Does regional anaesthesia improve outcome?

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Considerable research has been carried out over the last 30 years to investigate whether regional anaesthesia improves the quality of postoperative analgesia compared with systemic opioids, and whether it influences the outcome from surgery. Some benefits, such as the quality of postoperative analgesia, are easy to demonstrate but the intuitive belief that regional anaesthesia improves the outcome from surgery is more difficult to prove. Many studies have been inconclusive, with methodological weaknesses making it difficult to compare the results of different studies. Nevertheless, the weight of evidence suggests that regional anaesthesia has the potential to improve outcome from surgery.

Regional analgesia versus systemic analgesia
It is difficult to isolate the analgesic benefits of regional anaesthesia (compared with systemic opioid-based analgesia) from the anaesthetic benefits (compared with general anaesthesia). Regional anaesthesia is most commonly used for surgery and early postoperative analgesia and most studies do not distinguish between these components. If an epidural injection or a major peripheral nerve block is used as the sole anaesthetic technique or is combined with a light general anaesthetic, the use of intra-operative opioids is unnecessary, or reduced, compared with general anaesthesia alone. The depth of general anaesthesia also differs because of the influence of the local anaesthetic technique. These differences influence the early indicators of recovery such as time to consciousness, the incidence of postoperative nausea and vomiting (PONV), return of full cognitive function, and time to first supplementary analgesic. Therefore, while it is possible to compare improvements in pain scores, other benefits may occur purely as a result of avoiding opioids (Figure 1). The quality of analgesia with regional anaesthesia is significantly better than that with systemic opioids. Central and peripheral nerve blocks can prevent or abolish the neural transmission of nociceptive signals; opioids can only modulate the transmission.

The benefits of regional analgesia compared with systemic opioid-based analgesia
- Lower pain scores (visual analogue scores or verbal rating scores)
- Less time spent in post-anaesthesia recovery units (PACU)
- Longer time to first analgesic request
- Fewer requests for rescue analgesia and lower total dose required
- Less nursing time and lower nursing dependency in PACU
- Reduced opioid-based side-effects
  - Drowsiness/dysphoria
  - Respiratory depression
  - Nausea and vomiting
  - Ileus
- Earlier discharge home from day surgery units
- Reduced unplanned admission rate for day-surgery patients
- Increased patient satisfaction scores

Can anaesthesia influence outcome from surgery?
Regional anaesthesia has been used in all three perioperative phases to try to improve postoperative analgesia and influence surgical outcome.

Preoperative: regional anaesthesia has little influence on postoperative outcome though it improves the management of pre-existing pain.
Pre-emptive analgesia is the ability to reduce the severity and duration of postoperative pain by instituting effective analgesia before the onset of the pain. It has been demonstrated in animal models, but does not exist as a clinical entity, based on current understanding. Initial studies suggested that regional anaesthesia and systemic analgesia, administered before surgery, would improve postoperative pain, but this was not borne out in later studies.

Intraoperative: the morbidity and mortality associated with surgery and anaesthesia continue to decrease with advances in techniques. In the absence of avoidable errors, there is little difference in intraoperative risk between regional or general anaesthesia. Serious adverse outcomes from anaesthesia are extremely uncommon (0.1–1.5 deaths directly attributable to anaesthesia per 10,000 procedures). Preoperative fitness, patient age and the surgical procedure remain the most important risk factors for major non-fatal morbidity or mortality.

Postoperative phase: effective, continuous, postoperative analgesia is a worthwhile target for humanitarian reasons and for improving outcome. A large number of publications confirm the advantages of regional anaesthesia (both peripheral and central neural blockade) compared with systemic opioids (Figure 2). Regional anaesthesia may also prevent acute pain becoming chronic. A significant number of patients (about 50% for major breast surgery or thoracotomy) develop chronic pain following surgery owing to neuropathic nerve injury. A study of paravertebral blocks following thoracotomy showed a significant reduction in post-thoracotomy pain syndrome.¹

