Oxime therapy and outcomes in human organophosphate poisoning: an evaluation using meta-analytic techniques

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CRD summary
This review concluded that oxime therapy for organophosphate poisoning is associated with either no effect or possible harmful effects compared with standard therapy, and ongoing assessment is necessary. Given the poor reporting of review methods, the limited search strategy and variation between the included studies, the authors' conclusions should be interpreted with caution. However, the identified need for further assessment seems appropriate.

Authors' objectives
To evaluate the effectiveness of oxime therapy for organophosphate poisoning (OPP) in humans.

Searching
MEDLINE and TOXLINE were searched from inception to May 2005. The search terms were provided and no language restrictions were applied. Review articles were also examined for additional articles.

Study selection

Specific interventions included in the review
Studies that compared therapy with oximes and standard care (defined as atropine, ventilation, or other supportive care) to standard care alone were eligible for inclusion. In the included studies, varying doses of pralidoxime (3.5 g to 36 g) or obidoxime were used. The reported times from ingestion to oxime administration ranged from less than 6 hours to less than 24 hours.

Participants included in the review
Studies that evaluated humans with acute OPP were eligible for inclusion. The mean and median ages of the participants in the included studies ranged from 23 to 36 years, and the proportion of patients with severe poisoning was between 26 and 52%.

Outcomes assessed in the review
Studies that assessed hospital mortality rate or the need for mechanical ventilation were eligible for inclusion. The secondary outcomes included need for intensive care therapy and incidence of intermediate syndrome.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The validity of the included studies was assessed in an unblinded fashion and, although it was not reported how many reviewers performed the assessment, it was stated that disagreements were resolved by consensus. The included studies were assessed on the basis of mode of randomisation, definition of inclusion and exclusion criteria, objective criteria for intubation, need for intensive care and intention-to-treat analysis. No formal quality assessment (quality score) was conducted.

Data extraction
The data were extracted using a standardised data abstraction form. The authors did not state how many reviewers performed the data extraction. When necessary, the authors of the included studies were contacted to clarify study details. Data were extracted on a variety of baseline characteristics, such as the time from ingestion to oxime administration and the severity of poisoning. The measure of interest was the risk difference (RD) between treatment groups. However, it was not reported whether the authors extracted this or calculated it if unavailable.

Methods of synthesis
How were the studies combined?
The studies were categorised as retrospective or prospective and then a random-effects pooled estimate of RD, with 95% confidence intervals (CIs), was calculated for each group and all studies combined.

How were differences between studies investigated?
Heterogeneity was assessed using the Q statistic. A P-value of less than or equal to 0.1 indicated the presence of significant heterogeneity.

Results of the review
Seven studies were eligible for inclusion: two randomised controlled trials (RCTs; n=131), one historically controlled study (n=45), three retrospective studies (n=143) and one prospective trial (3 treatment arms; n=63).

Inclusion criteria were defined in six of the studies, and two studies were blinded. The studies were judged to be balanced at baseline in terms of a number of important characteristics.

Looking at the prospective studies alone, oxime therapy was associated with a statistically significant harmful effect compared with standard therapy in terms of mortality (RD 0.18, 95% CI: 0.06, 0.30; 3 studies), mechanical ventilation (RD 0.27, 95% CI: 0.14, 0.40; 3 studies), need for intensive care therapy (RD 0.29, 95% CI: 0.04, 0.53; 1 study) and incidence of intermediate syndrome (RD 0.31, 95% CI: 0.13, 0.49; 1 study). All of the retrospective studies showed no statistically significant effect of oxime therapy in comparison with standard therapy for any of the outcomes. The need for intensive care therapy was the only outcome for which oxime therapy remained statistically significantly more harmful than standard therapy when the retrospective and prospective studies were combined (RD 0.19, 95% CI: 0.01, 0.36; 3 studies).

Authors’ conclusions
Oxime therapy is associated with either no effect or a possible harmful effect. Ongoing assessment of the role of oximes in OPP is necessary.

CRD commentary
The review question was clear and explicit in terms of the interventions, participants, study designs and outcomes of interest. Although the search strategy that was employed had no language restrictions, it was limited and no attempts were made to locate unpublished studies; this means that potentially relevant articles might have been omitted from the review. The reporting of the review methodology employed was poor, so it is unclear whether there was a potential for bias or error to have been introduced throughout the review process. The methodological quality of the original studies was assessed but, again, limited reporting of methods and results make it difficult for the reader to judge the reliability of the assessment.

The use of meta-analyses for every outcome might have been inappropriate given the heterogeneity between studies, particularly in terms of the design and interventions. The lack of reporting of review methods, the limited search strategy, and the variation between the included studies mean that the authors’ conclusions should be interpreted with caution. However, the need for further assessment, as identified by the authors, seems appropriate.

Implications of the review for practice and research
Practice: The authors stated that caution must be exercised by the treating clinician when using oximes for human OPP.

Research: Further RCTs, with appropriate patient stratification, are needed to understand the role of oximes in human OPP more fully.

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