September 2017

AJMC
THE AMERICAN JOURNAL OF MANAGED CARE

Emerging Therapies and Preventive Treatments for Migraine

A migraine is often perceived as "just a bad headache." However, to those suffering from this disabling neurologic disease, it is an incapacitating and chronic illness.[1,2] Viewed as a hereditary disease that disproportionately affects females, migraines often begin in childhood. Puberty is a common trigger for their onset, and the frequency only increases with age.[1] Characterized as a throbbing headache, there are often accompanying sensory abnormalities, the most notable of which is an aversion to light.[3] According to the Migraine Research Foundation, migraines make up the third most prevalent disease in the world, affecting 1 billion people worldwide; in the United States, they affect 18% of women, 6% of men, and 10% of children.[1] In 2013, the World Health Organization updated the ranking of migraine among other conditions in the gloal burden of disease, placing it at the No. 6 spot for years lost to disability worldwide.[4] It is estimated that nearly 90% of migraine sufferers experience moderate to severe pain during an attack and 75% of suffers have a reduced ability to function normally during their attack.[5]

PATHOPHYSIOLOGY

Despite a growing amount of research, the underlying mechanisms that trigger and propagate the migraine cycle are not well understood. It is well known that migraine attacks are associated with triggers , which include stress, hormonal fluctuations, sleep disturbances, skipping meals, and sensory overload; however, the neural and vascular pathophysiology of a migraine is not well understood.[6] As such, the pathophysiology behind migraines is a highly debated topic. One theory for the origin of a migraine headache is that it is a vascular disorder and focuses on the dilation of blood vessels as the root cause during an attack.[6] However, newer evidence suggests the involvement of underlying mechanisms of the trigeminovascular system.[6] In this model, a migraine headache is thought to occur when meningeal pain networks are activated by signals emanating from the trigeminovascular system.[7] The cortex, brainstem, trigeminal nerve, meninges, and hypothalamus are also thought to play a role in migraine pathophysiology.[3] The hypothalamus is of particular interest for its role in maintaining homeostasis. While it not known whether the disease itself causes alterations in brain structure and function or if there is a genetic component, the brain of a migraine sufferer has abnormalities and differences from that of a person who does not experience migraines. It is believed that these abnormalities result in a greater sensitivity to changes in the neurochemical balance maintained within the brain, along with a decreased ability to adapt to fluctuations, which ultimately lead to repeated attacks.[7] Evidence suggests that repeated headaches are involved in the progression of disease and are linked to changes in brain anatomy and function.[7]

ROLE OF CALCITONIN GENE-RELATED PEPTIDE

Advancements in migraine research over the past few decades have led researchers to identify the possible role of calcitonin gene-related peptide (CGRP) in migraine pathophysiology. CGRP is a neuropeptide and a potent dilator of both peripheral and cerebral blood vessels.[3,8] Its effects vary widely; however, where migraines are concerned, it is most notably involved in the regulation of the cardiovascular