Canadian economic comparison of extended-release oxybutynin and immediate-release tolterodine in the treatment of overactive bladder

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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
Two pharmacological treatments for overactive bladder (OAB) were examined. These were the new extended-release (XL) formulation of oxybutynin (10 mg/day) and immediate-release (IR) tolterodine (4 mg/day).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a cohort of community-dwelling adults with OAB who were eligible for treatment with either drug.

Setting
The setting was secondary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from studies published between 2000 and 2002. Some resource use data came from studies published from 1997 to 2002. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies.

Modelling
A Markov model was constructed to examine the clinical and economic outcomes associated with the two treatments over the course of 1 year. The model was also used to extrapolate data derived from the OBJECT trial (which were limited to a 3-month observation period) to a longer timeframe. The probabilities of transition across states were defined by the severity of the condition over the course of 1 year. They were calculated biweekly over the first 4 weeks and monthly thereafter. Severity states were defined by weekly episodes of total urinary incontinence (TUI): 0 episodes weekly (total continence), 1 to 6 episodes (minimal incontinence), 7 to 21 episodes (mild incontinence), 22 to 42 episodes (moderate incontinence) and more than 42 episodes (severe incontinence).

Outcomes assessed in the review
The outcomes estimated from the literature were treatment efficacy and treatment persistence. Published data were also
used to extrapolate short-term data on the efficacy of treatment over one year.

Study design and other criteria for inclusion in the review
A review of the literature was undertaken to identify relevant primary studies. The inclusion and exclusion criteria were not reported. The majority of data came from the OBJECT trial of 378 patients (mean age 59.1 +/- 13.3 years; 83.3% female). Other data came from an observational study.

Sources searched to identify primary studies
MEDLINE was searched from 1990 to 2003. The key terms "incontinence", "overactive bladder", "oxybutynin" and "tolterodine" were combined with "trial", "cost", "economic", "Canada", "cost-effectiveness", "quality of life", "compliance", "persistence", "adverse events" and "review". The reference lists of relevant papers were also searched. Most of the data came from the OBJECT trial.

Criteria used to ensure the validity of primary studies
Not reported.

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

Number of primary studies included
Five primary studies provided clinical data.

Methods of combining primary studies
A narrative method appears to have been used to combine the primary estimates.

Investigation of differences between primary studies
Not reported.

Results of the review
Based on the results of the OBJECT trial, XL oxybutynin was significantly more effective in reducing episodes of urge incontinence, (p=0.03), TUI episodes, (p=0.02), and frequency of micturition, (p=0.02), than IR tolterodine. It also demonstrated an equivalent tolerability profile.

Based on other published evidence, it was assumed that no further changes in disease severity would take place between months 3 and 12 in patients who were compliant with treatment.

A dropout rate of 2.1% was used to define treatment persistence in the first 3 months, while the relative risk of discontinuation in the following 9 months was derived using an equation.

Measure of benefits used in the economic analysis
The summary benefit measure used was the number of incontinence episodes avoided. Other model outputs were the proportion of patients attaining complete continence, the proportion of patients achieving no or minimal incontinence, the total annual incontinence episodes, and the proportion of patients who continued drug treatment.

Direct costs
The cost analysis was carried out from the perspective of a comprehensive health care payer. The economic evaluation comprised the costs of drug therapy, physician visits, use of pads or other protection, and laundry costs. The unit costs were generally not reported separately from the quantities of resources used, although they were reported for some items. Resource use was estimated on the basis of authors’ opinions and some published evidence. The same acquisition cost appears to have been applied to the two drugs under study. The source of the costs was unclear, although some costs were derived from the Ontario physician fee schedules. The laundry costs were estimated as a proportion of the cost of incontinence products. Discounting was not relevant since the costs were incurred during one year. The price year was 2002.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
Sensitivity analyses were carried out to assess the robustness of the base-case estimates of costs and benefits to variations in some model assumptions. For example, all non-drug costs (25 to 400% of the base-case estimates) and treatment discontinuation rates (up to 400% higher than the base-case estimates). The price of XL oxybutynin was varied from 50 to 200% that of IR tolterodine. In addition, the effect of including co-morbidity and surgery costs was analysed using estimates from the USA and Australia.

