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Migraine - acute therapy

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DOES DIHYDROERGOTAMINE TREAT THE “WHOLE MIGRAINE”?

Sheena Aurora*, Sutapa Ray[1], Kelsey Satterly[1], Stephen Shrewsbury[1], John Hoekman[1]

[1]Impel NeuroPharma, Seattle, United States

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Introduction: Migraine is recognized as a complex, multifactorial brain network disease associated with 40 different gene loci. Despite a growing body of scientific evidence about the spectrum of migraine pathophysiology including autonomic dysfunction, advances in migraine therapeutics have become increasingly focused on headache pain which may be achieved by targeting a very narrow set of receptors i.e. 5HT1b/d or F or CGRP. Migraine however encompasses a spectrum of symptoms i.e. premonitory phase, aura, photo/phono and osmophobia as well as a postdrome. When a narrow receptor profile is targeted patients do not achieve a holistic migraine relief with lack of consistency, recurrence and accompanying nausea are the prominent reasons for discontinuation.

DHE has demonstrated a larger therapeutic gain compared to triptans [24hr sustained relief, central sensitization, no treatment window therefore it is likely that other receptor targets are involved at the various stages of the migraine cycle. A closer look at the receptor pharmacology of these agents in the context of the migraine cycle may provide insight into the total migraine benefits of treating with a broad receptor binding agent such as DHE versus the limitations of treating with a narrowly targeted therapy. This may further explain why DHE has such a high response rate even in the most difficult to treat migraines.

Objectives: To review the comparative pharmacology of acute treatments for migraine.

Methods: A literature review was conducted to compare the pharmacology and biological activity of new and existing migraine specific treatments.

Results: Comparative receptor binding of current and new migraine specific therapies is presented in tabular format. A model was created to show where in migraine progression each acute migraine specific therapeutic acts to address migraine symptoms.

Conclusion: Unlike other migraine therapeutics, DHE interacts with several different receptor subtypes and therefore is able to exert a greater influence over the pathophysiology of the migraine cycle (premonitory thirst, aura, allodynia, hypersensitivity, withdrawal, ictal pain, vasoconstriction, central sensitization, postdrome and interictal period). Moreover, the slow dissociation of DHE from target receptors is thought to sustain its anti-migraine effects therefore reducing headache recurrence rates and medication overuse headaches. Achieving dose-to-dose consistency and optimal plasma concentrations of DHE has been demonstrated to maximize therapeutic gain while providing safety and tolerability in addressing acute migraine. Advances in delivery systems for DHE will address these issues.

Disclosure of Interest: S. Aurora Conflict with: Employee and stock holder of Impel NeuroPharma, S. Ray Conflict with: Employee and stock holder of Impel NeuroPharma, K. Satterly Conflict with: Employee and stock holder of Impel NeuroPharma, S. Shrewsbury Conflict with: Employee and stock holder of Impel NeuroPharma, J. Hoekman Conflict with: Employee and stock holder of Impel NeuroPharma