemic ketamine [(R,S)-KET] is initially metabolized via nitrogen demethylation to norketamine [(R,S)-norKET], primarily by enzymes CYP2B6 and CYP3A4. Norketamine can then be further metabolized to form dehydronorketamine (DHNK) or the hydroxynorketamines (HNKs). Another metabolic pathway of ketamine is the direct hydroxylation of ketamine to 6-hydroxyketamine (HK). Approximately 80% of ketamine is excreted as the glucuronic acid-labile conjugates of HK and HNK which are eliminated in urine and bile.

The exact pathophysiology of ketamine cystitis is unknown, however, there are four proposed mechanisms that attempt to explain the urinary tract damage. These mechanisms were determined through retrospective analysis of 59 patients who abused ketamine, who were referred to the urology units of Princess Margaret and Tuen Mun Hospital, located in Hong Kong, from March 2000 to December 2007. The clinical presentations, pelvic pain and urgency/frequency scores, video-urodynamic studies, cystoscopy and radiological findings, and histological features of bladder biopsies of these 59 patients were gathered to propose these mechanisms.

The first proposed mechanism involves the direct effect of high concentrations of ketamine or its metabolites on bladder interstitial tissues. This may result in chronic submucosal inflammation. The inflammation could cause severe dysuria and diminished bladder capacity via submucosal edema, vascular ectasia, fibrosis, detrusor muscle inflammation, and fibrosis. Individuals who abuse chronic high doses of ketamine may even exhibit papillary necrosis due to irreversible toxicity effects on the papillary medullary interstitial cells. The damage to these cells can result in chronic renal insufficiency via interstitial fibrosis and structural damage. This is the same model used to explain aspirin-induced nephropathy.

The second proposed mechanism involves microvascular changes in the bladder and possibly in the kidneys, induced by ketamine and/or ketamine metabolites. These microvascular changes may cause endothelial cell injury of microvessels which may lead to either compromised intrinsic microcirculation or decreased microvascular density in the sub-endothelium. This proposed mechanism is supported by cystoscopic findings of...
neovascularization. Severe suprapubic pain and dysuria (pain on urination) may be accounted for by bladder ischemia during bladder filling. When bladder ischemia is present, interstitial fibrosis and diminished bladder capacity can occur over time. Micro-angiopathy or capillary sclerosis in the renal medulla resulting in hypoperfusion of the papilla can be induced by papillary necrosis. Papillary necrosis induced by diabetes or analgesic nephropathy may exhibit similar pathophysiology to papillary necrosis seen in ketamine cystitis.6

The third proposed mechanism entails an indirect effect of ketamine. An autoimmune reaction against the bladder urothelium and submucosa, due to circulating ketamine or urinary ketamine and its metabolites, may result in ketamine cystitis. This autoimmune reaction may explain raised erythrocyte sedimentation rate (ESR) and the complements (C3/C4) found in some patients. Vascular congestion, submucosal edema, and scarring result from the autoimmune-mediated reaction. This may lead to diminished bladder capacity and poor compliance (the ability of the bladder to accommodate large volumes of urine).5

The final proposed mechanism of ketamine cystitis is bacterial infection. However, it is stated that a bacterial infection is an unlikely cause for ketamine cystitis and papillary necrosis since the patients studied did not present with bacterial cystitis. Of all of the patients studied, only two patients subsequently had a positive bacterial culture due to a concomitant bacterial urinary tract infection. No patients showed improvement with antibiotic treatments.5

Risk factors of ketamine cystitis are difficult to determine because this unique condition has not been well studied and its exact mechanism is still unclear. However, a 2020 systematic review detailing ketamine-induced uropathy provides some potential insight regarding risk factors. The epidemiologic studies that were conducted revealed common trends and characteristics that are related to risk factors. It was determined that urologic injury may be dose-related, and may be related to an increased frequency of use and long-term abuse. Ketamine that is insufflated, or snorted, appeared to result in the development of more severe symptoms than smoking would cause. This systematic review also highlights that concomitant use of other substances is common in 35% of users, and these substances commonly include cocaine, heroin, cannabis, ecstasy, and alcohol.6 Of note, ketamine cystitis is commonly seen in younger patients (16-35 years old), as it coincides with the general age of patients who abuse ketamine.7

