Efficacy and adverse events of subcutaneous, oral, and intranasal sumatriptan used for migraine treatment: a systematic review based on number needed to treat

Tfelt-Hansen P

Authors' objectives

To assess the efficacy, speed of onset and adverse events of sumatriptan given using various routes of administration for migraine treatment.

Searching

The author searched MEDLINE (over the entire date range, performed in April 1997), using the terms 'migraine', 'sumatriptan', and 'clinical trials'. Printouts from the database on clinical trials on sumatriptan were obtained from Glaxo Wellcome Denmark. The journals 'Archives of Neurology', 'Neurology', 'Headache' and 'Cepalalgia' from 1990 on were handsearched for additional studies. Reference lists from retrieved studies and review articles were checked to identify possible unretrieved reports, and there were no language restrictions placed on the search.

Proceedings of international neurological and headache congresses were searched for reported published only as abstracts. Where necessary copies of the posters presented were obtained. Missing information was provided by the pharmaceutical industry.

If trials were reported as both a conference abstract and a complete paper, only the latter was included.

Study selection

Study designs of evaluations included in the review

Placebo-controlled double-blind randomised clinical trials (RCTs). Studies of doses other than 6 mg subcutaneous, 100 mg oral, and 20 mg intranasal were excluded.

Studies of:

1. Sumatriptan at 12 hours.

2. Recurrence of headache.

3. Comparative trials with other treatments without placebo control.

4. Success rates of oral sumatriptan after 4 hours.

5. Sumatriptan given in the aura phase.

6. Reports on three doses of sumatriptan without the inclusion of placebo, were all excluded from this review.

Specific interventions included in the review

Sumatriptan (6 mg subcutaneous, 100 mg oral, and 20 mg intranasal) versus placebo.

Participants included in the review

Patients being treated for migraine.

Outcomes assessed in the review

A successful response to sumatriptan (reported as response rates and number-needed-to-treat (NNT)) defined as a decrease in head pain from severe or moderate to none or mild at 1 hour for 6 mg subcutaneous sumatriptan, and at 2 hours for 100 mg oral and 20 mg intranasal sumitriptan. The adverse events response rate to sumatriptan (reported as response rates and number-needed-to-harm) was also reported.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The author does not state that they assessed quality.

Data extraction
The author does not state who, or how many of the reviewers, performed the data extraction. data were extracted for the categories of the number of patients responding to sumatriptan, the number of patients responding to placebo, the number of patients with adverse events with sumatriptan, and the number of patients with adverse events with placebo for each of the three methods and doses of administering sumatriptan.

The number of patients responding to sumatriptan and placebo was calculated from the percentages and total number given when the number of patients responding was not given.

Methods of synthesis
How were the studies combined?
The NNT for efficacy, and 95% confidence interval (CI) for efficacy and, when appropriate, for adverse events, were calculated for the combined data for the three forms of administration with a fixed-effect model. Therapeutic gain, response ratios and 95% CIs were calculated by taking the reciprocal of the corresponding NNT values.

How were differences between studies investigated?
The author does not state how differences between the studies were investigated.

Results of the review
Thirty RCTs were included in the review. Twelve trials compared 6 mg subcutaneous sumatriptan with placebo (1,927 participants with sumatriptan and 1,200 participants with placebo); twelve trials compared 100 mg oral sumatriptan with placebo (1,854 participants with sumatriptan and 1,036 participants with placebo); and six trials compared 20 mg nasal sumatriptan with placebo (917 participants with sumatriptan and 503 participants with placebo).

Subcutaneous sumatriptan had a higher therapeutic gain than intranasal and oral sumatriptan early after administration. Intranasal sumatriptan had a small therapeutic gain of 8% at 15 minutes, whereas for oral sumatriptan a similar small therapeutic gain of 10% was found after 30 minutes.

The combined therapeutic gain was 51% (95% CI: 48%, 53%) for subcutaneous sumatriptan at 1 hour, 33& (95% CI: 29.5%, 36%) for oral sumatriptan, whereas for intranasal sumatriptan it was 32% (95% CI: 27%, 38%). The combined therapeutic gains show that 6 mg sumatriptan at 1 hour is superior to either 100 mg oral or 20 mg intranasal sumatriptan at 2 hours.

The NNT for individual trials for a success for 6 mg subcutaneous sumatriptan at 1 hour varied from 1.3 to 2.6, and when the results from all 12 randomised trials were combined the NNT for a success was 2.0 (95% CI: 1.9, 2.1). The NNT for adverse events was 3.0 (95% CI: 2.7, 3.4).

The NNT for a success for 100 mg oral sumatriptan at 2 hours varied from 2.5 to 4.8, and when the results from all 12 randomised trials were combined the NNT for success was 3.0 (95% CI: 2.8, 3.4). The NNT for adverse events was 8.3 (95% CI: 6.3, 12.2).

The NNT for a success for 20 mg intranasal sumatriptan at 2 hours varied from 2.3 to 3.6, and when the results from all 6 randomised trials were combined the NNT for a success was 3.1 (95% CI: 2.7, 3.8). The NNT for adverse events was not reported.

Authors' conclusions

Subcutaneous sumatriptan has a higher efficacy and quicker onset of action than oral and intranasal sumatriptan in the treatment of migraine attacks. Intranasal sumatriptan has the same efficacy as oral sumatriptan and a quicker onset of action than oral sumatriptan, but the magnitude of this therapeutic effect of intranasal sumatriptan is limited in the first 30 minutes after administration.

CRD commentary

The author clearly stated the research question and the inclusion and exclusion criteria. The literature search is limited in its use of keywords and may have missed studies published outside the United States by focusing the electronic search on only the MEDLINE database. There were no language restrictions on the search and the author did seek unpublished data.

The data extracted is reported in tables and graphs and summarised in the text. The statistical analyses were appropriate. The quality of the included studies was not assessed and the author has not reported on how the articles were selected, or how many of the reviewers were involved in the data extraction.

The author has not tested for homogeneity but has only combined trials with specific dosages and routes of administration. The conclusions appear to follow from the results but should be viewed with caution because of the potential methodological limitations of the review.

Implications of the review for practice and research

The author did not state any implications for further research and practice.

Bibliographic details

Tfelt-Hansen P. Efficacy and adverse events of subcutaneous, oral, and intranasal sumatriptan used for migraine treatment: a systematic review based on number needed to treat. Cephalalgia 1998; 18(8): 532-538

PubMedID

9827244

Other publications of related interest

This additional published commentary may also be of interest. Making sense of migraine treatments. Bandolier 1999;59:1-4,7.

Indexing Status

Subject indexing assigned by NLM

MeSH

Administration, Intranasal; Administration, Oral; Double-Blind Method; Humans; Injections, Subcutaneous; Migraine Disorders /drug therapy; Randomized Controlled Trials as Topic; Safety; Serotonin Receptor Agonists /administration & dosage /adverse effects /therapeutic use; Sumatriptan /administration & dosage /adverse effects /therapeutic use; Treatment Outcome; Vasoconstrictor Agents /administration & dosage /adverse effects /therapeutic use

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