Perioperative supplemental oxygen therapy and surgical site infection: a meta-analysis of randomized controlled trials

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CRD summary
The authors concluded that compared with standard inspired oxygen concentration, perioperative supplemental high inspired oxygen therapy was associated with a significant beneficial effect in prevention of surgical site infections. The authors' conclusions reflected the evidence presented. However, a degree of caution might be required in interpreting the authors' conclusions given the methodological concerns about the review methods.

Authors' objectives
To compare the efficacy of high inspired oxygen concentrations with standard concentrations in the prevention of surgical site infections.

Searching
MEDLINE, EMBASE and unspecified Cochrane databases were searched without language restriction. MEDLINE was searched from January 1966 to September 2007; no search dates for other databases were reported. Search terms were reported. Symposia proceedings, poster presentations and abstracts from major surgical and anaesthetic meetings were searched from 1998 to 2007. Reference lists of relevant publications were screened.

Study selection
Randomised controlled trials (RCTs) that compared high inspired oxygen concentrations with normal inspired oxygen concentrations perioperatively were eligible for inclusion. Moribund, paediatric and neonatal patients were excluded, as were patients with obesity, hypercapnia and hyperbaric ventilation. Studies of purely laparoscopic procedures and minor outpatient surgery were excluded. The review outcome was surgical site infection defined using recognised clinical and/or microbiological criteria.

Most included trials were multicentre trials conducted in Europe and Australasia; others were single-center trials conducted in USA and Israel. All trials used 80% oxygen as the hyperoxic concentration. Most trials used 30% oxygen for the control concentration; one trial used 35% oxygen. Most trials continued oxygen supplementation for two hours postoperatively. Most trials used a nitrous oxide mixture for the control group. Most trials only included colorectal-specific procedures. Use of prophylactic antibiotics varied between studies.

The authors stated neither how papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The quality of studies was assessed using the Jadad five-point scale to evaluate randomisation, blinding, withdrawal and allocation concealment.

Three reviewers independently performed the validity assessment. Any disagreements were resolved by consensus.

Data extraction
Data on the number of patients who experienced an event were extracted using a standardised form. Relative risks (RRs) were calculated, with 95% confidence intervals (CIs).

Three reviewers independently extracted data from studies. Any disagreements were resolved by consensus.

Methods of synthesis
Studies were combined in meta-analyses using the fixed-effects model (Mantel-Haenszel method). Pooled relative risks
with 95% CIs were calculated. Relative risk reduction (RRR), absolute risk reduction (ARR) and number needed-to-treat (NNT), with 95% CIs, were calculated. Statistical heterogeneity was assessed using the \( I^2 \) statistic. Publication bias was investigated using a funnel plot and Egger regression test. Sensitivity analyses were conducted to examine the effect of excluding non-colorectal studies, nitrous oxide studies, the largest study and the study that used 35% inspired oxygen in controls.

**Results of the review**

Five double-blind RCTs (n=3,001) were included in meta-analyses. Four studies were judged as high quality (Jadad score of 5). The maximum follow-up duration was 30 days.

Compared with standard inspired oxygen concentration, high inspired oxygen concentration was associated with a significant reduction in surgical site infections (RR 0.74, 95% CI 0.60 to 0.92, NNT 33.0, 95% CI 18.8 to 90.9; five RCTs).

Sensitivity analyses showed that the beneficial effect from increasing oxygen concentration was greater in colorectal-specific procedures (RR 0.56, 95% CI 0.38 to 0.81; three RCTs). Although most sensitivity analyses did not materially affect results, sensitivity analysis with exclusion of the largest study resulted in a non-significant effect of high inspired oxygen concentration in the prevention of surgical site infections.

Significant heterogeneity was observed in the outcome of surgical site infections when combining all studies (\( I^2 = 65.6\% \)) and the sensitivity analysis by excluding the largest study (\( I^2 = 74.2\% \)). Potential publication bias was suggested by visual scanning of the funnel plot, but this was not supported by Egger's regression test.

**Authors' conclusions**

Perioperative supplemental high inspired oxygen therapy was associated with a significant beneficial effect in the prevention of surgical site infections compared with standard inspired oxygen concentration.

**CRD commentary**

This review's inclusion criteria were clear. Several relevant databases were searched. Efforts were made to find published and unpublished studies without language restriction, which minimised potential for publication and language biases. Potential publication bias was suggested by visual investigation of funnel plots, but evidence of publication bias was ruled out by Egger's regression test. Use of funnel plots to assess publication bias might not have been appropriate given the small number of studies. Steps were taken to minimise bias by having more than one reviewer undertake data extraction and validity assessment; it was unclear whether the process of study selection was also performed in duplicate. Relevant criteria were used to examine study quality. Statistical heterogeneity was assessed and significant heterogeneity was found in the primary outcome. Using a fixed-effects model to pool the outcomes in the presence of significant heterogeneity might not have been appropriate. The authors' conclusions reflected the evidence presented. However, a degree of caution might be required in interpreting the authors’ conclusions given the methodological concerns outlined above.

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

**Practice:** The authors stated that perioperative supplemental high inspired oxygen therapy should be used along with maintenance of normothermia, meticulous glycaemic control and preservation of intravascular volume perioperatively in prevention of surgical site infections. Use of hyperoxia to reduce wound infection, particularly during colorectal surgery, should be recommended.

**Research:** The authors did not state any implications for research.

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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.