Should intravenous steroids be administered during routine primary knee or hip arthroplasty?

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Response/Recommendation: There is strong evidence supporting the efficacy of intravenous steroids in reducing postoperative pain, opioid consumption, and nausea/vomiting in patients undergoing total joint arthroplasty. There is also evidence, that administration of intravenous steroids does not increase the risk of adverse or serious adverse events within the first 90 days postoperatively. We therefore recommend utilizing intravenous steroids whenever feasible at a dosage of 20-24mg intravenous dexamethasone during anesthesia induction, provided no contraindications are present.

Level of Evidence: High

Rationale

A vast number of articles have been published on this topic, including prospective and retrospective studies, meta-analyses, randomized controlled trials, and guidelines. Postoperative pain, nausea and vomiting (PONV) are common challenges for patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA). Inadequate pain control and PONV can significantly prolong recovery and diminish patient satisfaction post-surgery. Therefore, optimizing pain management and reducing PONV are critical for enhancing postoperative care protocols and patient outcomes.

In 2022, clinical practice guidelines from leading organizations including the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society, investigated the role of perioperative intravenous (iv) dexamethasone in total joint arthroplasty (TJA)[1]. Based on a review of fourteen high-quality studies and two moderate-quality studies, these guidelines found that iv dexamethasone reduces postoperative pain, opioid consumption, and incidence of nausea/vomiting after primary TJA. A direct meta-analysis of five studies with no heterogeneity ($I^2 = 0$) showed that patients receiving intravenous dexamethasone required significantly fewer opioids for breakthrough pain (relative risk [RR] 0.44; 95% confidence interval [CI] 0.28 to 0.68). Additionally, nine studies with moderate heterogeneity (I2 = 48.3%) demonstrated a significant reduction in postoperative nausea and vomiting with intravenous dexamethasone compared to placebo (RR 0.43; 95% CI 0.30 to 0.63). Recommendations based on three high-quality studies suggested that multiple doses of perioperative iv dexamethasone effectively reduce pain, opioid use, and PONV compared to a single dose.

In 2021, an update to the PROSPECT guidelines focused on procedure-specific pain management for THA and recommended intraoperative iv dexamethasone (8–10 mg)[2]. The guidelines also included an analgesic regimen comprising preoperative or intraoperative paracetamol, cyclo-oxygenase-2-selective inhibitors or non-steroidal anti-inflammatory drugs, and opioids as rescue analgesics postoperatively.

Subsequent to these publications, a comprehensive systematic review and meta-analysis involving 32 RCTs (involving 3521 patients) assessed perioperative systemic glucocorticoids versus placebo

or no intervention for analgesic pain management in TJA[3]. The meta-analysis demonstrated that glucocorticoids significantly reduced 24-hour cumulative morphine consumption by 5.0 mg (95% CI 2.2 to 7.7; P=0.0004). Pain at rest decreased by 7.8 mm (VAS) at 6 hours (95% CI 5.5 to 10.2; P<0.00001) and by 6.3 mm at 24 hours (95% CI 3.8 to 8.8; P<0.00001), while pain during mobilization decreased by 9.8 mm at 6 hours (95% CI 6.9 to 12.8; P<0.00001) and by 9.0 mm at 24 hours (95% CI 5.5 to 12.4; P<0.00001). Although the incidence of adverse events was generally lower in the glucocorticoid group, serious adverse events were rare. However, the GRADE rating was generally low to very low, and study follow-up periods ranged from 1 day to 1 year.

Recent RCTs published since the aforementioned systematic review have further confirmed the safety and efficacy of iv steroids in TJA[4-15]. Two high quality RCTs including 1060 primary THAs[4] and 485 TKAs[9], respectively, confirm the safety and efficacy of intravenous steroids with a 90-day follow-up. Steiness et al. [4] found that a single dose of 24 mg iv dexamethasone, in combination with paracetamol and ibuprofen, significantly reduced 24-hour morphine consumption compared to paracetamol plus ibuprofen and paracetamol plus dexamethasone in THA. A lower incidence of serious and non-serious adverse events (primarily driven by differences in nausea, vomiting, and dizziness) were found compared to the regimen not containing dexamethasone. Gasbjerg et al.[9] compared a single preoperative versus preoperative plus postoperative dosing of 24 mg iv dexamethasone in TKA, showing reduced morphine consumption and postoperative pain over 48 hours with both regimens compared to placebo. Median morphine consumption at 0-48 hours was 37.9 mg (IQR 20.7-56.7) with single dose, 35.0 mg (20.6-52.0) for repeated dose, and 43.0 mg (28.7-64.0) for placebo, with significant differences between both dexamethasone groups and placebo but not between single dose and repeated dose. Reduction in morphine consumption in patients receiving repeated dose, exceeded the predefined minimal important difference of 10 mg (10.7 mg; 4.0 to 17.3; (P<0.001)) compared to placebo. There were no differences in adverse events among the groups.

Moreover, two RCTs[8; 10] and a network meta-analysis encompassing 34 studies[16] affirm the advantages of administering repeated doses of intravenous steroids over a single dose during the initial postoperative phase in THA and TKA, respectively. Lei et al.[11], in their RCT, demonstrated that a single preoperative high dose of 20 mg dexamethasone was more effective than two perioperative low doses of 10 mg in managing pain and recovery outcomes in patients undergoing TKA. A study of the 3-year follow-up of the trial by Gasbjerg et al. demonstrated that while dexamethasone effectively manages acute pain and improves immediate recovery after TKA, it does not influence chronic pain development or long-term functional outcomes[17]. Additionally, a prospective questionnaire for postoperative days 3–7 found that neither 1 or 2 doses of iv dexamethasone demonstrated prolonged effects on overall pain or sleep quality and there was no effect on patient satisfaction significantly impact overall patient satisfaction in the long term[18].

Both the study by Steiness et al and Gasbjerg et al included patients with diabetes, in which the condition was considered regulated. The investigators did not examine postoperative blood glucose levels. Regarding safety considerations, while perioperative corticosteroids can transiently elevate blood glucose levels, recent studies like the PADDI trial suggest these increases are minimal and unlikely to clinically impact outcomes in non-acute, noncardiac surgery[19]. Perioperative corticosteroids may lead to increased postoperative blood glucose levels and there is no evidence in TJA for its use in patients with uncontrolled diabetes mellitus, it should therefore be used with caution in these patients. Recent retrospective studies confirm that a second dose of dexamethasone reduces postoperative opioid consumption[20] but increases postoperative blood glucose levels[21]. However, the clinical benefits may outweigh this effect. Additionally, an analysis of 70,000

high-risk patients found that a second dose is associated with a decreased risk of pulmonary embolism and deep vein thrombosis following TJA[22].

Currently, there is limited evidence regarding the impact of high versus low doses of iv steroids on postoperative outcomes such as pain, opioid use, nausea/vomiting, or complications. Nielsen et al.[7] found that administering 1 mg/kg of dexamethasone before surgery reduced moderate-to-severe pain 24 hours after TKA and improved recovery specifically in patients with a low pain threshold or regular opioid use, compared to a dose of 0.3 mg/kg. This difference was not observed in patients with a or regular opioid use undergoing THA[5] nor TKA[6] with a high pain threshold or no regular opioid use. Further studies are needed to validate these findings.

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