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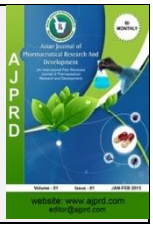

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Review Article

Drug Information of Lasmiditan and Its Effectiveness for Maigraine

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A B S T R A C T

Migraine is the leading cause of disability in people under 50 years of age and the second highest cause of disability worldwide with significant impact on the daily lives of patients and their families, 50-200mg lasmiditan is a serotonin (5-HT) 1F receptor agonist new class of medication needed for treatment of migraine, A latest drug with recent studies showns to be efficacious and safe for the prevention of migraine in adults, Lasmiditan was more effective than placebo for the acute treatment of migraine in patients concurrently using migraine preventive medications. Lasmiditan efficacy and safety measures were similar for patients using and not using preventive medications.

KEY WORDS: lasmiditan, maigraine, efficacy of lasmiditan.

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INTRODUCTION

Migraine is a neurological disease that can be incapacitating and affects 12% of the US population, including children.[1] It typically manifests as severe throbbing pain on one side of the head, but can be bilateral in up to 1 in 3 adults and in a higher proportion in children. Migraine attacks generally last between 4 and 72 hours when untreated or unsuccessfully treated.[1,2] Migraine is the leading cause of disability in people under 50 years of age [3] and the second highest cause of disability worldwide with significant impact on the daily lives of patients and their families [4]. Migraine disease management includes preventive treatments to reduce attack frequency and acute medications to treat attacks. The American Migraine Prevalence and Prevention (AMPP) study found that an estimated 39% of patients with migraine experience attack frequency or migraine-related disability that would make them eligible for preventive treatments [5,6]. Multiple classes of drugs are currently used to prevent migraine attacks including antiepileptic, antidepressant, and beta-adrenoceptor blocking medications [7]. The American Academy of Neurology (AAN) and the American Headache Society (AHS) developed evidence-based recommendations to help guide the use of migraine preventive medications in clinical practice [6], as has the European Headache Federation (EHF) [8]. However, not all patients respond sufficiently to triptans and NSAIDs, and in some patients, triptans are contraindicated due to their vasoconstrictive effects [9]. Lasmiditan is a novel serotonin receptor agonist, distinct from triptans in that it is selective for the 5-hydroxytryptamine (5HT)1F receptor and does not result in vasoconstriction [10].

Until 30 years ago, migraine was believed to be caused by dilatation of blood vessels, and the aura of migraine, which affects about 20% to 33% of patients, was thought to result from vasoconstriction.[11] However, neuroimaging studies have refuted these assumptions, leading to the current belief that migraine is a primary neuronal (central nervous system [CNS]) dysfunction that involves sensitization and activation of trigeminovascular pathways.[12-14] In addition, researchers examining migraine-associated genes [15] have identified the important role of neuropeptides in the pathophysiology of migraine. Migraine aura, which is usually visual in nature but can also involve sensory, motor, or verbal disturbances, has been linked to cortical spreading

depression (CSD) of Leão.[16-19] CSD is a phenomenon involving a self-propagating wave of extreme depolarization of glial and neuronal cell membranes that leads to a transient increase and then decrease in cerebral blood flow.[16,17] In addition, CSD is believed to activate trigeminal nerve afferents, resulting in inflammatory changes in the pain-sensitive meninges, which ultimately leads to headache pain.[20,21].The basis of this pain is the activation of peripheral nociceptive trigeminal sensory afferents that surround cranial blood vessels and innervate the eye, dura mater, dural venous sinuses, and cerebral and pial blood vessels. Secondary transmission occurs in neurons in the trigeminocervical complex, which are integrated through the thalamus and transmitted to the brainstem, subcortical, and cortical regions. [16,17] It has been hypothesized that migraine without aura is associated with CSD in other areas of the brain, such as the cerebellum. Stimulation of the trigeminal ganglion leads to the release of vasoactive neuropeptides such as substance P, calcitonin gene-related peptide (CGRP), and neurokinin A.[18] Release of these neuropeptides, in turn, has been linked to neurogenic inflammation that may be associated with migraine pain intensification and prolongation. CGRP is a primary neurotransmitter expressed in trigeminal ganglia nerves; it has strong vasodilation effects of cerebral and dural vessels.[19] Stimulating the trigeminal ganglion causes the release of CGRP, which can then cause a migraine attack in persons with migraine.[20] The role of serotonin (5-HT) in the pathophysiology of migraine remains unclear, but there is evidence that activation at serotonin receptors is important in the acute treatment of migraine. Triptans are highly selective 5-HT1B/1D receptor agonists that act to prevent the release of CGRP.[21,22]

MANAGEMENT OF MAIGRAINE

Three novel agents have been approved by the FDA in the past year using the FDA 2018 requirements for the treatment of acute migraine the selective 5-HT 1F receptor agonist lasmiditan and 2 small-molecule CGRP receptor antagonists, ubrogepant and rimegepant. Another CGRP receptor antagonist, intranasal vazegepant (BHV-3500), is under investigation and has been shown to be superior to placebo in a phase 2/3 study.[23] In addition, 4 CGRP monoclonal antibodies—eptinezumab, erenumab, fremanezumab, and galcanezumab have been approved by the FDA for the prevention of migraine. These agents have all been shown to be efficacious and safe for the prevention of migraine in adults.[23]

DRUG INFORMATION OF LASMIDITAN

LASMIDITAN(REYVOW) is a serotonin (5-HT) 1F receptor agonist indicated for the acute treatment of migraine with or without aura in adults but not indicated for the preventive treatment of migraine. The recommended dose of REYVOW is 50 mg(light grey), 100 mg(light purple), or 200 mg taken orally, as needed. Not more than one dose should be taken in 24 hours, and dosing interval is 8 hours while driving or operating machinery.

