Physostigmine as a treatment for gamma-hydroxybutyrate toxicity: a review

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Authors' objectives
To assess the effect of physostigmine in the treatment of sedation caused by gamma-hydroxybutyrate (GHB).

Searching
MEDLINE was searched for studies published in any language. The reference lists of identified studies were also checked.

Study selection
Study designs of evaluations included in the review
The inclusion criteria were not explicitly defined in terms of the study design. All of the included studies were case series.

Specific interventions included in the review
Studies of physostigmine were eligible for inclusion. In the included studies, physostigmine was administered intravenously at doses of 2 mg one or more times, 1.0 mg, and 0.5 mg times three doses.

Participants included in the review
Studies of patients with GHB-induced sedation were eligible for inclusion. The included studies were of patients with GHB poisoning who were being treated in emergency departments and surgical patients who had been given GHB as part of an anaesthetic regimen. Some patients with GHB poisoning were given naloxone or flumazenil. In the studies of surgical patients, the cointerventions included combinations of diazepam, regional anaesthesia, morphine, alcuronium, neostigmine, naloxone, and thiopentone or althesin.

Outcomes assessed in the review
Studies that reported the reversal or attenuation of sedation were eligible for inclusion. The included studies appeared to assess time till 'awake', 'regained consciousness' or 'recovered' and respiratory rate.

How were decisions on the relevance of primary studies made?
Three authors selected the studies for inclusion

Assessment of study quality
Validity was not formally assessed, but some aspects of validity were discussed in the text, e.g. study design, blinding and confounding by cointerventions.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The data extracted included study design, sample size, study setting and cointerventions.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken.

How were differences between studies investigated?
The differences between the included studies were described in the text.
Results of the review
Four case series (73 patients) were included.

Methodological limitations included the lack of a control group, the use of unblinded studies, and the concurrent use of diazepam in 90% of the patients.

Small case series: there were 2 case series with a total of six patients with GHB overdose. Five of the six patients were reported as improving after the administration of physostigmine.

Larger case series: there were 2 case series with a total of 67 patients undergoing surgery. The first case series reported that 24 of the 25 patients awoke within 10 minutes of being given physostigmine. The second case series found that 36 of the 42 patients awoke within 10 minutes of being given physostigmine.

Authors' conclusions
There was insufficient evidence to assess whether physostigmine should be used routinely for treating toxicity due to GHB.

CRD commentary
The review question was clear in terms of the intervention, participants and outcomes. The inclusion criteria were not defined in terms of the study design. Studies in any language were included and the search terms were stated. The authors acknowledged that limiting the search to studies listed in only one database may have resulted in the omission of other relevant studies. Three reviewers independently selected the studies and this reduced the potential for bias and errors. The methods used to extract the data were not described, so it is not known whether efforts were made to reduce errors and bias. Validity was not formally assessed, but some methodological limitations of the studies were discussed in the text. A narrative synthesis was appropriate given the small number of studies. The evidence presented appears to support the authors' conclusions.

Implications of the review for practice and research
Practice: The authors stated that there was insufficient evidence to recommend the routine use of physostigmine in toxicity due to GHB.

Research: The authors stated that further research is required to assess whether physostigmine should be used to treat toxicity due to GHB.

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MeSH
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.