OnabotulinumtoxinA for the treatment of chronic migraine

Chronic migraine is defined as 15 or more headache-days per month for more than 3 months within the previous 12 months, with at least 8 migraine-days per month. Chronic migraine usually evolves from episodic migraine, with peripheral and central sensitization in the trigeminovascular system contributing to the pathophysiology.

The first-line treatment of chronic migraine is pharmacological. Acute medications treat migraine symptoms, and preventative therapies help reduce the frequency, severity, and duration of migraine attacks. Unfortunately, several of these medications show inadequate efficacy, tolerability, and adherence to treatment. This has led to the development of novel therapies such as onabotulinumtoxinA, a preventative option formulated from botulinum toxin type A.

In the peripheral neuron, onabotulinumtoxinA targets SNAP-25, an essential protein of the SNARE complex. This complex mediates the release of neurotransmitters associated with the genesis of pain from vesicles in neurons. After which, pain-sensitive ion channels are inserted into the membrane and remain active. By cleaving SNAP-25, the drug disrupts SNARE-mediated vesicle trafficking.

Pericranial injection of onabotulinumtoxinA may reduce the peripheral sensitization and consequently the central sensitization associated with chronic migraine by modulating two SNARE-dependent processes: decreasing the release of pro-inflammatory and excitatory neurotransmitters that transmit nociceptive pain and decreasing the up-regulation of pain-sensitive ion channels.

OnabotulinumtoxinA is administered intramuscularly by a health professional every 12 weeks. One hundred fifty-five units are injected into 31 sites across seven head and neck muscle areas. Up to 8 additional injections of 5 units each may be given in up to 3 muscle areas.

Clinical studies show that onabotulinumtoxinA is effective in preventing headache in those with chronic migraine, including in patients with overuse of acute medications and regardless of whether patients have previously used recognized prophylactic medications.

Compared with placebo in the PREEMPT studies, onabotulinumtoxinA administered every 12 weeks was associated with sustained and clinically meaningful improvements in multiple assessments of headache symptoms,

including the frequency of monthly headache-days; headache-related impact and/or disability; and migraine-specific health-related quality of life.

Reductions in headache and migraine-days per week were seen within one week of treatment with onabotulinumtoxinA in the PREEMPT studies, and cumulative prophylactic effects were evident with successive treatment cycles over 1 year in the PREEMPT studies and 2 years in the COMPEL study.

In clinical practice, onabotulinumtoxinA shows efficacy similar to that observed in clinical trials. For instance, in the multinational REPOSE study in Europe, treatment with the drug significantly and progressively decreased the number of headache-days per month and improved quality of life measures related to migraine and general health over a period of 2 years.

The most common adverse events reported with onabotulinumtoxinA have been neck pain, muscle weakness, and eyelid ptosis. These are consistent with the known pharmacology and tolerability profile of the drug, which is more favorable than that of oral topiramate, an anticonvulsant approved for preventing migraine.

Effective and well-tolerated, onabotulinumtoxinA is one of the most widely used preventative options available for chronic migraine. And it continues to be a central component of chronic migraine management.