A systematic review and meta-analysis of the Chinese literature for the treatment of achalasia
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CRD summary
The authors found that Heller myotomy was the most effective treatment for achalasia in China and appeared safe and durable. The small number and very small sample sizes of controlled studies in the meta-analyses and their questionable quality means that these conclusions may not be reliable.

Authors’ objectives
To evaluate the effectiveness of different treatments for achalasia in China.

Searching
The Chinese Biomedical Database and Chinese Scientific Journals Database were searched to March 2008. Search terms were reported.

Study selection
Controlled or uncontrolled studies of any form of treatment of achalasia were eligible for inclusion, provided that diagnosis was confirmed by clinical, manometric, radiographic and endoscopic means and that studies had more than 10 participants and at least 12 months’ follow up. Outcomes of interest were symptom improvement at one year and treatment failure (defined as lack of improvement in symptom grade of at least 1, or recurrence of symptoms at one year).

The median age of participants ranged from 31 to 53 years; just over half were female. Interventions in the review included botulinum toxin (BoTx) injection of the lower oesophageal sphincter, pneumatic dilation, Heller myotomy, laparoscopic myotomy and/or thoracoscopic myotomy, with or without fundoplication. Response was defined as good-to-excellent response sustained to the end of the observation period without further therapy. Review outcomes included adverse effects. Duration of follow-up ranged from one to 178 months.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
Study quality was evaluated using the Jadad scale, which assesses randomisation, blinding, and management of withdrawals and dropouts. Each study was awarded a score out of a maximum of 5 points. The authors did not state how the assessment was performed.

Data extraction
For controlled studies, risk ratios were calculated from the numbers of events in the two groups of each study, with 95% confidence intervals (CIs). For uncontrolled studies, event rates were extracted as percentages. Data on the type and number of adverse events in each study group were extracted. Two reviewers extracted the data.

Methods of synthesis
Data from controlled studies were combined to calculate pooled risk ratios and 95% CIs. Heterogeneity was assessed using the X² test and I² statistic. If I² was 50% or less, a fixed-effect model was used, otherwise a random-effects model was used. Data from uncontrolled studies were combined to calculate a pooled mean event rate weighted by sample size, with standard errors. Subgroup analysis was conducted to examine the effect of study design (controlled versus uncontrolled).

Results of the review
Forty-three studies were included (n=1,791, range 10 to 125): 12 RCTs (n=587) and 31 uncontrolled studies. Two RCTs were deemed high quality (Jadad score 3) and 10 were deemed low quality (Jadad score 2); three reported their
randomisation method; all explained withdrawals; and none were clearly blinded or described allocation concealment.

**RCTs:**

The remission rate was significantly higher in the pneumatic dilation group than in the BoTx group (risk ratio 1.47, 95% CI 1.23 to 1.77, p<0.0001, I^2=7.8%; seven RCTs) and the relapse rate was significantly lower (risk ratio 0.32, 95% CI 0.16 to 0.65, p<0.001, I^2=0%; three RCTs).

Remission was significantly more likely with a combination of BoTx and pneumatic dilation than with pneumatic dilation alone (p<0.05; one RCT, n=43).

Remission rate was significantly superior with Heller myotomy than with pneumatic dilation (risk ratio 1.48, 95% CI 1.15 to 1.99, p=0.002, I^2=49.7%; two RCTs), with no statistically significant difference in the complication rate.

There was no statistically significant difference in the remission rate between laparoscopic and thoracoscopic myotomy (two RCTs).

**Uncontrolled studies:**

Pneumatic dilation had a weighted mean remission of 86.6% (standard error 23.9) and a relapse rate of 10.7% (standard error 21.0) (five studies, n=667).

Heller myotomy had a weighted mean remission of 94.8% (standard error 10.6) and a relapse rate of 1.5% (standard error 6.3) (five studies, n=354).

Thoracoscopic myotomy had a weighted mean remission of 92.0% (standard error 10.0%) and a relapse rate of 4.91% (standard error 9.0) (three studies, n=64).

**Adverse effects of treatment:**

These included chest pain (associated with BoTx) and perforation and gastro-oesophageal reflux (associated with pneumatic dilatation).

**Subgroup analysis:**

Pneumatic dilation was significantly more effective in uncontrolled than in controlled studies.

**Authors’ conclusions**

Heller myotomy was the best choice for treatment of achalasia in China and appeared safe and durable.

**CRD commentary**

The objectives of the review were clear, but inclusion criteria were poorly defined with respect to both the timeframe for assessing outcomes and the specific measures used. Relevant sources were searched for studies, but only two databases were used. It was unclear whether the search was restricted by language or publication status. Steps were taken to minimise potential reviewer bias and error by having more than one reviewer undertake study selection and data extraction; it was unclear whether this also applied to validity assessment. Some relevant components of validity were assessed, but insufficient details were provided on the quality of individual RCTs (for example, drop-out rates), and it did not appear that the quality of uncontrolled studies was assessed. Appropriate statistical techniques appeared to have been used to combine the controlled studies and to assess for heterogeneity between them, although it did not appear that publication bias was assessed. The large differences in response rates in the uncontrolled studies and the large standard errors associated with the pooled effect measures suggested that it was not appropriate to combine these data. The small number and very small sample sizes of controlled studies in the meta-analyses and their questionable quality means that the authors’ conclusions may not be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that although Heller myotomy appeared to be the most effective treatment for achalasia in China, BoTx was recommended if multiple injections were given or when combined with another treatment modality. Pneumatic dilation was more effective than BoTx, but carried a risk of perforation.

Research: The authors stated that their findings required validation and confirmation and that RCTs were needed to assess the effectiveness of repeated BoTx injections and of BoTx combined with other treatments. RCTs were also needed to determine the effectiveness of laparoscopic myotomy (with or without anti-reflux procedures and/or partial or total fundoplication) and whether it was superior to thoracoscopic myotomy in China. A uniform standard for outcomes assessment in this area of research was needed.

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