Estimated benefits used in the economic analysis
The proportion of patients attaining complete continence was 20.4% with XL oxybutynin and 17.2% with IR tolterodine.

The proportion of patients achieving no or minimal incontinence was 54.3% with XL oxybutynin and 48.7% with IR tolterodine.

The number of days per year with no incontinence episodes was 162.5 with XL oxybutynin and 146.0% with IR tolterodine.

The total annual incontinence episodes were 584.6 with XL oxybutynin and 679.8 with IR tolterodine.

The proportion of patients continuing drug treatment (treatment persistence) was 79.1% with XL oxybutynin and 81.5% with IR tolterodine.

The number-needed-to-treat (NNT) with XL oxybutynin for one additional patient to attain total continence by the end of the year would be 32. The NNT for attaining no or minimal incontinence would be 18.

Cost results
The mean annual costs per patient were Can$656 with XL oxybutynin and Can$688 with IR tolterodine. The difference was Can$23 per patient per year. This increased to Can$42 when the costs of co-morbidities and surgery were included.

Synthesis of costs and benefits
The costs and benefits were not combined in the base-case analysis because XL oxybutynin was the dominant treatment. In effect, it was more effective and less costly than IR tolterodine.

The sensitivity analysis showed that the base-case results were robust to variations in the model assumptions, although increases in the discontinuation rate reduced the additional continence days with XL oxybutynin.

Only changes in the cost of XL oxybutynin altered the conclusions of the analysis. If oxybutynin XL cost $0.11 more than IR tolterodine, net savings would be eliminated.

Authors' conclusions
At price parity, extended-release (XL) oxybutynin reduced costs and provided better results than immediate-release (IR) tolterodine over 1 year of treatment.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear since only pharmacological treatments were considered. The authors stated that pharmacotherapy and bladder retaining represented the two most common conservative approaches to the treatment of OAB. Doses were reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical evidence came from the literature. However, most of the evidence was derived from a published clinical trial, the design of which should ensure the validity of the primary data. The characteristics of the patients included in the trial were reported. Some data were also estimated from other published studies that were found when reviewing the literature. The inclusion and exclusion criteria employed when selecting the primary studies were not reported and, generally, no information on the designs and characteristics of such studies was provided. The exception was an open-label study of XL oxybutynin. The methods used to extract and then combine the primary estimates were not described. Similarly, the comparability of the primary studies was not discussed. Some model inputs were varied in the sensitivity analysis.

Validity of estimate of measure of benefit
Several benefit measures were used in the economic analysis to assess the impact of the interventions on several aspects of health. However, the impact of the treatments on quality of life was not addressed, although this might represent an important issue for patients with OAB.

Validity of estimate of costs
The cost analysis was restricted to those health services relevant to the service provider. The costs associated with the subsequent management of patients were considered in the sensitivity analysis, which demonstrated the weak impact of such costs. Cost items were listed, but information on the unit costs and resource consumption was unclear. This limits the possibility of replicating the analysis in other settings. The source of the data was reported only for few items. Thus, it was unclear whether the costs reflected charges, reimbursement rates, or actual prices. The price year was reported, which aids reflation exercises in other time periods. The cost estimates were specific to the study setting but were varied in the sensitivity analysis.

Other issues
The authors stated that few pharmacoeconomic studies on the treatment of OAB had been carried out. The differences between current findings and a published US model were discussed. The issue of the generalisability of the study results to other settings was not explicitly addressed, but some sensitivity analyses were performed. This enhanced, in part, the external validity of the analysis. The study sample referred to patients with OAB and this was reflected in the authors' conclusions. The authors noted some limitations of their analysis, such as the fact that the clinical estimates were mainly
derived from a single study. In addition, the use of persistent data from clinical trials might not reflect real-world estimates. Finally, the authors stated that they did not investigate the scenario where doses were not fixed.

Implications of the study
The study results support the use of XL oxybutynin for the treatment of OAB in Canada when priced equivalently to IR tolterodine. The authors stated that further clinical trials comparing the two treatments would be required to increase the reliability of the results. Moreover, comparisons of XL oxybutynin with the new long-acting formulation of tolterodine could be of some interest.

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Other publications of related interest


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MeSH
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