The Mortar & Pestle:

MD Custom Rx's monthly e-newsletter

May 2019

MD Custom Rx
Quality Matters

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Greetings!

Thank you for entrusting in the compounding services at MD Custom Rx to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to continuing to be your medication problem solvers. Please don't ever hesitate to let us know how we can be of further assistance to you and your practice.

Sincerely,
Dan, Monica and John

Intranasal Ketamine for Treatment-Resistant Depression: Glutaminergic Inhibition for Patients who are Refractory to MAOI Antidepressants

Depressive disorders represent diverse psychiatric illnesses with heterogeneous clinical manifestations and a multitude of comorbidities that can lead to severe disability. In spite of decades of research on the pathogenesis of these disorders, the wide variety of pharmacotherapies currently used to treat them is based on the modulation of monoamines, whose alteration has been considered the neurobiological foundation of depression, and consequently of its treatment. However, approximately from one third to a half of patients respond partially or become refractory to MAO inhibitors, thereby jeopardizing the therapeutic effectiveness in the real world of clinical practice. Recent scientific evidence has been pointing out the essential role of other biological systems beyond monoamines in the pathophysiology of depressive disorders, in particular, the glutamatergic neurotransmission, which can be inhibited by ketamine.

Ketamine is approved by the FDA to be used as an anesthetic; however, recent reports have shown its success in the treatment of major depressive disorder (MDD). Studies have suggested that a sub-anesthetic dose produces rapid antidepressant activity, providing significant symptomatic relief particularly in patients with a history of treatment resistant depression (TRD). Many reports have been published on the intranasal efficacy of ketamine in the treatment of depression.

In a randomized, double-blind, placebo-controlled, crossover trial conducted in 20 patients with major depression, Lapidus et al. of the Icahn School of Medicine at Mount Sinai, New York, tested the safety, tolerability, and efficacy of intranasal ketamine in patients with depression who had failed at least one prior antidepressant trial. Eighteen patients completed 2 treatment days with intranasal ketamine hydrochloride or saline solution. The researchers found that a single intranasal dose of ketamine (50 mg) outperformed saline by 7.6 points on the Montgomery-Asberg Depression Rating Scale as assessed 24 hours after dosing; the response rate was 44% vs 6%, respectively. Anxiety ratings also decreased significantly more with ketamine. Patients showed significant improvement in depressive symptoms at 24 hours after ketamine compared to placebo. Intranasal ketamine was well tolerated with minimal psychotomimetic or dissociative effects and was not associated with clinically significant changes in hemodynamic parameters.

J Psychiatr Res. 2019 May;112:7-11.
Curr Pharm Des. 2019 Mar 11. [Epub ahead of print]
PLoS One. 2019 Mar 13;14(3):e0213721.
Biol Psychiatry. 2014 Dec 15;76(12):970-6.

Estrogen, Cardiovascular Health, & Sexual Function

The Kronos Early Estrogen Prevention Study (KEEPS) was designed to address gaps in understanding the effects of timely menopausal hormone treatments (HT) on cardiovascular health and other effects of menopause after the premature termination of the Women's Health Initiative (WHI).

The Kronos Early Estrogen Prevention Study (KEEPS) was a randomized, double-blinded, placebo-controlled trial to test the hypothesis that initiation of hormone therapy (HT) in healthy, recently postmenopausal women (n?=?727) would slow the progression of atherosclerosis. After 4 years, there were no severe adverse effects, including venous thrombosis. Several ancillary studies demonstrated reduced hot flashes, improved sleep, and maintenance of bone mineral density. Sexual function improved with transdermal 17ß-estradiol (t-E2). There were no significant effects on cognition, breast pain, or skin wrinkling. KEEPS and its ancillary studies have supported the value and safety of the use of HT in recently postmenopausal women and provide a perspective for future research to optimize HT and health of postmenopausal women. The KEEPS continuation study continues to pursue these issues.

