Subcutaneous sumatriptan compared with usual acute treatments for migraine: clinical and pharmacoeconomic evaluation

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Subcutaneous sumatriptan 6mg in acute treatments for migraine. Subcutaneous sumatriptan was chosen because of its high biodisposibility and its proven efficacy in relieving pain more quickly than the oral form.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Outpatients who met the International Headache Society criteria for migraine with or without aura and who were between 18 and 55 years of age with at least a 6-month history of 1 to 6 migraine attacks per month of moderate to severe intensity were recruited by neurologists. Women who were pregnant and lactating were excluded. In addition, any patient who met at least one of the following criteria was excluded from the study: use of sumatriptan within the previous 6 months; start or change of prophylactic medication within 3 months prior to the study; a history suggestive of an ischaemic heart and/or atherosclerotic disease; non-controlled hypertension or supine diastolic blood pressure over 95 mmHg; a history within the last year of abuse of alcohol (more than 315 g/week), ergotamine, opiate analgesics, major tranquillisers or other drugs; a history of significant psychiatric illness; any contraindication due to concurrent medical conditions and known hypersensitivity or contraindication to the use of sumatriptan.

Setting
Outpatient clinics in a hospital. The economic analysis was carried out in Belgium.

Dates to which data relate
The dates of the data were not reported.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was prospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. A total of 212 patients satisfied the inclusion criteria.
and were randomised to either the customary treatment group (CTG) or the sumatriptan treatment group (STG). 186 patients completed the pharmacoeconomic cards; 89 of them with a mean (SD) age of 36 (10) years were allocated to the CTG and 97 with a mean (SD) age of 38 (9) years to the STG.

Study design
This was a multicentre open randomized controlled trial, carried out in 18 centres. The follow-up visits took place at 6 and 12 weeks after the initial visit. In each group, 20 patients did not complete the 3-month trial. Some failed to return for the follow-up visit (CTG, 11; STG, 10), some withdrew due to an adverse event (STG, 7) or discontinued for other reasons (CTG, 9; STG, 3). At the initial visit, patients were instructed to use their allocated treatment in the acute phase of a migraine attack. They were asked to use diary cards to record, for each attack, the time of onset, the time of patient-defined meaningful relief, headache severity (from 3 severe to 0 none) before and 2 hours after the first treatment, the medications and therapy used to relieve symptoms, any side effects and the impact of migraine on professional and non-professional activities.

Analysis of effectiveness
The principle used in the analysis of effectiveness was treatment completers only. The health outcome measures were the reduction of headache severity after all attacks from grade 2/3 to grade 0/1 during the first 2 hours after treatment, the time needed for alleviation of migraine, the percentage of patients using medication for adverse events, and the percentage of patients suffering from associated migraine symptoms (vomiting, nausea and photo-/phonophobia) after 1 and 2 hours of treatment. The Migraine and Quality of Life Questionnaire was used to assess the patient's quality of life. The impact on social life was assessed using measures such as number of hours of diminished work-efficiency and suspension of non-professional activity. At the final visit, the STG patients were asked if they wanted to return to their customary treatment. The study groups were comparable in terms of demographic and clinical characteristics.

Effectiveness results
Within 2 hours, headache severity decreased to none/mild in 86% of all attacks in the STG compared to 25% in the CTG. Migraine was alleviated earlier in the STG than in the CTG (median 3.78 versus 13.39 hours, p<0.0001). Significantly more sumatriptan patients reported an improvement in quality of life of more than 20% (61.6 versus 20.6% patients, p<0.001). The STG patients used less medication for adverse events (6.2 versus 22.5%, p<0.001) and suffered less from associated migraine symptoms. The median number of hours of diminished work-efficiency (3 versus 7 hours, p<0.01) or of suspension of non-professional activity (10 versus 24 hours, p<0.001) was also significantly lower in the STG. After 3 months of treatment, 79.5% of the STG patients preferred the subcutaneous drug compared with 12.5% who chose to return to their customary treatment; 8% of the STG patients had no preference.

Clinical conclusions
This randomised open study, which included patients consulting their neurologists for severe headache, shows that subcutaneous sumatriptan 6mg is a well tolerated, well accepted and more effective medication than customary treatment in the acute treatment of migraine during a three-month period. It also gives the patients a better quality of life.

