Real-world data suggests that adding CGRP inhibitors to onabotulinumtoxinA provides additional efficacy for the preventive treatment of chronic migraine

Chronic migraine is defined as having at least 15 monthly headache days, of which 8 or more are migraine days. This high attack frequency can seriously impair everyday activities and reduce quality of life.

Unfortunately, the disease's complexity makes treatment difficult, and many patients have far more than 15 monthly headache days.

Two approved preventive treatments for chronic migraine include onabotulinumtoxinA and antibody-based inhibitors of calcitonin gene-related peptide, or CGRP.

OnabotulinumtoxinA is administered to muscles surrounding the head and neck and near sensory nerves.

At the nerve terminal, it disrupts pain signals by reducing synaptic release of various neurotransmitters and neuropeptides, including CGRP, and by inhibiting insertion of pain-sensitive ion channels.

In contrast, CGRP inhibitors, in the form of monoclonal antibodies, primarily act directly on CGRP receptors or the CGRP ligand and prevent ligand-to-receptor binding.

Preclinical data suggest that the two types of agents inhibit different types of pain fibers implicated in migraine: onabotulinumtoxinA primarily inhibits C-fibers, while CGRP inhibitors primarily inhibit Aδ-fibers.

The different mechanisms of action suggest that adding CGRP inhibitors to onabotulinumtoxinA treatment may produce additive or synergistic effects, which could be useful for patients who don't achieve sufficient relief from onabotulinumtoxinA alone due to disease severity.

Clinical reports have indicated benefits of this combination therapy, but no randomized controlled trials have been performed.

A retrospective longitudinal chart review recently assessed the effects of onabotulinumtoxinA treatment and subsequent combination treatment with CGRP inhibitors and onabotulinumtoxinA among 257 patients at a single center. Safety, tolerability, and outcome measures were assessed for up to 1 year after the CGRP inhibitors were prescribed.

OnabotulinumtoxinA alone effectively decreased headache frequency, and the addition of a CGRP inhibitor significantly reduced the number of monthly headache days even further at all visits.

Combined treatment also resulted in significantly lower headache intensity scores at all visits and clinically meaningful improvements in migraine-related disability over 6-12 months compared with the baseline values achieved with onabotulinumtoxinA alone.

The combination treatment regimen was well tolerated, with no new safety signals reported. The most common adverse event was constipation, which was reported primarily by patients receiving the CGRP inhibitor erenumab.

Approximately one-quarter of patients discontinued one or both treatments, primarily CGRP inhibitors. Lack of insurance reimbursement was the most common reason for CGRP inhibitor discontinuation, followed by lack of effect.

Additional studies, including controlled trials, are warranted to confirm the findings and to address the limitations of this retrospective study.

Overall, however, this real-world study did not identify safety concerns with adding CGRP inhibitors to onabotulinumtoxinA treatment and suggests that the combination provides clinically meaningful benefits for patients with chronic migraine.