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Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) for the prevention of tension-type headache in adults.

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Abstract

BACKGROUND: This is an updated version of the Cochrane review published in 2005 on selective serotonin re-uptake inhibitors (SSRIs) for preventing migraine and tension-type headache. The original review has been split in two parts and this review now only regards tension-type headache prevention. Another updated review covers migraine. Tension-type headache is the second most common disorder worldwide and has high social and economic relevance. As serotonin and other neurotransmitters may have a role in pain mechanisms, SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) have been evaluated for the prevention of tension-type headache.

OBJECTIVES: To determine the efficacy and tolerability of SSRIs and SNRIs compared to placebo and other active interventions in the prevention of episodic and chronic tension-type headache in adults.

SEARCH METHODS: For the original review, we searched the Cochrane Central Register of Controlled Trials (CENTRAL 2003, Issue 4), MEDLINE (1966 to January 2004), EMBASE (1994 to May 2003), and Headache Quarterly (1990 to 2003). For this update, we revised the original search strategy to reflect the broader type of intervention (SSRIs and SNRIs). We searched CENTRAL (2014, Issue 10) on the Cochrane Library, MEDLINE (1946 to November 2014), EMBASE (1980 to November 2014), and PsycINFO (1987 to November 2014). We also checked the reference lists of retrieved articles and searched trial registries for ongoing trials.

SELECTION CRITERIA: We included randomised controlled trials comparing SSRIs or SNRIs with any type of control intervention in participants 18 years and older, of either sex, with tension-type headache.

DATA COLLECTION AND ANALYSIS: Two authors independently extracted data (headache frequency, index, intensity, and duration; use of symptomatic/analgesic medication; quality of life; and withdrawals) and assessed the risk of bias of trials. The primary outcome is tension-type headache frequency, measured by the number of headache attacks or the number of days with headache per evaluation period.

MAIN RESULTS: The original review included six studies on tension-type headache. We now include eight studies with a total of 412 participants with chronic forms of tension-type headache. These studies evaluated five SSRIs (citalopram, sertraline, fluoxetine, paroxetine, fluvoxamine) and one SNRI (venlafaxine). The two new studies included in this update are placebo controlled trials, one evaluated sertraline and one venlafaxine. Six studies, already included in the previous version of this review, compared SSRIs to other antidepressants (amitriptyline, desipramine, sulpiride, mianserin). Most of the included studies had methodological and/or reporting shortcomings and lacked adequate power. Follow-up ranged between two and four months.Six studies explored the effect of SSRIs or SNRIs on tension-type headache frequency, the primary endpoint. At eight weeks of follow-up, we found no difference when compared to placebo (two studies, N = 127; mean difference (MD) -0.96, 95% confidence interval (CI) -3.95 to 2.03; I(2)= 0%) or amitriptyline (two studies, N = 152; MD 0.76, 95% CI -2.05 to 3.57; I(2)= 44%).When considering secondary outcomes, SSRIs reduce the symptomatic/analgesic medication use for acute headache attacks compared to placebo (two studies, N = 118; MD -1.87, 95% CI -2.09 to -1.65; I(2)= 0%). However, amitriptyline appeared to reduce the intake of analgesic more efficiently than SSRIs (MD 4.98, 95% CI 1.12 to 8.84; I(2)= 0%). The studies supporting these findings were considered at unclear risk of bias. We found no differences compared to placebo or other antidepressants in headache duration and intensity.SSRIs or SNRI were generally more tolerable than tricyclics. However, the two groups did not differ in terms of number of participants who withdrew due to adverse events or for other reasons (four studies, N = 257; odds ratio (OR) 1.04; 95% CI 0.41 to 2.60; I(2)= 25% and OR 1.55, 95% CI 0.71 to 3.38; I(2)= 0%).We did not find any study comparing SSRIs or SNRIs with pharmacological treatments other than antidepressants (e.g. botulinum toxin) or non-drug therapies (e.g. psycho-behavioural treatments, manual therapy, acupuncture).

AUTHORS' CONCLUSIONS: Since the last version of this review, the new included studies have not added high quality evidence to support the use of SSRIs or venlafaxine (a SNRI) as preventive drugs for tension-type headache. Over two months of treatment, SSRIs or venlafaxine are no more effective than placebo or amitriptyline in reducing headache frequency in patients with chronic tension-type headache. SSRIs seem to be less effective than tricyclic antidepressants in terms of intake of analgesic medications. Tricyclic

antidepressants are associated with more adverse events; however, this did not cause a greater number of withdrawals. No reliable information is available at longer follow-up. Our conclusion is that the use of SSRIs and venlafaxine for the prevention of chronic tension-type headache is not supported by evidence.

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