General Anesthesia

Best evidence in anesthetic practice

Prevention: supplemental oxygen reduces the incidence of surgical-wound infection

Article appraised

Grief R, Akça O, Horn E-P, Kurz A, Sessler DI, for the Outcomes Research Group. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 2000; 342: 161–7.

Structured abstract by Peter Choi, Department of Anesthesia, McMaster University, Hamilton, Ontario, Canada.

Question: Can supplemental administration of oxygen during the perioperative period decrease the incidence of postoperative wound infections in patients undergoing colorectal resection?

Design: Multicenter, randomized, double-blind, controlled trial.

Setting: Three hospitals in Europe (Austria and Germany).

Patients: Five hundred patients between 18 to 80 yr of age (mean age 57 yr, 44% women) undergoing elective open colorectal resection. Exclusion criteria were minor colon surgery, recent history of fever or infection, serious malnutrition, and bowel obstruction.

Intervention: Two hundred fifty patients were allocated to 30% oxygen / 70% nitrogen (30% O₂ group); 250 patients were allocated to 80% oxygen / 20% nitrogen (80% O₂ group). Both received the assigned concentrations during anesthesia until immediately before extubation when oxygen was increased to 100%. After extubation, as soon as deemed safe by the anesthesiologist, the oxygen concentration was returned to the allocated levels for the first two hours of recovery.

Main outcomes: Fifteen-day incidence of surgical-wound infection was the primary outcome. ASEPIS score, white-cell counts, time to first solid food, time

to staples removal, duration of postoperative hospitalization, proportion of ICU admission, and 15-day mortality were secondary outcomes. Amounts of collagen and protein deposition were measured in a subgroup of patients (32 receiving 30% O₂; 22 receiving 80% O₂).

Main results: Analysis was intention-to-treat. Clinical characteristics, diagnoses, surgical procedures and duration, hemodynamic values, use of anesthetics, and types and duration of prophylactic antibiotic administration were similar between both groups. Overall incidence of surgical wound infections was 8%. The 80% O₂ group had fewer wound infections (5.2%) compared to the 30% O₂ group (11.2%) [absolute risk reduction 6.0%; 95% confidence interval 1.2–10.8%; number-needed-to-treat 17; *P*=0.01]. Similarly, the mean ASEPIS score was lower in the 80% O₂ group (3 ± 7) compared to the 30% O₂ group (5 ± 9; *P*=0.01). There were no statistically significant differences between groups for the other outcomes.

Conclusion: Administration of 80% supplemental oxygen during colorectal resection and for two hours afterwards halved the 15-day incidence of surgical-wound infection.

Funding: U.S. National Institutes of Health, Fonds zur Förderung der wissenschaftlichen Forschung, Joseph Drown Foundation, Anesthesia Patient Safety Foundation, Max Kade Foundation, Erwin-Schrödinger Foundation, Bürgermeister Fond der Stadt Wien, Austrian National Bank Fund.

Correspondence: Dr. Sessler, Outcomes Research Group, Department of Anesthesia, 374 Parnassus Avenue, Third Floor, University of California – San Francisco, San Francisco, CA 94143-0648, USA. Email: sessler@anesthesia.ucsf.edu

Commentary by A. Denault, D. Fréchette

Greif *et al.* demonstrated that the use of supplemental oxygen reduced the frequency of surgical-wound infections in colorectal surgery patients by half from 11.2% to 5.2%. In evaluating a randomized controlled trial on therapy, validity and applicability of the results to my population are the critical issues.¹

In this single-blind randomized trial, the surgeons evaluating the wounds were blinded to oxygen concentration and all patients entering the trial were accounted for. Both groups were treated equally, apart from a higher end-tidal isoflurane concentration in the 80% O₂ group. This difference was small and clinically insignificant. Thirty-eight patients in the 30% O₂ group required higher FiO₂ but the duration of exposure is unknown. The definition of malnourished patients, who were excluded, is unclear. This group is unlikely to be immunocompetent and could be the one that benefits most from an intervention aiming to reduce rates of infection. The authors do not give a rationale for selecting two hours of 80% O₂ as the intervention.

How large is the treatment effect? This was significant for the 80% O₂ group with an absolute risk reduction in surgical wound infection of 6%, which represents a number-needed-to-treat of 17. However, the confidence intervals for surgical wound infection rates did overlap between the 30% O₂ group (7.3% to 15.1%) and the 80% oxygen group (2.4% to 8.0%). Patients with postoperative infections had longer duration of hospitalization but the duration did not differ between the study groups.

