

INDIVIDUAL PATIENT DATA META-ANALYSIS OF RCTS OF ANTICHOLINERGIC DRUG TREATMENT.

Aims of Study

Our recent systematic review of randomized controlled trials of anticholinergic drug treatment left as many questions unanswered as it answered(1,2). We were unable to draw any conclusions about whether anticholinergic drug treatment had different effects in different patient groups, such as idiopathic compared to neurogenic overactive bladder syndrome. Or if the effect of treatment varied with age or the drug used. There was a considerable amount of clinical heterogeneity between these studies, but surprisingly little statistical heterogeneity. In an attempt to address these unanswered questions we endeavoured to get the individual patient data from the included studies. An individual patient data meta-analysis is regarded as the gold standard for studies of this type(3), being able to adjust for co-variables measured at the individual level.

Methods

The authors of the original trials were contacted by letter, asking for non-identifiable data to be sent to us. The data of particular interest was specified and a variety of possible formats given. We offered to enter the data if it was only on paper and not in a computer file. A reminder letter was sent to non-responders. Those that still did not reply were sent an e-mail asking for the reasons for non-response. Options were: not enough time, no longer had the data, disagreed with meta-analysis, did not think it ethical, or other.

It was intended to analyse the individual patient data using either a mixed model, or a generalized linear mixed model, with study as a random factor, and the covariates of interest as fixed factors.

Results

Fifty-two studies were included in the original systematic review. One author was responsible for three of these studies and three authors were the first author on two studies each. Addresses were found for the first author of 45 of these out of a potential 46. The results of requesting individual patient data are given in the flow chart. Only two useable data sets were received.

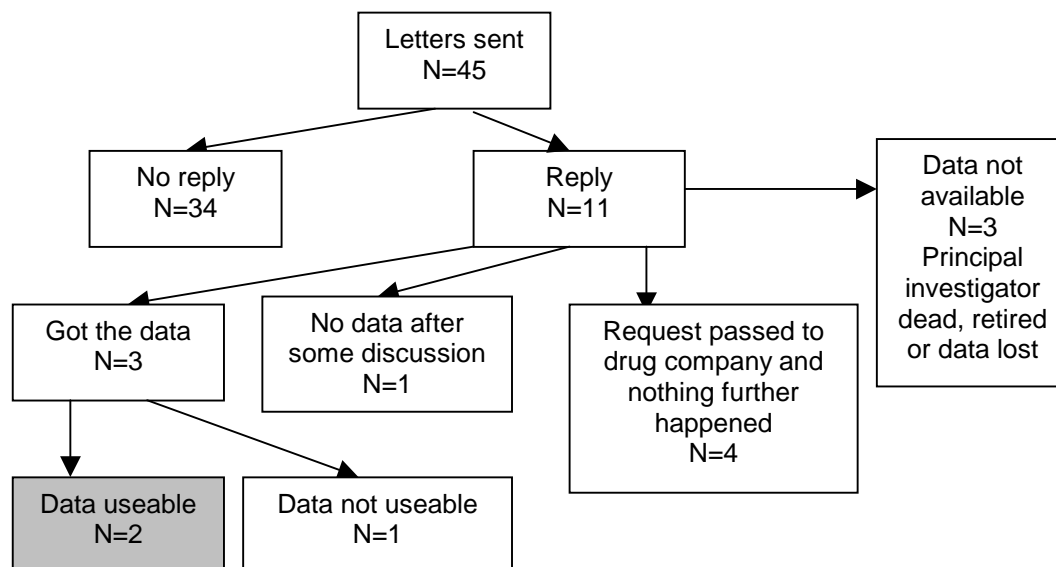


Figure: Results of requesting individual patient data.

E-mails were sent to 21 of the 34 non-respondents whose e-mail addresses we could find. Nine replies were received. Seven of these said that the reason for not responding was that it would take too much time, and two could not find the data. There were no concerns about the ethics of individual patient data meta-analyses, and no one disagreed with the use of meta-analysis.

Conclusions

It was impossible to do an individual patient meta-analysis with the level of response demonstrated here. In the absence of an individual patient meta-analysis the results from the systematic review must be considered the best evidence about the effectiveness of anticholinergic drug treatment. In that review it was found that anticholinergic drug treatment produced statistically significant improvements in the outcomes measured, with no important increase in residual volume, but increased dry mouth. However, the advantage over placebo was small, at one fewer episode of leakage every two days, and one fewer void every two days. This would have to be regarded as the best evidence of treatment differences for all people who receive treatment, regardless of drug and formulation, patient sex and age, and cause of the overactive bladder syndrome.

If individual patient data analyses are considered worthwhile, then a better response than this is necessary. To enable them to happen, the awareness of the benefits needs to become accepted. Some help with transforming the data to a common format would be desirable, so that it does not take much time from the original principal investigator.

Anticholinergic drugs versus placebo for overactive bladder syndrome in adults (Cochrane Review). In: The Cochrane Library, Issue 4, 2002. Oxford: Update Software.

Anticholinergic drugs versus placebo in the treatment of overactive bladder: a systematic review . *BMJ* 2003 (In Press)

Stewart LA, Parmar MKB. Meta-analysis of the literature or of individual patient data: is there a difference? *The Lancet* 1993;341:418–22.