The use of nitrates in chronic stable angina

Perras C

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
Prophylactic nitrates (isosorbide dinitrate tablet (ISDN); ISDN sustained release (SR) tablet; nitroglycerin (NTG) ointment; NTG patch; NTG SR tablet; isosorbide mononitrate (ISMN) tablet; ISMN SR tablet; and pentaerythritol (PETN) tablet).

Type of intervention
Secondary prevention; treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with chronic stable angina.

Setting
Secondary care. The economic study was carried out in Canada.

Dates to which data relate
The efficacy data were based on a meta-analysis of clinical trials, the dates of which were not reported. Data from 1992 to 1994 for British Columbia's Pharmacare, and from 1989 to January 1996 for New Brunswick Prescription Drug Program and Blue Cross for the Atlantic Provinces were used to find surrogate indicators for effectiveness. 1995 prices were used in the economic analysis.

Source of effectiveness data
Effectiveness data were based on a review of previously completed studies and analysis of three provincial drug databases to determine duration of therapy and evidence of tolerance. Prescribing patterns and trends were obtained from intercontinental medical statistics data.

Link between effectiveness and cost data
The cost data were not based on the same patients as used in the effectiveness study and the costing was undertaken retrospectively.

Outcomes assessed in the review
In the meta-analysis the outcomes assessed were performance at stress tests, frequency of angina attacks, use of sublingual nitroglycerin, tolerance, patient preferences and adverse effects. In the database analysis the outcomes measured to determine duration of therapy and evidence of tolerance were dose escalation of the prophylactic nitrate
and use of sublingual nitroglycerin over time to determine tolerance, relative duration of nitrate therapy, and switching to a different type of nitrate.

**Study designs and other criteria for inclusion in the review**
Randomized controlled trials comparing nitrates against other nitrates were included in the review.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Not stated.

**Methods of combining primary studies**
Primary studies were combined using meta-analysis.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
No evidence could be found to show the superiority of the newer nitrate preparations compared to ISDN. No studies have evaluated the impact of nitrates on important outcomes such as mortality, myocardial infarction, or quality of life. Each nitrate was not necessarily evaluated for all outcomes and was not necessarily compared to all other nitrates. Patient characteristics, disease severity, co-morbidity and concomitant treatment were often poorly described in the trials. It was determined that patches were the most frequently prescribed nitrate preparation for each of the three databases. NTG-SR and ISDN were the second and third most prescribed nitrates respectively. For these three medications, patients infrequently switched to another nitrate. There were no significant differences between the three nitrates in dose escalation or use of sublingual nitroglycerin. Results of placebo-controlled trials were not incorporated in the meta-analysis, although a review of abstracts indicated that no nitrate appeared to be superior. Overall, results of the databases analyses did not indicate that one nitrate is better.

**Measure of benefits used in the economic analysis**
Given that there was no evidence that any nitrate was superior a cost-minimization analysis was conducted.

**Direct costs**
Estimated costs included drug acquisition costs, mark up, and prescription fees. A mean cost per nitrate type was obtained for each province by summing cost per individual nitrate's strength weighted by their relative volume of claims. Cost data were obtained from 1995 provincial formulary claims from seven provinces, a survey of 1996 prices, and from 1994 IMS cost data.
Currency
Canadian dollars (Can$).

Estimated benefits used in the economic analysis
Not applicable.

Cost results
ISDN had the lowest cost per unit of nitrate for all provinces (ranging from Can$0.0235 in Alberta to Can$0.0458 in Ontario). Patches were the most expensive (Can$1.4308 in Manitoba (0.8mg/h), except in two provinces where ISDN SR tablets were within the range of cost for patches.

Synthesis of costs and benefits
Not applicable.

Authors’ conclusions
In 1995, isosorbide dinitrate had the lowest cost per unit in the provinces. Patches were the most expensive. Large differences in usage patterns between provinces probably reflected whether other nitrates were reimbursed by provincial drug plan. National savings of Can$9 million could be achieved if ISDN replaced other nitrates 50% of the time.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. Isosorbide nitrate (isosorbide dinitrate tablet (ISDN) and ISDN sustained release (SR) tablet) has been a widely prescribed standard and is cheaper than newer nitrate preparations. You, as a user of this database, should consider whether these are widely used technologies in your setting.

Validity of estimate of measure of benefit
The estimate of the measure of benefit was based on a review of clinical trials, but few details are provided about the details of the meta-analysis in this overview. Only a small number of head to head trials with no placebo control were available for the meta-analysis. The use of administrative databases for effectiveness data is subject to a selection bias. This problem was acknowledged and measures were undertaken to correct for it, but no details were provided about the methods applied.

Validity of estimate of costs
Resource quantities were reported separately from the costs. Unit costs of each type of nitrate were, however, reported, and adequate details of the methods of quantity/cost estimation were given.

Other Issues:
The authors’ conclusions were justified, given that there is no difference in effectiveness. Since very few details were provided of the trials included in the meta-analysis, it is not possible to assess whether adequate power was achieved in order to detect any difference in side-effects or tolerance production. Observational data from administrative databases does not provide reliable evidence for this issue either. The costs were based on Canadian provincial formulary claims and hence are not directly generalisable to other countries.

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Bibliographic details

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http://www.ccohta.ca

Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

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