How can we explain that exposure to higher oxygen concentration reduces the risk of infection but not the duration of hospitalization? Safety was documented in a subgroup of 30 patients receiving 80% O₂. There were no significant side effects such as atelectasis. This would reassure clinicians about the safety of such a treatment. Kotani *et al.* have shown that hyperoxia (100% FiO₂) can prevent a decrease in antimicrobial therapy of alveolar macrophages and increase pro-inflammatory cytokines.² However, several studies have demonstrated that hyperoxia can be harmful to the lung and inactivate surfactant. This cellular damage would not be seen necessarily with conventional imaging studies such as chest radiograph or computed tomography. Caution to the universal application of high oxygen concentrations has been suggested by Knight and Holm.³

Do the results apply to all postoperative patients? On one hand, the study population had a non-sterile surgical site that is different from the wound from an elective orthopedic procedure in which surgery is performed in a sterile environment. In the latter, would a

benefit be observed? On the other hand, the treatment is so simple and inexpensive that one could argue that the cost-effectiveness of such a strategy is not prohibitive. In the era of evidence-based medicine, the administration of 80% O₂ for two hours for all patients undergoing colorectal surgery can be considered level I evidence (large randomized trial with clear-cut results).⁴ However, the universal application of such a strategy cannot be generalized to all postoperative patients unless a higher oxygen concentration is indicated.

André Denault MD FRCPC

Denise Fréchette MD MPH

Montréal, Québec

References

- 1 Cook DJ, Levy MM. Evidence-based medicine. A tool for enhancing critical care practice. *Crit Care Clinics* 1998; 14: 353–8.
- 2 Kotani N, Hashimoto H, Sessler DI, *et al.* Supplemental intraoperative oxygen augments antimicrobial and proinflammatory responses of alveolar macrophages. *Anesthesiology* 2000; 93: 15–25.
- 3 Knight PR, Holm BA. The three components of hyperoxia (Editorial). *Anesthesiology* 2000; 93: 3–5.
- 4 Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest* 1989; 95(suppl. 2): 2–4.

Commentary by Y. Skrobik

Five percent of all surgical procedures, and 10 to 20% of colorectal surgical interventions, are complicated by wound infections. Predictable increases in morbidity and cost ensue. Infectious outcome depends on the invading organism's load and virulence, and the ability of the host's tissue to protect itself. Tissue oxygenation is felt to be significant in host defense because of neutrophil-activated oxidative killing, in which bactericidal superoxide radicals play an important role.

The study by Grief *et al.* compares 30% FiO₂ to 80% FiO₂ during surgery and in the immediate postoperative period in patients undergoing elective colonic resection. The results indicate that administration of the higher oxygen concentration is associated with a lower incidence of postoperative wound infection. In the subset of patients in whom tissue oxygen concentration is measured (*sc* or intramuscularly), interstitial pO₂ levels are higher in the 80% O₂ group. This finding provides a physiologic explanation for the improved outcome in patients given 80% O₂.

The authors randomized 500 patients. Severely malnourished, or clinically infected patients, as well as those

suffering from bowel obstruction, were excluded. Chronic inflammatory disease and bowel cancer patients, whose immune status could influence infectious outcome, numbered equally in both groups, as did factors such as age and the American Society of Anesthesiologists physical status score. Risk factors for wound infection, other than imminent colon surgery, were thus evenly distributed in the two groups. Perioperative management was carefully tailored to allow maximal tissue perfusion pressures by generously infusing *iv* crystalloid. Body temperature was fastidiously maintained at 36.5°C, since the benefit of normothermia with regards to wound infections is known.¹ Thirty-eight of 250 patients in the 30% O₂ group and only one in the 80% O₂ group required perioperative increase in oxygen administration. Hemodynamics were similar in the two groups, implying perioperative instability was not masked in the 80% oxygen group. Potential adverse effects of 80% O₂ administration were addressed. Frequency of postoperative atelectasis, carefully evaluated with roentgenograms and computed tomography in a subgroup of patients, was not different between the two groups.² Unexpectedly, the 80% O₂ group showed a marked (50%) decrease in postoperative nausea and vomiting.³

Wound healing rates were no different between groups. The authors carefully and objectively documented postoperative wound infection. Wound infection rates were significantly worse in the lower oxygen group (11.2% in 30% O₂ group *vs* 5.2% in the 80% O₂ group; *P*=0.01). This translated into significant morbidity (sepsis, multi-organ failure, and ICU admissions) and cost.

This study shows a simple, safe, and inexpensive way of minimizing wound infections. Benefits to the patient extend to how they feel in the immediate postoperative period. The paper's message emphasizes the role of anesthesiologists as active participants in the outcome of the whole disease process,⁴ in addition to their role as providers of perioperative stability and analgesia.

Yoanna Skrobik MD FRCPC
Montréal, Québec

References

- 1 Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *N Engl J Med* 1996; 334: 1209–15.
- 2 Akça O, Podolsky A, Eisenhuber E, *et al*. Comparable postoperative pulmonary atelectasis in patients given 30% or 80% oxygen during two hours after colon resection. *Anesthesiology* 1999; 91: 991–8.
- 3 Grief R, Laciny S, Rapf B, Hickie RS, Sessler DI. Supplemental oxygen reduces the incidence of postoperative nausea and vomiting. *Anesthesiology* 1999; 91: 1246–52.
- 4 Buggy D. Can anaesthetic management influence surgical wound-healing? *Lancet* 2000; 356: 355–7.