EVIDENCE THAT'S GOOD ENOUGH TO CHANGE YOUR PRACTICE

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Evidence-based medicine (EBM) depends on well-designed studies with reliable results. Spurious findings, clinically irrelevant findings, surrogate endpoints, and biased studies hinder the application of new knowledge derived from published research, but EBM continues to identify how to best to identify, critique and apply useful interventions in anaesthesia.

Good quality evidence from randomised trials and systematic reviews is available, and their uptake into anaesthetic practice can work, and should be adopted to reduce serious complications after surgery. Systematic review (SR) and meta-analysis are useful in that they provide a minimally biased estimate of effect. The key is an understanding of the value and purpose of the 95% CI: this describes the "best" estimate of effect and a measure of the precision (reliability) of that estimate. If either 95% confidence limit would change the conclusion of the study, then we are left with uncertainty.

The main problems confronting most patients after surgery are surgical pain, restricted physical functions, and emesis. Multimodal analgesic techniques can provide effective pain relief, and this will assist restoration of activity. The latter is particularly important after major surgery where respiratory complications may ensue if there are limitations of ventilatory capacity and ability to cough.

Other serious complications of surgery and anaesthesia include myocardial infarction, stroke, renal failure, sepsis and death. There are some simple, effective techniques that should be used more widely.

Prophylactic Treatment for PONV

Anti-emetic prophylaxis should be used selectively (1-5). Targeted prophylaxis of high-risk patients is more rational in that they are much more likely to benefit from treatment – a concept neatly summarised by the statistic, *number needed to treat* (NNT) (6). High-risk patients include those with a history of PONV and motion sickness, non-smokers, young women undergoing most types of surgery, and with high opioid requirements after major surgery.

At least double-, if not triple-therapy should be used, combining a 5-HT_3 antagonist, droperidol and dexamethasone (1,5). Ondansetron is an effective prophylactic treatment for the prevention of PONV. In an earlier systematic review of 53 RCTs (n=12,889 pts), a dose response for oral and IV ondansetron was demonstrated, with at least 4 mg being required for effective prophylaxis (2). Ondansetron had greater effect at preventing vomiting than nausea.

Droperidol appears to be an equally effective drug at preventing PONV (3). In a systematic review of 54 RCTs (n=7324), both ondansetron, odds ratio (OR) 0.43 (95% CI: 0.31-0.6), and droperidol, OR 0.68 (0.54- 0.85), were more effective than metoclopramide. Ondansetron was more effective than droperidol in preventing vomiting OR 0.70 (0.52-0.94), but not nausea OR 0.99 (0.66-1.47).

Recent evidence suggests that dexamethasone is probably the most rational first choice to prevent PONV (4). In a systematic review of 17 RCTs in 1946 patients, there was a 20%-30% reduction in PONV, equating to a NNT of 7. Given dexamethasone is a cheap drug with no recognised side effects from single-dose treatment, it should be recommended as a first line therapy.

Chlorhexidine for Skin Antisepsis

More than 90% of all intravascular cannula-related septicaemias are due to central venous or arterial catheters. Maki et al. (7) compared three antiseptic solutions in an RCT of 668 catheters comparing 10% povidone-iodine, 70% alcohol, or 2% aqueous chlorhexidine. Chlorhexidine was associated with the lowest incidence of local catheter-related infection (2.3 per 100 catheters vs 7.1 and 9.3 for alcohol and povidone-iodine, respectively, p = 0.02) and catheter-related bacteraemia (0.5 vs 2.3 and 2.6). Of the 14 infusion-related bacteraemias one was in the chlorhexidine group and 13 were in the other two groups (OR 0.16, p = 0.04). They concluded that use of 2% chlorhexidine, rather than 10% povidone-iodine or 70% alcohol, can substantially reduce the incidence of catheter-related infection. Chlorhexidine-based solutions should be used for intravascular cannulations and regional blockade (8,9).