Across databases, such as UpToDate8, Micromedex9, and AHFS Essentials located within Lexicomp10, general urologic injury and cystitis are listed as adverse effects of chronic ketamine abuse. AHFS Essentials also references cystitis as a potential risk of long-term exposure that should be considered when undergoing ketamine infusion therapy for mood disorders.10 The drug monograph for esketamine (Spravato ®) found on UpToDate and Lexicomp lists ulcerative and interstitial cystitis under warnings and precautions. Further discussion reveals that ulcerative cystitis cases have been reported in individuals with long-term off-label use or misuse/abuse of ketamine,8,10 Lexicomp also states that while clinical trials have shown higher rates of LUTS, they had not shown any cases of esketamine-related interstitial cystitis in patients treated for up to one year.10

There are various treatment modalities that can be employed for the management of ketamine cystitis, ranging from complete cessation of ketamine to pharmacologic interventions to even surgical interventions. These treatment modalities have been developed through trials of therapy with each unique patient case. It is important to note that the treatment of ketamine-associated cystitis depends on the severity of the disease. In all cases, the first-line, and mainstay, of treatment begins with pharmacologic interventions to complete cessation of ketamine to pharmacologic interventions to even surgical interventions. These treatment modalities have been developed through trials of therapy with each unique patient case. It is important to note that the treatment of ketamine-associated cystitis depends on the severity of the disease. In all cases, the first-line, and mainstay, of treatment begins with ketamine cessation. In mild cases, cessation alone may even be sufficient.6

Since ketamine cystitis is rare, and the mechanism of injury is still being investigated, treatment modalities focus on symptom management. First-line medications include a trial of non-steroidal anti-inflammatory drugs (ex: diclofenac) and anticholinergic agents (ex: solifenacin), followed by tramadol in the case of a partial response to these initial agents.6 One study showed that high dose antimuscarinics (oxybutynin 10mg by mouth three times daily or tolterodine 4mg by mouth twice daily) had no response.5 A separate study demonstrated that anti-inflammatory agents or corticosteroids may only achieve a partial response and are not curative.11 Second-line options include re-epithelization, intravesical injection, bladder hydrodistension, or oral pentosan polysulfate sodium (Elmiron®).6
Pentosan polysulfate appears to adhere to the bladder wall mucosa where it may act as a buffer to protect the tissues from irritating substances in the urine which may play a role in treating interstitial cystitis. Pentosan polysulfate sodium is standardly dosed at 100 mg by mouth three times daily for cases of cystitis. Surgery is also an available option as a last-line treatment for patients with late-phase disease after failing all other options. Surgical options include partial cystectomy, reconstruction, and augmentation enterocystoplasty. These procedures are performed in order to reduce inflammation and preserve micturition, as well as to improve bladder capacity and decrease pressure. However, relapse in ketamine use will more often than not result in symptom relapse.6

Published case reports support the current treatment recommendations for ketamine cystitis. Shahani et al was the first article published regarding ketamine-associated ulcerative cystitis. One case provided details of a 28-year-old male who presented with a six-month history of urinary symptoms that began shortly after the daily use of ketamine. The patient was unresponsive to both antibiotic and steroid therapy, while cessation of ketamine reduced some, but not all symptoms. This article also mentions the case of a 25-year-old female presenting with a two-year history of urinary symptoms associated with initial ketamine use. Here, ketamine cessation was successful in that the patient had marked improvements in symptoms. Another patient, a 17-year-old male, presented with recurrent episodes of urinary symptoms over the span of several months associated with ketamine use. However, in this case, discontinuation of ketamine had no effect and pentosan polysulfate therapy was needed to relieve irritative symptoms.12 Surgery is also an available option as a last-line treatment for patients with late-phase disease after failing all other options. Surgical options include partial cystectomy, reconstruction, and augmentation enterocystoplasty. These procedures are performed in order to reduce inflammation and preserve micturition, as well as to improve bladder capacity and decrease pressure. However, relapse in ketamine use will more often than not result in symptom relapse.6