### Regional anaesthesia compared with ‘on-demand’ systemic opioids or intravenous patient-controlled analgesia

<table>
<thead>
<tr>
<th>Technique</th>
<th>Surgery</th>
<th>Benefits compared with systemic analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interscalene brachial plexus</td>
<td>Shoulder replacement or major arthroscopic surgery</td>
<td>Improved pain scores, earlier discharge, improved rehabilitation</td>
</tr>
<tr>
<td>Paravertebral</td>
<td>Breast surgery</td>
<td>Less pain, earlier discharge, less postoperative nausea and vomiting (PONV)</td>
</tr>
<tr>
<td></td>
<td>Thoracotomy</td>
<td>Less pain, improved oxygenation, less haemodynamic dysfunction (compared with epidural), decreased risk of chronic pain</td>
</tr>
<tr>
<td></td>
<td>Renal surgery</td>
<td>Less pain, less haemodynamic dysfunction (compared with epidural)</td>
</tr>
<tr>
<td>Thoracic epidural</td>
<td>Pulmonary/cardiac surgery</td>
<td>Less pain, improved pulmonary mechanics, faster recovery, reduced risk of perioperative ischaemia</td>
</tr>
<tr>
<td></td>
<td>Upper abdominal surgery</td>
<td>Decreased pain, ileus, PONV, pulmonary dysfunction</td>
</tr>
<tr>
<td>Lumbar epidural and spinal</td>
<td>Lower abdominal, urogenital</td>
<td>Decreased pain, ileus, blood loss, risk of deep vein thrombosis, PONV</td>
</tr>
<tr>
<td></td>
<td>Lower limb surgery (hip/knee joint surgery)</td>
<td>Decreased pain and blood loss, earlier mobilization, improved rehabilitation</td>
</tr>
<tr>
<td>Lower limb block</td>
<td>Lower limb surgery (knee joint/foot and ankle)</td>
<td>Less pain, earlier mobilization, improved rehabilitation</td>
</tr>
</tbody>
</table>

Data from published studies.

Regional versus general anaesthesia

In the last 30 years, numerous prospective, randomized, controlled trials have compared regional with general anaesthesia and their effects on outcome from surgery. In addition to improved analgesia, continuous lumbar epidural blocks for lower abdominal, pelvic and lower limb surgery significantly modify the surgical stress response, which is responsible for much postoperative morbidity (Figure 3).

The effects of thoracic epidural blockade on the stress response are not so marked because of less complete block of the lumbar autonomic nerve supply to the abdominal viscera and lower limbs. Intravenous patient-controlled analgesia (PCA) and other opioid-based analgesic techniques do not influence outcome from surgery despite satisfactory analgesia and a high degree of patient and staff satisfaction scores.

Regional anaesthesia, using local anaesthetic drugs alone or in combination with low doses of opioid drugs, has significant advantages over epidural or intravenous opioid-based analgesia.²
A number of clinical benefits can be predicted from the effects that regional anaesthesia has on the stress response. It is easier to investigate the influence of regional anaesthesia on a single variable of the stress response than to investigate its overall influence. Consequently, stronger data are available to show that regional anaesthesia has a beneficial effect on single systems during and after surgery (Figure 4) than for its overall effects on outcome. The influence of regional anaesthesia on cognitive function remains unclear.

### The effects of continuous lumbar epidural anaesthesia/analgesia on the surgical stress response compared with general anaesthesia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Factors</th>
<th>Effect of lumbar epidural compared with general anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroendocrine response</td>
<td>Adrenocorticotrophin (ACTH), anti-diuretic hormone (ADH), growth hormone, cortisol, renin, glucagon, catecholamines, insulin, lactate</td>
<td>Plasma levels remain stable or decrease in response to stress</td>
</tr>
<tr>
<td>Glucose metabolism</td>
<td>Less insulin resistance, normal glucose tolerance test, normal plasma glucose level</td>
<td>Reduced hyperglycaemic response to surgery</td>
</tr>
<tr>
<td>Nitrogen balance</td>
<td>Modification of neuroendocrine response</td>
<td>Reduced nitrogen losses</td>
</tr>
<tr>
<td>Electrolyte and water balance</td>
<td>Sodium excretion increased, potassium excretion decreased</td>
<td>Less water retention and electrolyte imbalance</td>
</tr>
<tr>
<td>Coagulation/fibrinolysis</td>
<td>No inhibition of fibrinolysis, inhibition of platelet aggregation</td>
<td>Less hypercoagulation and thrombogenesis</td>
</tr>
</tbody>
</table>