Avoidance of Intraoperative Hypothermia

Intraoperative hypothermia is common and may lead to reduced drug metabolism, and so may slow recovery time. It also reduces thermal comfort, increases bleeding and transfusion requirements, and increases myocardial ischaemia (10). There is strong evidence that avoiding intraoperative hypothermia can reduce wound infection (10). In an RCT of 200 patients, have clearly demonstrated that avoidance of intraoperative hypothermia, using forced air warming, reduces wound infection in patients undergoing colorectal surgery. They also demonstrated improved wound healing and a reduction in hospital length of stay. Avoiding hypothermia is a widely used clinical indicator in anaesthesia (10,11).

Avoidance of Nitrous Oxide

The ENIGMA trial identified probable adverse effects of nitrous oxide in patients undergoing major surgery (12). We found that patients in the nitrous oxide-free group suffered significantly lower rates of major complications (OR 0.71; 95% CI: 0.56-0.89; P=0.003), and severe nausea and vomiting (OR 0.40; 95% CI: 0.31-0.51; P<0.001), but median duration of hospital stay did not differ substantially between groups (7.0 versus 7.1 days, P=0.06). Among patients admitted to the intensive care unit postoperatively, those in the nitrous oxide-free group were more likely to be discharged from the unit on any given day than those in the nitrous oxide group (hazard ratio 1.35; 95% CI: 1.05-1.73; P = 0.02).

Nitrous oxide-induced inactivation of methionine synthetase increases plasma homocysteine concentrations after surgery (13), and this may pose a risk in patients with cardiovascular disease. We have thus begun a follow-up trial in 7,000 patients to confirm or refute these findings (14).

Supplemental Oxygen Therapy?

Wound infection is a common complication of surgery and has significant cost implications because of greater resource utilisation and increased hospital stay. The use of high inspired oxygen concentration during the perioperative period has theoretical benefits because of improved tissue oxygenation and bactericidal activity. At least four trials with conflicting results have been published (15).

A meta-analysis of four randomized trials has concluded that supplemental oxygen does reduce wound infections, but they omitted some other negative studies in their analysis and in any case the results were no longer significant when using the more valid random effects model, [RR 0.74 (95% CI 0.39-1.43), P = 0.37]. It therefore remains unclear as to whether supplemental oxygen reduces wound infection and other complications after abdominal surgery. Supplemental oxygen does not reduce the incidence of PONV (5).

Beta-blockers Should Be Used Selectively

An influential clinical practice guideline (16), updated in 2007, made a Class I recommendation for perioperative beta-blockade in patients with documented ischaemia having vascular surgery and a Class IIa recommendation for patients with, or at risk of, ischaemic heart disease having non-cardiac surgery. Earlier trials and SRs suggest

possible benefits of perioperative beta-blockade (17,18). However, the definitive POISE study (19), despite confirming a significant reduction in MI found this came at a cost of more strokes and death. POISE enrolled 8351 patients and found a reduction in MI (HR 0.73, 0.60-0.89; p=0.0017) but an increased risk of death (HR 1.33, 1.03-1.74; p=0.03). and stroke (41 [1.0%] vs 19 [0.5%] patients; 2.17, 1.26-3.74; p=0.005) in the beta-blocker group.

A post-POISE SR of 33 trials in 12,306 patients (20) seems to discount the adverse effect on mortality, but confirms an increased risk of stroke (OR 2.01, 1.27-3.68), with a number needed to harm [NNH] 293. The authors of this evidence-based review concluded that evidence does not support the use of beta-blocker therapy for the prevention of perioperative clinical outcomes in patients having non-cardiac surgery. The ACC/AHA guidelines, therefore, will need to be modified.

Clonidine and other alpha$_2$-agonists may reduce the risk of renal impairment in vascular and cardiac surgery (21,22). The evidence supporting a myocardial protective effect of clonidine is quite strong (23). These possible benefits are being evaluated in a definitive large trial being planned by the POISE group.

Volatile Agents for CABG Surgery

SR of 22 trials in 1922 patients (24) found that volatile anaesthetics are associated with significant reductions of myocardial infarctions (OR 0.51 [0.32-0.84], p = 0.008) and mortality (OR 0.31 [0.12-0.80], p = 0.02). These data show for the first time that the choice of an anaesthetic regimen based on administration of halogenated anaesthetics is associated with a better outcome after cardiac surgery. At this stage there is no evidence that volatile agents are protective in noncardiac surgery (25).

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