A small randomized control trial found that the use of botulinum toxin A injections in combination with bladder hydrodistension was an effective form of management for ketamine cystitis. In this study, thirty-six patients (30 males and 6 females) between ages 19-38 with ketamine-associated cystitis were treated with intravesical botulinum toxin A injection (dose: 200UI) combined with bladder hydrodistension. All patients failed to achieve symptomatic relief with previous antimuscarinic and/or antibiotic therapy prior to the trial. All subjects had a history of ketamine abuse ranging from 1-5 years. In order to quantify any improvements in symptomatology, urodynamic testing, the O’Leary−Sant interstitial cystitis symptom index (ICSI), and problem index (ICP) were used to evaluate both baseline and post-treatment values. There were significant improvements (p-value <0.001) in many urinary symptoms from baseline to one-month post-treatment including nocturia, interval between micturition, void volume, maximum flow rate, and bladder capacity. There was also a notable decrease from baseline in ICSI and ICP following 1 month of post-treatment.15

Though the exact mechanism of ketamine cystitis is unknown, available literature suggests that it is most likely not caused by a bacterial infection. Therefore, the use of antibiotics is not a recommended treatment method. Available treatments focus on symptomatic management rather than disease cure. NSAIDs, anticholinergics, and opioids are the first modalities recommended for symptomatic relief, followed by more invasive means in the case of treatment failure. That being said, it has often been reported that symptoms typically resolve upon discontinuation of ketamine use and reappear with relapse. Due to the variable presentations of ketamine cystitis and unknown pathophysiology, it is essential for healthcare clinicians to recognize the various symptoms associated with ketamine cystitis and utilize different treatment modalities for patients experiencing this unique drug-associated adverse event.
References:


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Human immunodeficiency virus (HIV) is a single-stranded retrovirus that attacks the immune system, predisposing the host to opportunistic infections and malignancies. If not properly treated, HIV can progress to Acquired Immunodeficiency Syndrome (AIDS). Goals of therapy include restoration of immune function, suppression of HIV viral load, prolonged survival, and transmission prevention. Most preferred HIV-1 treatment regimens entail the use of daily oral antiretroviral (ARV) medications. The mainstay of current treatment consists of two nucleoside reverse transcriptase inhibitors (NRTIs) combined with a third ARV medication from one of the following drug classes: a non-nucleoside reverse transcriptase inhibitor (NNRTI), a protease inhibitor (PI), or an integrase strand transfer inhibitor (INSTI).

Adherence to ARV therapy is imperative for successful management of HIV. Interruption of therapy can result in virologic failure, drug resistance, elevated healthcare costs, and increased morbidity/mortality. Simplification of ARV regimens with the emergence of combination medications promotes long-term medication adherence, reduces risk of treatment failure, and improves quality of life. Approved by the Food and Drug Administration (FDA) in January 2021, cabotegravir/rilpivirine (Cabenuva®) is the first extended-release injectable indicated for the treatment of HIV-1. This promising new ARV regimen consists of an INSTI (cabotegravir) and an NNRTI (rilpivirine), and is intended to replace current therapy in adult patients who are virologically suppressed (HIV-1 RNA < 50 copies/mL) with no history of treatment failure/resistance to either component of the combination drug.

Prior to the initiation of cabotegravir/rilpivirine injections, patients must take a trial regimen of oral cabotegravir 30 mg and rilpivirine 25 mg tablets once daily for one month (at least 28 days) to assess tolerability. This is referred to in the package insert as the “Oral Lead-in” period. After this oral-lead in period, patients will take the “initiation” injections which consist of long-acting cabotegravir (600 mg/3mL) and rilpivirine (900 mg/3mL). These injections must be administered by a healthcare provider in separate gluteal sites either on opposite sides or 2 cm apart. For the third month and beyond, patients will be given the continuation doses of the 2 injections which consist of cabotegravir 400 mg (2 mL) and rilpivirine 600 mg (2 mL). Important for patients and clinicians to consider are the unique missed dose instructions for cabotegravir/rilpivirine. As always, patients should be strongly encouraged to take their medications as prescribed. In the event that a patient misses their dose of medication, there are specific sets of instructions outlined in the package insert. There are two categories: “planned missed injections” and “unplanned missed injections”. If a patient plans to miss a scheduled injection visit by > 7 days, they are instructed to administer oral therapy to replace up to 2 consecutive monthly injections. The first dose of oral therapy should be administered at least 1 month after the last injections, and continued until the day the injection dosing is restarted. If monthly injections are unintentionally missed or delayed by >7 days and oral therapy has not been administered in the interim, patients should be clinically reassessed to determine appropriateness of resuming injection dosing. If injection dosing will be continued, administer as follows: continue with cabotegravir 400 mg and rilpivirine 600 mg IM monthly injections if it has been less than or equal to 2 months since the last injection. If it has been greater than 2 months, reinitiate with cabotegravir 600 mg and rilpivirine 900 mg IM injections, then continue to follow the cabotegravir 400 mg and rilpivirine 600 mg IM monthly injection dosing schedule.