Measure of benefits used in the economic analysis
The measures of benefit were the time needed to achieve pain relief on a migraine treated day and successfully treated patients.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the cost of treatment of migraine (consultation of medical professional, technical examination, hospitalisation, and medication) and treatment of adverse events. The
The perspective adopted in the cost analysis was that of the payer and the health care system. The patients were asked to record all cost-inducing items on a pharmacoeconomic diary card. The sources of unit costs were national or local institutions. The only information reported regarding the price year was that the drug price was based on a source from 1994.

**Statistical analysis of costs**
The Pearson chi-square test was used to compare the difference in costs between the groups.

**Indirect Costs**
Indirect costs were not discounted due to the short time frame of the cost analysis. Quantities were reported separately from the costs. Cost items were reported separately. The cost analysis covered the cost of number of days lost from work as well as the decreased work efficiency during an attack. Calculation of the mean gross wage was based on data gathered from the questionnaire completed by patients at the initial visit. The additional costs paid by the employer were included in the mean monthly gross wage. The perspective adopted in the cost analysis appears to have been that of the society. The price year was not given.

**Currency**
Belgian francs (Bfr).

**Sensitivity analysis**
A sensitivity analysis was not conducted.

**Estimated benefits used in the economic analysis**
The incremental effectiveness in terms of the difference in time needed to achieve pain relief on a migraine treated day was 9.62 hours (13.39 hours in the CTG; 3.78 hours in the STG). The percentage of all attacks successfully treated was significantly higher in the STG (86%) than in the CTG (25%, p< 0.01).

**Cost results**
The direct and total cost of treatment was Bfr133 and Bfr2,012, in the CTG and Bfr1,400 and Bfr2,522 in the STG.

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratios for sumatriptan compared to the usual therapy for were Bfr132 (direct costs) and Bfr53 (total costs) per hour of relieved pain. The total cost per successfully treated patient was lower in the STG.

**Authors' conclusions**
Sumatriptan is more effective, provides a better quality of life, reduces health care resource utilisation, and improves work productivity as compared to the CTG, thereby resulting in a favourable cost-effectiveness ratio.

**CRD COMMENTARY - Selection of comparators**
Usual therapy (customary treatment group) was regarded as the comparator. Customary treatment included analgesics, ergotamine and derivatives, non-steroidal anti-inflammatory drugs, anti-emetics, narcotic analgesics. You, as a database user, should consider whether these are widely used medications in your own setting.

**Validity of estimate of measure of effectiveness**
Whilst the internal validity of the effectiveness results is likely to have been enhanced by the randomised nature of the
study design, it may have been adversely affected by the fact that no power analysis was performed and that the effectiveness analysis was based on treatment completers only. Furthermore, as the authors acknowledged, the effectiveness results have to be interpreted cautiously because the benefits observed in the STG in non-blinded studies might be due to a non-pharmacological effect such as improved medical care or a patient's perception of a new drug. The study groups were comparable in terms of demographic and clinical characteristics and the study sample appears to have been representative of the study population.

**Validity of estimate of measure of benefit**
The estimate of benefits was obtained directly from the effectiveness analysis. This choice of estimate was justified.

**Validity of estimate of costs**
The authors provided sufficient details on the methods applied in the cost analysis. Furthermore, quantities were reported separately from the costs and the perspective adopted in the cost analysis was reported. The effects of alternative procedures on indirect costs were addressed in the analysis. Statistical analyses were performed on cost data and resource consumption. However, the price year was not reported. It should be noted that cost results may not be generalisable outside of the study setting.

**Other issues**
The authors’ conclusion appears to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. It was, however, reported that the data could not be extrapolated to other formulations of sumatriptan. Appropriate comparisons were made with other studies. The degree to which the study sample was representative of the study population was not discussed and the authors noted that the study patients had more severe disease requiring higher consumption of medical care and drugs. Also the migraine patients in this study were relatively young.

**Implications of the study**
This study suggests that sumatriptan should be prescribed to migraineurs who require, or demand, a more rapid onset of relief, or for those who wish to remain at work but are not concerned that their symptoms will recur once they return home. By contrast, dihydroergotamine may prove useful to the migraineur who does not require a rapid onset of relief, but needs to maintain functionality for a longer period of time.

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