Transdermal estradiol treatment was associated with a significant increase in mean lubrication and decreased pain compared with placebo. Transdermal estradiol treatment resulted in fewer women with low sexual function compared with placebo, while oral conjugated equine estrogens (CEE) produced no significant benefit.

Menopause. 2019 Apr 1. [Epub ahead of print]
JAMA Intern Med. 2017 Oct 1;177(10):1471-1479

Estriol Treatment for Vulvovaginal Atrophy

Despite its frequency, recognition and therapy of vulvovaginal atrophy (VVA) remains suboptimal. Wet mount microscopy, or vaginal pH testing, allows VVA diagnosis in menopausal or

postpartum women, but also in young contraception users or after breast cancer. The basis of good treatment is a correct and complete diagnosis, using a microscope to study the maturity index of the vaginal fluid. Many experts believe that minimal doses of estriol with or without lactobacilli can be used intravaginally after breast cancer and in women with history of thromboembolic disease. Ultra-low-dose vaginal estriol is beneficial in most cases, even in breast cancer patients.

A literature review was conducted to evaluate the efficacy and safety of estriol for the treatment of vulvovaginal atrophy in postmenopausal women, and confirmed the efficacy of local estrogens to treat symptoms of vulvovaginal atrophy with few adverse effects reported. Following treatment, serum estriol levels rose, peaking at 1?hour. At the 6-month follow-up, there was no increase in serum estriol in treated women. The available evidence (of low and moderate quality) shows that, when administered vaginally, estriol preparations may be considered as a treatment option for women who have risk factors related to systemic estrogen therapy.

An Italian study evaluated the effectiveness of the application of 0.005% estriol gel to the vulvar vestibule to relieve sexual pain. Postmenopausal women with dyspareunia were enrolled in the study and instructed to use a fingertip to apply estriol vaginal gel to the vulvar vestibule daily for three weeks and then twice weekly for up to 12 weeks. Assessment of symptoms and signs of vestibular atrophy were performed, and changes between baseline and weeks 3 and 12 were assessed. Adverse events were recorded. A total of 63 women were included. Fifty-nine women completed the 12-week treatment period, and four dropped out for vestibular burning (which may have been a result of the base used for this particular preparation). Dyspareunia improved or resolved by week 12 in 81.4% of patients. The women also showed a statistically significant reduction in vestibular atrophy at the end of treatment.

Hyaluronic acid therapy may help women who cannot or do not want to use hormones. The use of a hyaluronic acid topical liquid preparation for vaginal use (Justgin®, Just Pharma, Rome, Italy) three times per week for 8 weeks produced statistically significant improvements in symptoms, both objectively via the use of the Vaginal health Index (VHI) and subjectively with a Visual Analogic Scale (VAS). The most significant improvements concerned vaginal dryness and painful intercourse, therefore strongly improving the Quality of Life of these women. The patients' degree of satisfaction at the end of the trial was high (95%).

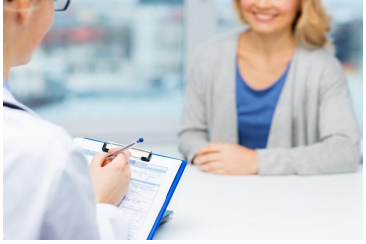
In contrast, laser therapy requires validation and safety data, as it can potentially cause vaginal fibrosis and stenosis.

Expert Opin Pharmacother. 2019 Mar 21:1-15.
Eur J Obstet Gynecol Reprod Biol. 2016 Dec;207:121-124.
Climacteric. 2017 Aug;20(4):321-330.
https://www.europeanreview.org/wp/wp-content/uploads/4190-4195-Hyaluronic-acid-improves-VVA-symptoms.pdf

Your questions are welcome!

MD Custom Rx Educational Events

We regularly offer educational events at the pharmacy. Be sure to share our events with your patients. **VISIT OUR WEBSITE** to see our schedule and to register. If you are interested in speaking on a topic, please contact the pharmacy.



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