Mechanism of Action of Abortive Migraine-Specific Medications

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BACKGROUND

Conventionally, different drugs used to treat a specific medical condition are classified into categories or classes based on their mechanism of action. For example, aspirin, which acts by blocking the uptake of serotonin from the synaptic cleft, is referred to as a selective serotonin reuptake inhibitor (SSRI), to differentiate it from other drugs that inhibit the uptake of both serotonin and norepinephrine, commonly referred to as serotonin and norepinephrine reuptake inhibitors (SNRIs).

Drugs used for the acute treatment of migraine, however, have traditionally been classified based on their chemical structure as opposed to their mechanism of action. For example, ergots, which act by blocking the uptake of both serotonin and norepinephrine, are classified into categories or classes based on their chemical structure. DHE and ergotamine are chemically similar, however there are substantial differences in their clinical effects and potentially help physicians select the appropriate class of drugs in treating their patients. Here, we review the published mechanisms of action of representative molecules, DHE and sumatriptan, from these two classes of migraine-specific drugs.

OBJECTIVE

To present a review of the literature that supports different mechanisms of action for these two classes of abortive migraine-specific drugs.

MOLECULAR STRUCTURES

As presented in Table 1, DHE targets some of the same receptors that sumatriptan targets. The mechanisms of action of these drugs through these receptors are similar. They include:

- Both DHE and sumatriptan cause seasoconstruction due to 5-HT 2A receptor activation.
- Both DHE and sumatriptan block Calcitonin Gene-Related Peptide (CGRP) release and kinins from trigeminal nerve endings due to 5-HT 1B/1D receptor activation.
- Both drugs block pain transmission from the trigeminal nuclei to the anterior cingulate cortex (ACC) via 5-HT1D receptor activation.

The effects of DHE through a variety of receptors beyond serotonergic receptors allow it to modulate multiple nociception pathways. These mechanisms of action of DHE differentiate it from sumatriptan.

MECHANISMS OF ACTION

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- DHE causes vasodilatation due to activity at adrenergic receptors.
- DHE reverses central sensitization of the TNC.
- Prolonged dilatation and severe pain of migraine can lead to sensitization of the TNC, resulting in spontaneous firing of TNC neurons.
- DHE has an anti-inflammatory effect via modulation of the MAP kinase/phosphatase system (Figure 2). DHE also has been shown to modulate glial cells.

REFERENCES

5. Headache Society (IHS); 2009; Philadelphia, PA.

ADDITIONAL REFERENCES