### The benefits of regional anaesthesia compared with general anaesthesia

#### Primary effect of regional anaesthesia
- Improved systemic blood flow, decreased platelet stickiness, decreased inhibition of fibrinolysis
- Reduced perioperative blood loss
- Improved coronary blood flow
- Reduced myocardial oxygen demand
- Reduced duration of ileus
- Reduced risk of respiratory depression, improved lung mechanics

#### Benefit compared with general anaesthesia
- Reduced incidence of deep vein thrombosis
- Reduced risk of pulmonary embolism
- Reduced rate of blood transfusion
- Reduced risk of myocardial ischaemia
- Reduced incidence of postoperative nausea and vomiting (PONV), early return of bowel function
- Improved partial pressure of oxygen in arterial blood ($\text{PaO}_2$) and oxygen saturation, earlier extubation, reduced pulmonary infection

### The role of Systematic Reviews

It is difficult to measure differences in outcome between regional anaesthesia and general anaesthesia for rare but important variables such as perioperative mortality. A very large sample size is required for prospective randomized trials to demonstrate any significant differences (too large even for multi-centre trials when studying these rare outcome events). Systematic Reviews are a useful method of analysing large numbers of smaller studies to evaluate any potential benefits of regional anaesthesia.

Several important meta-analyses of the effects of regional anaesthesia on outcome from surgery have been published recently. A review of hip fractures showed reduced 1-month mortality in favour of regional anaesthesia plus a reduction in the rate of deep vein thrombosis,

confirming earlier work that regional anaesthesia offers an early advantage over general anaesthesia, though this advantage reduces with time. At 3 months, mortality is the same as for general anaesthesia. Patients who had a thoracic epidural infusion for at least 24 hours postoperatively had improved postoperative analgesia and a reduction in postoperative myocardial infarction risk.

Jorgensen showed improvements in the return of gastrointestinal function as well as improved pain scores.

A meta-analysis of the effects of various postoperative analgesic regimens on pulmonary outcome confirmed the benefits of local anaesthetic-
based epidural infusions. The largest and most significant meta-analysis evaluated 144 published papers, involved over 9500 patients, and confirmed several benefits of regional anaesthesia (alone or in combination with general anaesthesia) compared with general anaesthesia alone. There was a reduction in the risk of mortality from all causes after major surgery of 30% in the regional anaesthesia group compared with the general anaesthesia group.

Clinical relevance of regional anaesthesia
The important question is whether the benefits associated with regional anaesthesia lead directly to measurable clinical improvements such as fewer complications, lower mortality and better outcome from surgery. High quality analgesia is an important achievement but does not improve outcome directly. For example, an epidural infusion for postoperative analgesia following major abdominal surgery produces low pain scores, a shorter duration of ileus, a reduced need for postoperative blood transfusion and results in high levels of patient satisfaction. However, unless efforts are made to use the analgesia and other benefits of the epidural to mobilize the patient and encourage early return to full nutrition, there are no long-lasting benefits once the infusion is discontinued. Traditional surgical postoperative practice such as the routine use of nasogastric tubes, the slow return to enteral nutrition and other fixed determinants of the recovery pathway may also delay recovery and fail to maximize the potential improvements in surgical outcome that regional anaesthesia can offer.

The significant risks associated with spinals, epidurals and major peripheral nerve blocks must be balanced against the potential benefits if the anticipated improvement in outcome for an individual patient is to be realized. The key features of regional anaesthesia (quality of analgesia, avoidance of opioid side-effects and minimizing the impact of the surgical stress response), combined with new surgical techniques and ward routines, make it possible to reduce the incidence and severity of complications (e.g. hypoxaemia, fatigue, weight loss) and delayed recovery, and encourage early nutrition, increased mobility and reduced hospital stay.

KEY REFERENCES

FURTHER READING

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