Adverse reactions for cabotegravir/rilpivirine mainly consisted of injection site reactions, fatigue, sleep disorders, and dizziness. Aside from hypersensitivity reactions to the medication, precautions included hepatotoxicity (for which liver function tests should be monitored and the medication discontinued if hepatotoxicity is suspected), and depressive disorders (for which medication evaluation is warranted). Cabotegravir/rilpivirine should not be co-administered with UGT1A1 inducers (for example, phenobarbital and rifampicin) or CYP 3A4 inducers (for example, clarithromycin, erythromycin, ketoconazole, diltiazem, verapamil). The reasoning is that these medications will reduce the serum concentration of cabotegravir/rilpivirine, which will lead to suboptimal patient outcomes. Furthermore, because this medication is considered a complete HIV therapy regimen, it should not be administered concomitantly with other antiretroviral therapies. It is important to note that although the injectable dosage form of cabotegravir/rilpivirine may be considered by some to be inconveniencing, its monthly dosing frequency provides therapy simplification, a huge advantage for patients.
with a history of non-adherence. Injections must be administered by a healthcare provider, therefore patients with poor follow-up may not be ideal candidates for therapy. Given the novelty of cabotegravir/rilpivirine, conventional ART may also be more cost-effective for uninsured patients.

In conclusion, cabotegravir/rilpivirine is a novel form of therapy that has the potential to impact the lives of many patients living with HIV-1 who struggle with nonadherence. There are advantages and disadvantages which should be taken into consideration, as previously discussed. Ultimately, the decision to initiate cabotegravir/rilpivirine should be a shared decision making process between the patient and the healthcare provider. Pharmacists, as the most accessible healthcare providers, play an essential role in the delivery of healthcare, and should be cognizant of such drug updates when they occur.

References:

We are always looking for creative and motivated students to join our team!

If you are interested in becoming a Rho Chi Post editorial team member, visit:

rhochistj.org/RhoChiPost/Application
Throughout my time in the PharmD program, my understanding of pharmacy as a profession has evolved and deepened as much as my desire to create awareness, particularly to non-science students, about the diverse role pharmacy plays in various healthcare and non-healthcare settings. I have always had an affinity for writing and look forward to combining my interests in literary composition, editing and pharmacy to produce relevant issues which both pharmacy students and non-pharmacy students alike will find relatable and take an interest in.

Pharmacy is a constantly evolving profession. Writing for the Rho Chi Post gives me the opportunity to enlighten my peers and myself on changes occurring in the field that we are often not taught in the classroom. The Rho Chi Post serves as a creative outlet where students can express their opinions and share new information by combining their passion for writing and the pharmacy profession. I hope that my contribution to this newsletter inspires others to improve patient outcomes by staying up to date on recent changes.

I am excited to be a part of Rho Chi Post, a place for pharmacy students to share insights, opinions, and new discoveries. As future pharmacists, the issues that exist in the US healthcare system will have to be addressed and improved by us. Rho Chi Post informs students on all aspects of pharmacy and serves as an example and inspiration for others. Pharmacy is an ever-changing and dynamic field, and there are vast career opportunities and pathways for pharmacy students. I look forward to working, listening, and learning from my fellow students and future colleagues, and I hope to serve as a guidance to others as others have.