ADVERSE DRUG REACTIONS

Driving Impairment, Central Nervous System Depression, Serotonin Syndrome, Medication Overuse Headache are adverse effects. The most common side effects are tingling and less than 2% vertigo, limb discomfort, cognitive changes, confusion, euphoric mood, chest discomfort, speech abnormalities, dyspnea, and hallucinations .In 0.2% of patients treated Events of hypersensitivity, including angioedema, rash and photosensitivity reaction. It was associated with mean decreases in heart rate of 5 to 10 bpm and may increase blood pressure following a single dose.

DRUG INTERACTIONS

Drug interactions include Concomitant use with alcohol or other CNS depressant drugs cause sedation, as well as other cognitive and/or neuropsychiatric adverse reactions, other drugs like e.g., SSRIs, SNRIs, TCAs, MAO inhibitors, trazodone, etc., over-the counter medications (e.g., dextromethorphan), or herbal supplements (e.g., St. John's Wort) that increase serotonin may increase the risk of serotonin syndrome. Use cautiously in patients taking concomitant medications that lower heart rate if this magnitude of heart rate decrease may pose a concern. It inhibits P-gp and BCRP in vitro. Concomitant use is avoided.

USE IN PREGNANCY AND LACTATION

There are no adequate data on the developmental risk associated with the use of REYVOW in pregnant women. There are no data on the presence in human milk, effects of on the breastfed infant, or the effects on milk production. Safety and effectiveness in pediatric patients have not been established. Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

DOSE ADJUSTMENT IN ORGAN IMPAIRMENT

No dosage adjustment is needed for patients with mild or moderate hepatic impairment. Not recommended in severe hepatic impairment. Evaluate patients for risk of drug abuse and observe them for signs for misuse or abuse as it produce adverse events of euphoria and hallucinations. Physical withdrawal was not observed in healthy subjects following abrupt cessation after 7 daily doses of 200 mg or 400 mg. It presumably exerts its therapeutic effects in the treatment of migraine through agonist effects at the 5-HT1F receptor; however, the precise mechanism is unknown.

PHARMACOKINETICS

Absorption orally rapidly absorbed, tmax of 1.8 hours. Plasma protein binding of 55% to 60%. It is primarily eliminated via metabolism, with ketone reduction as major pathway. Renal excretion is a minor route of clearance. It undergoes hepatic and extrahepatic metabolism primarily by non-CYP enzymes. Recovery of unchanged in urine was low and accounted for approximately 3% of the dose. No drug-related tumors were observed following oral administration. No drug related mutagenesis is seen. In animal studies no adverse effects on fertility or reproductive performance is seen.

EFFECTIVENESS OF LASMIDITAN

Lasmiditan dosed at 200 and 100 mg was efficacious and well tolerated in the treatment of acute migraine among patients with a high level of cardiovascular risk factors.[24]

Loo et al. The Journal of Headache and Pain (2019) 20:84 research shows Lasmiditan was more effective than placebo for the acute treatment of migraine in patients concurrently using migraine preventive medications. Lasmiditan efficacy and safety measures were similar for patients using and not using preventive medications. In these trials, 698 of 3981 patients (17.5%) used migraine preventive treatments. Among patients using preventives, all lasmiditan doses resulted in significantly more patients being pain-free at 2 h, compared to placebo ($p < 0.05$). Primary efficacy outcome (pain-free at 2 h), key secondary outcome (most bothersome symptom-free at 2 h) and all other efficacy outcomes were not significantly different between patients using or not using migraine preventives (all interaction p-values ≥ 0.1). Rates of adverse events were similar for patients using and not using preventive medications [25].

The two (SAMURAI and SPARTAN) large studies were conducted in adults diagnosed with migraine with or without aura with a history of 3-8 migraine attacks and less than 15 headache days per month. Patients were told to wait until pain was moderate to severe to treat, an FDA requirement for these trials. The SAMURAI study did not include patients with known coronary artery disease, heart rhythm abnormalities, or uncontrolled hypertension. However, the other study, SPARTAN, included this group with heart and vascular disease, and these patients did equally well with lasmiditan, with no heart or blood vessel issues caused by the drug. [25,26] lasmiditan is an exciting new class of medication for treatment of migraine. It can be used in those with vascular disease. It does require health care providers to write it as a special prescription since it is a scheduled medication. When patients waited to take lasmiditan until they had moderate to severe levels of migraine pain, over 1/3 of them were pain free by 2 hours. A mild intoxicated feeling is the most common side effect, and patients should not drive for 8 hours after taking the medication.[26]

CONCLUSION

Migraine is the leading cause of disability in people under 50 years of age and the second highest cause of disability worldwide with significant impact on the daily lives of patients and their families, 50-200mg lasmiditan is a serotonin (5-HT) 1F receptor agonist new class of medication needed for treatment of migraine, A latest drug with recent studies showns to be efficacious and safe for the prevention of migraine in adults

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