Achalasia treatment in the elderly: is botulinum toxin injection the best option?

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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
The use of a botulin toxin injection (BTI) for the treatment of achalasia, a primary oesophageal motor disorder consisting in the incomplete relaxation of the lower oesophageal sphincter (LOS). BTI was injected through a sclerotherapy needle into quadrants up to a total of 80 units.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised elderly patients with clinical, radiographic and manometric features of achalasia.

Setting
The setting was secondary care. The economic study was carried out in Barcelona, Spain.

Dates to which data relate
The effectiveness and resource use data were gathered from January 1998 to December 2000 for the BTI group and between January 1985 and December 1997 for the ED group. No price year was reported.

Source of effectiveness data
The effectiveness evidence came from a single study.

Link between effectiveness and cost data
The costing was performed on the same sample of patients as that used in the effectiveness study. It was carried out prospectively in the BTI group and retrospectively in the ED group.

Study sample
Power calculations to determine the sample size were not performed. Eligible consecutive patients over the study periods were considered. Seventeen patients with an age of 77.6 (+/- 6.4) years (range: 66 - 89) were included in the BTI group. Sixteen patients with an age of 73.9 (+/- 5.3) years (range: 65 - 83) were included in the ED group. There were 7 men in the BTI group and 10 in the ED group. It was not stated whether some patients refused to participate in the study and if the sample was representative of the study population.
Study design
This was a comparative study with a historical comparison group, which was carried out in a single centre. Information on the comparison group came from medical records. In both groups, the patients were evaluated at baseline, and 1, 6, 12 and 18 months after the interventions. The same investigator performed all the interventions. The follow-up assessment was by telephone or at the hospital using a standardised questionnaire. The length of follow-up ranged from 12 to 36 months in the BTI group, and from 12 to 108 months in the ED group. Follow-up data were available for all patients, with the exception of 10 patients who did not provide data on manometries performed before and after treatment in the BTI group. No blind assessment was performed.

Analysis of effectiveness
Except for the analysis on manometries, all patients included in the study were accounted for in the effectiveness analysis. The health outcomes used in the analysis were LOS pressure, change in global symptom score, complications and duration of symptom alleviation. The global symptom score assessed the severity of dysphagia, regurgitation, chest pain and heartburn using a scoring system of 0 (never), 1 (occasionally), 2 (daily) and 3 (with every meal or more than three times a day). The study groups were shown to be similar at baseline in terms of the demographics and clinical conditions.

Effectiveness results
The LOS pressure values changed from 30.7 (+/- 10.6) mmHg at baseline to 16.7 (+/- 5.9) mmHg at the one-month evaluation in the ED group, (p<0.001). In the BTI group these values changed from 29.7 (+/- 12.9) mmHg to 27.4 (+/- 9.4) mmHg, (p=0.7).

After one month, the global symptom score decreased from 5.2 (+/- 1.5) to 1.0 (+/- 1.0) in the BTI group, and from 4.9 (+/- 1.3) to 0.6 (+/- 0.9) in the ED group. The difference did not reach statistical significance, (p=0.08). However, after one year, the average global symptom score was statistically different in the BTI group and in the ED group. The mean score was 2.7 (+/- 1.9) in the BTI group versus 0.7 (+/- 1) in the ED group, (p=0.04).

No major complications were observed.

The duration of symptom alleviation was 48 (+/- 33) months in the ED group and 13.8 (+/- 9.5) months in the BTI group. Thus, keeping patients in clinical remission required 0.26 procedures/patient per year with ED and 0.98 procedures/patient per year with BTI, (p<0.001).

Clinical conclusions
The effectiveness analysis showed that the ED approach for the treatment of achalasia was more effective than the new BTI-based approach in terms of global symptoms and duration of symptom alleviation.

Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was the duration of symptom-free periods with both treatments. It was derived from the effectiveness analysis.

Direct costs
Discounting was not performed. It was unclear whether it was relevant since the time horizon of the cost analysis was not explicitly reported. The unit costs were reported separately from the quantities of resources used. The cost/resource boundary adopted in the study appeared to be that of the health service. The health services included in the economic evaluation were BTI, ED, endoscopic approach for BTI, and hospitalisation. The cost of BTI included only botulin and the endoscopic procedure, while the cost of ED included the endoscopic approach and two days of hospitalisation. The costs were estimated using actual data derived from the Barcelona Medical Council. The resource consumption was estimated from patients' charts collected over the two study periods. No price year was reported.
Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Euros (Euro).

Sensitivity analysis
No sensitivity analyses were conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost per procedure was Euro 355.41 with BTI and Euro 430.34 with ED.

Synthesis of costs and benefits
An average cost-effectiveness ratio was calculated to combine the costs and benefits of the two treatments. The yearly cost per symptom-free patient was Euro 348.31 with BTI and Euro 117.47 with ED.

Authors' conclusions
In the long term, endoscopic dilation (ED) was more cost-effective than the new treatment (botulin toxin injection, BTI) for the treatment of old patients with achalasia. BTI patients required re-interventions and the number of symptom-free days was significantly lower than for the ED patients. Further, the high cost of botulin made it a less attractive option.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. ED was selected because it represented the standard approach for the treatment of patients with achalasia. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a comparative study with a historical control group. The authors justified this in terms of the rarity of the disease. However, there is a significant potential for bias and confounding with this design. There is also a possibility that the results were due to chance since no power analysis was reported and the sample size was small. The fact that the comparison group was historical means that there was a potential for performance bias and selection bias. The groups were comparable for the characteristics assessed at baseline. Hence, some confounding factors were eliminated as a potential problem. There was potential for measurement bias as the presence of the study may have influenced the outcome assessors. These issues may limit the internal validity of the analysis.

Validity of estimate of measure of benefit
The benefit measure was derived directly from the effectiveness analysis. It did not appear to represent a final outcome measure. Thus, its comparability with the benefits of other interventions was limited.
Validity of estimate of costs

The perspective adopted in the study was not reported. Thus, it was unclear whether all the relevant categories of costs were included in the analysis. This affects the internal validity of the results. The actual costs were used, which is good, but discounting was not discussed and the time horizon for the costs was not clear.

The unit costs were reported separately from the quantities of resources used, but no price year was given. This makes reflation exercises in other settings difficult. The cost estimates were specific to the study setting. Uncertainty in the cost results was not investigated, as the costs were treated deterministically and no sensitivity analyses were conducted. All these issues make it hard to generalise the results to other settings.

Other issues

The authors made several comparisons of their findings with those from other studies. However, they did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were not performed, thus the external validity of the analysis was low. The study referred to elderly patients with achalasia and this was reflected in the conclusions of the analysis.

Implications of the study

The study suggests that ED should be considered the most cost-effective treatment for patients with achalasia. BTI does not appear to offer the best therapeutic option, especially in populations, such as the Spanish population, with long life expectancy.

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