I am excited to have the honor of serving on the Executive Board as Social Media Manager, eager to showcase the award-winning work of our editorial team, staff and contributing writers alike. Since joining the Rho Chi Post as a Staff Writer, I have been a frequent contributor to the newsletter, those who may be hesitant to do so might benefit more from a firsthand account of newsletter writing, with the added bonus of guidance from one of our own media manager and staff editor for the Rho Chi Post informed students on all aspects of pharmacy. As a member of our team, I will strive to keep up with all updates. Rho Chi Post provides a platform for students to share their insights, opinions, and new discoveries. As future pharmacists, the issues that exist in the US healthcare system will have to be addressed and improved by us. Rho Chi Post informs students on all aspects of pharmacy and serves as an example and inspiration for others. Pharmacy is an ever-changing and dynamic field, and there are vast career opportunities and pathways for pharmacy students. I look forward to working, listening, and learning from my fellow students and future colleagues, and I hope to serve as a guidance to others as others have.
The Rho Chi Post offers a place for students, alumni, and faculty to collaborate and share their experiences. Each bringing their own perspectives and opinions. I am very excited to be part of the Rho Chi Post team. As someone who has always had a love for writing, I am grateful for the voice that the Rho Chi Post has given me. I have also had the opportunity to learn from the articles published by my peers. I hope that I can encourage more students to contribute to the Rho Chi Post. After all, without conversations, there can be no change.

The Rho Chi Post gives pharmacy students the opportunity to explore their interests, whether it be editing, writing, or graphics, while also enhancing their skills and knowledge as student pharmacists. I am excited to be a part of the Rho Chi Post because it is a great way to expand on what I have learned during my time in pharmacy school and also keep developing my writing skills. Being a writer gives me an outlet to raise awareness on the advancements that are constantly happening in the field of pharmacy and allows me to be part of an amazing team in hopes of providing other students with our best work.

The pharmacy profession treasures the continuous search for knowledge in the fast-paced, ever-changing catalog of old, new, and developing drugs and therapies, whilst maintaining a manner of grace and compassion in everyday settings among patients, medical professionals, and higher associates. The St. John’s University Rho Chi Post is an emblem of this pursuit, bringing together an incredibly talented team of pharmacy students and graduates to present the latest pharmacy news to our fellow colleagues. I’m incredibly honored to be part of such an esteemed newsletter as a staff editor, which has since given me the opportunity to connect with a network of truly influential colleagues. I pledge to help aspiring student writers speak directly to the pharmacy community, in a voice that further empowers the words they convey.

Rho Chi Post is an amazing student-operated newsletter publication that is doing an astonishing job delivering updated news as well as giving students the opportunity to give back to the pharmacy community. As a staff writer, I hope to play a key role in educating students on the different aspects of pharmacy and how much growth takes place in this field. Reading the Post since freshman year has helped me gain a better understanding of what it means to be a pharmacist and I hope to achieve that same understanding in students who read my articles.

There are two things I am passionate about one which is pharmacy and the second which is writing. The Rho Chi Post is a professional newsletter, which allows students to educate as well as learn more about the field of pharmacy as it evolves. I am beyond excited to contribute to this newsletter and provide my fellow classmates and peers interesting news about pharmacy. I have always enjoyed reading The Rho Chi Post articles throughout pharmacy school. The articles were interesting and educational. This allows me to make an important contribution to society and spread awareness not only of new drugs and advancements in the field, but current issues in the pharmacy world. Having a voice is very important and writing for this newsletter allows me to have one.
The field of pharmacy is constantly growing and improving with every coming day. Today’s headlines become tomorrow’s history. As healthcare leaders in a dynamic field, it is important to stay up to date. The Rho Chi Post serves as an excellent tool to help students become more informed about our profession, as well as providing them with the opportunity to contribute their own two cents to the conversation. I am excited to join the team and look forward to contributing to keeping students on top of current pharmacy advancements.

My desire to learn about medicine and its effect on the human body began with a nebulizer. I had asthma as a young girl. At the age of ten, the vaporous gases from the pump never ceased to amaze me. My sickness, although unfortunate, fueled my interest in the functions, limitations, and exploitations of drugs. I have always had a passion for advocating for change and believe the Rho Chi Post adds great value to the community. As the world grows and develops, each individual has an opportunity to express their thoughts on its development. Having the chance to become a Staff Writer provides me an opportunity to learn information about my peers to better assess the nature of their situation. When people begin discussing concepts at a younger age, they are able to influence people of their generation to care more about their own health. Combining concepts learned from pharmacy school with the mission to help those in need will create a stronger foundation for future healthcare professionals.

