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Editorial comment

Intravenous non-opioids for immediate postop pain relief in day-case programmes: Paracetamol (acetaminophen) and ketorolac are good choices reducing opioid needs and opioid side-effects

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In this issue of the *Scandinavian Journal of Pain* Anand et al. report on their study comparing intravenous 1 g of paracetamol (acetaminophen) (Perfalgan® in the Nordic countries Ofirmev® in the USA) with intravenous 30 mg ketorolac (Toradol®) given during the procedure in order to reduce pain in the immediate post-anaesthesia/post-operative period [1]. They found no difference in the first half-hour, but after 45 min the pain intensity was somewhat less in the ketorolac treated patients who had an ambulatory parathyroidectomy. Opioid use for rescue analgesia was not different, but there was a bit more nausea in the paracetamol-treated patients [1].

1. Is this interesting enough to warrant publication?

The procedure is a minor one, but as stated recently by Joshi and Kehlet in an editorial in Anaesthesiology the pain experienced after different types of surgical procedures is often not related to our preconceptions of the degree of tissue damage and need for post-operative pain relief [2]. The study by Anand et al. had an adequate number of patients in each group (total 180) so that this procedure, parathyroidectomy with or without thyroid nodule removal, can now confidentially be added to the long list of surgical procedures (n = 179 procedures in 115,775 patients) where the degree of postoperative pain problems has been well documented [3].

2. Movement-related pain is always more problematic than pain at rest

Surgical procedures in the neck leave traumatised tissues that the patient cannot prevent from moving: during deep breathing and coughing, swallowing, talking, moving the head-neck provoke movement-related pain in a surgical wound. Nausea and vomiting cause venous pressure to increase, aggravating any ongoing bleeding in the wound. A haematoma in the deep tissue layers of the neck can rapidly become a serious airway problem.

3. Increased risk of wound-bleeding with NSAIDs compared with paracetamol

All NSAIDs have unfavourable effects on platelet adhesiveness and may increase the risk of postoperative wound bleeding [4]. This is less so with the COX-2-specific NSAIDs, but there are no injectable COX-2-specific inhibitors in the Nordic countries after parecoxib (Dynastat®) became less popular because of the risk of precipitating an anaphylactoid reaction in sulfa-allergic patients [5].

4. NSAIDs increase the risk of haematoma and airway-obstruction after thyroid surgery

Ketorolac is a potent COX-1 inhibitor, easily dissolved in water, and the injectable form of ketorolac has been popular on both sides of the Atlantic for several years. However, ketorolac, like all COX-1 inhibitors, diminishes platelet stickiness [4], and it has caused increased incidence of haematoma after thyroid surgery [6]. Therefore, the present study is important in that it in fact documents a similar effect of 1 g intravenous paracetamol on the immediate post-parathyroidectomy pain compared with intravenous ketorolac 30 mg.

5. Intravenous, oral, or rectal paracetamol administration for immediate postoperative pain?

Is it necessary to give paracetamol (acetaminophen) intravenously? Preoperative oral administration of 1.5–2 g paracetamol could conceivably give a similar effect as 1 g given intravenously during the procedure. However, paracetamol has to reach the small intestine before it can be absorbed. The pre-anaesthesia period is stressful to most patients and this may easily stop gastric emptying. Paracetamol is not absorbed from the gastric mucosa.

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Rectal administration of paracetamol is possible, but absorption is slow, often incomplete. Thus, the patient in the perioperative period is left with uncertain effects of all other administration forms than the intravenous infusion of paracetamol. Intravenous administration gives a much more reliable therapeutic plasma- and CNS-concentrations and effect of paracetamol compared with oral or rectal administration [7].

6. The conundrum of pain-relieving mechanisms of paracetamol are now being resolved

Paracetamol is a weak inhibitor of prostaglandin synthesis and therefore is not an NSAID. We have known for a while that paracetamol, and its metabolites must be present in the CNS to cause pain relief; paracetamol is not a peripherally acting analgesic. Recent research by Andersson et al. has documented that metabolites of paracetamol have effects on TRPV1 and TRPA1-receptors in pain modulating neurons in the CNS, as well as effects on the cannabinoid systems in the brain [9,10]. A COX-2 inhibiting effect in the CNS may also contribute to paracetamol's central nervous system analgesic effects. In diabetic neuropathy with pain, another TRPA1 antagonist is effective and may even be a disease-modifying drug in that it prevents loss of thin afferent nerve fibres in diabetic mice [11].

For surgery in the neck, especially on thyroid and parathyroid glands, reducing risk of postoperative haematoma formation and compromised airways is one of the most important aspects of safe postoperative care. Paracetamol should therefore be the analgesic drug of choice. Paracetamol results in reduced pain, reduced need for opioids as rescue analgesics, thereby reducing the dose-related opioid-induced adverse effects, nausea and vomiting in particular [8]. For day-case or ambulatory surgical procedures in the neck the benefits of adequate doses of paracetamol resulting in pain relief and less risk of bleeding compared with NSAIDs, are especially important.

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