Immunosuppressive therapy in lung injury due to paraquat poisoning: a meta-analysis
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CRD summary
This review aimed to determine the efficacy of immunosuppressive therapy in lung injury due to paraquat poisoning. The authors’ conclusion that further research was required seems reasonable.

Authors' objectives
To determine the efficacy of immunosuppressant therapy in the management of lung injury due to paraquat poisoning.

Searching
MEDLINE and CINAHL were searched from 1980 to 2006 without language restriction; search terms were reported. References of selected articles and reviews as well as personal files were also checked for additional relevant studies.

Study selection
Randomised controlled trials (RCTs) and non-randomised studies with or without historical controls that investigated immunosuppressive therapy with glucocorticoids and cyclophosphamide in patients with paraquat poisoning and which reported mortality data were eligible for inclusion in the review. Any control group was required to be managed with supportive care alone.

Two reviewers independently selected papers for inclusion in the review. Disagreements were resolved by consensus.

Assessment of study quality
The validity of the included studies was evaluated using the Jadad scale (a 5-point scale that assesses the adequacy of reported randomisation, blinding and withdrawals/dropouts). A study with a score of 2 or more was considered to be of low quality. Studies with a score of 3 or more were deemed to be of high quality.

The authors stated neither how the papers were assessed for validity nor how many reviewers performed the validity assessment.

Data extraction
Binomial proportions were extracted from observational studies in order to calculate the efficacy of immunosuppressive therapy (the expected proportion was the success rate of each study included) and 95% confidence intervals (CI) were calculated using the Newcombe-Wilson method. Relative risks and 95% CIs were extracted from all RCTs.

Data were extracted onto a standard extraction form. The authors stated neither how data were extracted nor how many reviewers performed the data extraction.

Methods of synthesis
Studies were pooled using meta-analysis. A random-effects model was used for the controlled studies. Summary estimates from observational studies were reported as success rates with 95% CI. Estimates from controlled studies were reported as relative risk with 95% CI. The number needed to treat was calculated. Statistical heterogeneity was assessed using Cochrane's Q statistic (significance p=0.1), $X^2$ test, $I^2$ statistic and visual inspection of the forest plots. Publication bias was assessed using Begg's funnel plot.

Results of the review
Twelve studies were included in the review (n=497): four observational studies without controls (n=39); six observational studies with historical controls (n=314); and two RCTs (n=144). Jadad scores for the two RCTs were 1 and 3.
No statistically significant between-group difference for mortality was found for the two RCTs (relative risk 0.6, 95% CI: 0.27 to 1.34). Evidence of statistical heterogeneity was found with Cochran Q (p=0.045), but not with $X^2$ (p=0.21). In the non-randomised studies with historical controls, a statistically significant effect in favour of immunosuppressive therapy was found (relative risk 0.55, 95% CI: 0.39 to 0.77). Evidence of statistically significant heterogeneity was found (Cochran Q p=0.001, $X^2$ p=0.001 and I$^2$=72.9%). The survival rate in the four uncontrolled studies was 74.4% (95% CI: 58.9% to 85.4%). Visual inspection of the forest plot indicated heterogeneity.

The number needed to treat for observational studies was three (95% CI: 3 to 4) and for RCTs was five (95% CI: 3 to 14); when combined, one out of four patients (95% CI: 3 to 5) were treated successfully with immunosuppressive therapy.

The funnel plot showed evidence of significant publication bias for the outcome of mortality in all the controlled trials.

Authors' conclusions
One in four patients were treated successfully with immunosuppressive therapy for paraquat poisoning, but significant heterogeneity and publication bias was found. A large RCT was recommended to confirm the role of immunosuppression in paraquat poisoning.

CRD commentary
The review question was supported with clear inclusion criteria. Several sources were searched without language restriction. Publication bias was assessed. Methods used to select studies were likely to minimise the possibility of reviewer error and bias, although it was unclear whether similar methods were undertaken to extract data and assess internal validity. The quality of the included studies was assessed, but the Jadad was not an appropriate choice of tool for observational studies. Studies were combined using standard meta-analytic techniques and statistical heterogeneity was evaluated. The authors did not attempt to assess possible reasons for the heterogeneity that was found. The treatment of small uncontrolled observational studies as a single population to provide an overall treatment success rate did not seem appropriate. However, despite some limitations with the review, the authors' conclusion that further research was required seems reasonable given the limited available evidence.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that a large RCT was required to confirm the efficacy of immunosuppressive therapy for paraquat poisoning.

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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.