

## **ANTIDEPRESSANTS ARE THE BEST DRUGS TO TREAT FREQUENT MIGRAINE**

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Frequent migraine and especially chronic migraine is a disabling illness that has substantial impact on patients' ability to perform routine daily activities and on their quality of life. The management of frequent and chronic migraine requires a multidisciplinary team and includes strategies directed to the identification and management of risk factors, the frequent use of nonpharmacological treatment and assessment and treatment of the frequent neuropsychiatric and comorbid conditions.

There are several pharmacological strategies in the management of frequent migraine but we will concentrate our discussion on the antidepressants as drugs of first line in the management of this condition.

Antidepressants consist of a number of different classes of drugs with different mechanisms of action. For the purpose of this discussion we will concentrate our interest in the monoamine reuptake inhibitors, including the non-selective tricyclic antidepressants (TCAs), the selective serotonin reuptake inhibitors (SSRIs) and the dual compounds: the selective serotonin and norepinephrine reuptake inhibitors (SNRIs). Antidepressants are useful in treating many chronic pain states, including headache, independent of the presence of depression, and the response occurs sooner than the expected antidepressant effect.

TCAs were first shown to be effective in preventing tension type headaches in 1964. In a recent meta-analysis of TCAs in headache 37 studies were included: 17 studies in tension-type headache, 13 in migraine and 6 in chronic headache (mixed migraine and tension-type, probably most of them chronic migraine). It was found that tricyclic antidepressants substantially reduced the pain from both migraine and tension-type headaches. Patients treated prophylactically with tricyclics experienced about 1 standard deviation of improvement in headache burden, a clinically large effect. Patients with tension-type or migraine headaches were 40-70% more likely to report at least a 50% improvement in headaches. Most of the studies used amitriptyline and in fact this drug is the antidepressant with most consistent support for efficacy in migraine prevention. Other TCAs with positive results in some trials have been clomipramine, nortriptyline, doxepin and protriptyline. Another important finding of the meta-analysis is that the effect of the TCAs seems to increase over time; patients in the first month of treatment had less improvement than those treated for six months; this is consistent with clinical practice.

Amongst the SSRIs fluoxetine worked better than placebo in some trials and the results with other SSRIs are more controversial. When we compare the efficacy of TCAs against the SSRIs, the TCAs are superior in achieving 50% reduction in headaches in the few studies published.

Venlafaxine, a SNRI, has been shown to be effective in a double-blind, placebo-controlled trial and also in a separate placebo and amitriptyline controlled trials in which venlafaxine was equally effective than amitriptyline in reducing pain outcomes in migraine.

Along our presentation we will discuss in detail all the published data about the use of the different antidepressants in frequent migraine: comparative trials with placebo or other compounds, use in clinical practice, clinical guidelines recommendations and use in combination with other drugs.... We are sure that after our presentation the audience will be convinced that antidepressants, alone or in combination with other compounds, are a first line of treatment in the management of frequent migraine.