Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials


Authors' objectives
To obtain reliable estimates of the effects of neuraxial blockade with epidural or spinal anaesthesia on post-operative morbidity and mortality

Searching
Current Contents (from 1995 to 1996), EMBASE Excerpta Medica (from 1980 to 1996), MEDLINE (from 1966 to 1996) and the Cochrane Library (1998) were searched. The keywords were 'regional anaesthesia', 'regional anaesthesia', 'spinal' or 'epidural', and the Cochrane Collaboration search terms for randomised trials. The authors' names and study titles of identified trials were then used as search terms. Other sources were reference lists of all identified papers and handsearches of selected conference proceedings. Authors were also asked about other relevant studies (published or unpublished). Published and unpublished studies reported in any language were eligible.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included. Trials were excluded if data were not available before 1 January 1997.

Specific interventions included in the review
Studies in which intra-operative neuraxial blockade (with thoracic or lumbar epidural or spinal anaesthesia) was compared with no neuraxial blockade were eligible. Combinations of general anaesthesia and neuraxial blockade and regimes where neuraxial blockade was continued post-operatively were included.

Participants included in the review
The included studies were in patients undergoing general surgery and orthopaedic, urology, vascular and other types of surgery.

Outcomes assessed in the review
Post-operative morbidity and mortality were assessed. Post-operative morbidity included vascular events, bleeding, infection, respiratory failure and renal failure. Mortality included the overall mortality within 30 days of randomisation, and death from pulmonary embolism, cardiac events, or stroke, other causes and unknown causes. The definitions of events were those used by the original authors.

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

Assessment of study quality
No formal validity assessment was undertaken, although the influence of some aspects of validity (number of patients originally randomised not available, more than 5% of patients lost to follow-up, and more than 5% of neuraxial blockade group excluded after randomisation) on the results was assessed.

Data extraction
Two reviewers independently extracted the data, on an intention-to-treat basis where possible. Standard data collection sheets were used. A third reviewer compared the two sets of data collection sheets and any differences were resolved by
discussion. Attempts were made to contact the authors to verify the data and obtain additional unpublished data. The data extracted were: study characteristics; type of surgery; the number of patients per treatment arm; intervention details; concurrent use of general anaesthesia; and the number of patients with each outcome event. [A: Details of the included studies were presented in tables that are available on the BMJ web site (see URL)].

Methods of synthesis
How were the studies combined?
Odds ratios (ORs) with 95% confidence intervals (CIs) and a two-sided P-value were calculated for each outcome, using Peto's modification of the Mantel-Haenszel method (see Other Publications of Related Interest).

How were differences between studies investigated?
Statistical heterogeneity was assessed using a chi-squared test. The influence of type of anaesthesia on mortality was examined for: spinal versus epidural anaesthesia; neuraxial blockage continued post-operatively versus not; and neuraxial blockage combined with general anaesthesia versus neuraxial blockage alone. Sensitivity analyses assessed the effect of the following factors on total mortality: methodological problems in the trials; exclusion of trials that were stopped before scheduled completion; exclusion of unpublished data; and trial size. The authors also used indirect comparisons to compare mortality rates between spinal and epidural anaesthesia.

Results of the review
A total of 141 RCTs (9,559 patients) were included.

Neuraxial blockage significantly reduced overall post-operative mortality within 30 days of randomisation; the OR was 0.70 (95% CI: 0.54, 0.90, P=0.006). No clear difference was observed between different surgical groups. No significant heterogeneity was found (P=0.50).

Spinal and epidural anaesthesia were compared directly in 7 trials that found no difference in mortality (the event rates were very low). The authors then reported indirect comparisons which may be seriously misleading. The results for neuraxial blockage continued post-operatively versus not continued, and for neuraxial blockage combined with general anaesthesia versus neuraxial blockage alone, also appear to be based on indirect comparisons of groups of patients treated in different trials.

Venous thrombosis, cardiac events and stroke.

Deep vein thrombosis (18 RCTs) was significantly reduced with neuraxial blockage (OR 0.56, 95% CI: 0.43, 0.72). Pulmonary emboli (23 RCTs) were significantly reduced with neuraxial blockage (OR 0.45, 95% CI: 0.29, 0.69). Myocardial infarction (30 RCTs) was reduced with neuraxial blockage (OR 0.67, 95% CI: 0.45, 1.00), but the reduction did not reach statistical significance. There was no significant difference in stroke (OR 0.85, 95% CI: 0.46, 1.57).

Bleeding.

Peri-operative transfusion requirements (16 RCTs) significantly reduced with neuraxial blockage; the OR for peri-operative transfusion of greater than 2 units was 0.50 (95% CI: 0.39, 0.66). Post-operative bleeds requiring transfusion (12 RCTs) were significantly reduced with neuraxial blockage (OR 0.45, 95% CI: 0.29, 0.70). No clear differences were found across surgical groups.

Post-operative infection. There was no significant difference in wound infection (14 RCTs); the OR was 0.79 (95% CI: 0.47, 1.33). Pneumonia (28 RCTs) was significantly reduced with neuraxial blockage (OR 0.61, 95% CI: 0.48, 0.76; heterogeneity P=0.05). There was no significant difference in death from other infective causes (6 RCTs); the OR was 0.33 (95% CI: 0.10, 1.07).

Other events.

Respiratory failure (8 RCTs) was significantly reduced with neuraxial blockage (OR 0.41, 95% CI: 0.23, 0.73).
was no significant difference in renal failure (10 RCTs); the OR was 0.57 (95% CI: 0.32, 1.00). Other results were also reported.

The testing of the influence of methodological problems and the type of anaesthesia was hampered by the lack of power to detect even moderate differences.

**Authors' conclusions**

Neuraxial blockade reduces post-operative mortality and other serious complications. The size of some of these benefits remains uncertain, and further research is required to determine whether these effects are due solely to the benefits of neuraxial blockade or due partly the avoidance of general anaesthesia.

**CRD commentary**

The review question was clear in terms of the study design, participants and intervention. The possibility of publication bias and the omission of relevant studies was reduced by searching for published and unpublished studies without language restriction. The methods used to select the studies were not described and the adequacy of the methods used cannot, therefore, be assessed. Only RCTs were included, but no formal validity assessment was undertaken. Thus, the quality of the evidence cannot be judged. The data were extracted in duplicate, which reduces the potential for bias and errors [A: and relevant information on the included studies were presented in tables on the BMJ web site]. The data were appropriately combined in a meta-analysis, statistical heterogeneity was assessed and some aspects of validity were explored in the sensitivity analyses. The discussion considered some limitations of the review, such as the probability of missing some occurrences of events, the underestimation of the incidence of undiagnosed nonfatal events, and the lack of data for many outcomes resulting in wide confidence intervals. The data shown appear to support the conclusion about overall mortality, but the analysis of mortality by type of anaesthesia is very dubious because it is based on indirect comparisons. For the subgroup analyses and the morbidity outcomes, it is not entirely clear if the data were appropriately pooled or if the events were just added as if from one large trial and then used to calculate the OR. These results require cautious interpretation.

**Implications of the review for practice and research**

**Practice:** The authors state that the findings of the review support more widespread use of neuraxial blockade.  

**Research:** The authors state that further research is required to determine whether the effects shown are due solely to the benefits of neuraxial blockade or due partly to the avoidance of general anaesthesia. Research is also required to determine whether neuraxial blockade is indicated or contraindicated in patients at risk of cardiac complications.

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**Other publications of related interest**

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