The profession of pharmacy is constantly evolving and adapting to the ever-changing field of healthcare. The Rho Chi Post serves as an amazing outlet for students to be informed, as well as to inform others, on the most up to date and relevant information. I could not be more excited to join the Rho Chi Post. This opportunity allows myself and my peers to take initiative and raise awareness of the advancements in the field of pharmacy. As a staff writer, I look forward to contributing to the Rho Chi Post and am grateful for the opportunity to educate students on the growth within our profession.

Joining the Rho Chi Post is an opportunity to remain updated with new advancements in the science of pharmacy. The Post provides students with a platform to present the rest of the student body with interesting articles regarding new medications and important changes in the field. Keeping up with new developments and innovations is key to becoming a capable pharmacist. I am quite excited to join a team that is a voice of research and knowledge and look forward to contributing in a way that will benefit the pharmacy community.

As an avid reader, I have always taken an interest in how things were written. Whether it be novels, journal articles, or magazine columns, there is always a peculiar way in which a writer tells a story. The real story is only 50% of what is written and the rest is in how the writer decides to disseminate that information. The Rho Chi Post serves as an amazing outlet for student pharmacists, allowing us to delve into the intricacies of different perspectives and ideas in the world of pharmacy. It also gives us the opportunity to decide how we want to detail these new found perspectives and ideas to our audience. As an incoming editor for The Rho Chi Post, I hope to enhance and curate the way each writer tells their stories and help them reach their audience at new levels.

As future drug experts, we student pharmacists have a responsibility to take initiative and educate ourselves on advancements in healthcare, so as to improve the quality of patient care. The Rho Chi Post serves as a great platform for students to get information that is both accessible and accurate. To be a voice for my future, fellow pharmacists is to be heard and my patients cared for—as pharmacists are their best, sometimes their only, advocates. I hope that my contributions to the RCP spark readers’ curiosity, and inspire conversations of how we may become better pharmacists.

I am so excited to be a part of the Rho Chi Post team. This opportunity allows both myself and my peers to be well informed about the ever-changing profession of pharmacy and the vital developments in science and healthcare. Beyond the classroom setting, this newsletter fills in the gaps for the most up-to-date and current advancements for students and faculty. As a staff writer, I look forward to acting as an educator, a motivator, and an executor to further the mission and goals of the Rho Chi Post.
The profession of pharmacy is continuously expanding to meet new demands and offer novel platforms for innovation in healthcare. With an abundance of new information and guidance being published everyday, it can become difficult for students and professionals to stay updated with relevant information and find new outlets to learn. The Rho Chi Post not only allows us to be informed about the current state of our profession, but also allows students to voice their opinions and connect with each other through literature. I am excited to be part of its team, and hope to provide meaningful and resourceful contributions.

My name is Edwin and I am a Doctor of Pharmacy student at St. John’s University. My favorite aspect of pharmacy school is learning about the clinical and therapeutic components of drugs and diseases. As a kid, I was interested in both the math and sciences. The reason I chose pharmacy over other health care professions is because a lot of people rely on their medications to make them feel better. Pharmacists are the most accessible healthcare providers and are able to help patients optimize their drug therapy in order to improve their health. Throughout the beginning of pharmacy school, I volunteered at Columbia University Medical Center on the oncology department for one year. After that, I have been working as a pharmacy intern at Sandcastle Pharmacy, which is primarily an HIV specialty pharmacy. As a staff writer, I want to highlight the critical role of clinical pharmacists within an interdisciplinary team, in improving and enhancing a patient’s quality of life.
The Rho Chi Post is an award-winning, monthly, electronic, student-operated, faculty-approved publication that aims to promote the pharmacy profession through creativity and effective communication. Our publication is a profound platform for integrating ideas, opinions, and innovations from students, faculty, and administrators.

The Rho Chi Post aims to become the most exciting and creative student-operated newsletter within St. John’s University College of Pharmacy and Health Sciences.

Our newsletter continues to be known for its relatable and useful content.

Our editorial team continues to be known for its excellence and professionalism.

The Rho Chi Post essentially sets the stage for the future of student-operated publications in pharmacy.

Opportunity
Teamwork
Respect
Excellence

To provide the highest quality student-operated newsletter with accurate information.

To maintain a healthy, respectful, challenging, and rewarding environment for student editors.

To cultivate sound relationships with other organizations and individuals who are like-minded and involved in like pursuits.

To have a strong, positive impact on fellow students, faculty, and administrators.

To contribute ideas and innovations to the Pharmacy profession.

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