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Should Intravenous Corticosteroids Be Administered Routinely During Primary Knee or Hip Arthroplasty to Impart Analgesic and Anti-Inflammatory Properties?

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Should intravenous corticosteroids be administered routinely during primary knee or hip arthroplasty to impart analgesic and anti-inflammatory properties?

Response/Recommendation: There is strong evidence supporting the efficacy of intravenous corticosteroids in reducing postoperative pain, opioid consumption, and nausea/vomiting in patients undergoing total joint arthroplasty. There is also evidence, that the administration of intravenous corticosteroids does not increase the risk of adverse events within the first 90 days postoperatively. We, therefore, recommend utilizing intravenous corticosteroids (dexamethasone) during anesthesia induction, provided no contraindications are present.

Level of Evidence: High.

Vote: Agree 90.4%, disagree 6.0%, abstain 3.6%.

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 markedly prolong recovery and diminish patient satisfaction postsurgery. 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, the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Orthopaedic Surgeons, the Hip Society, and the Knee Society, investigated the role of perioperative intravenous (IV) dexamethasone in total joint arthroplasty (TJA) [1]. Based on a review of 14 high-quality studies and two moderate-quality studies, these guidelines found that IV dexamethasone reduced postoperative pain, opioid consumption, and the incidence of nausea/vomiting after primary TJA. A direct meta-analysis of five studies with no heterogeneity ($I^2 = 0$) showed that patients receiving IV dexamethasone required significantly fewer opioids for breakthrough pain (relative risk 0.44; 95% confidence interval

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[CI] 0.28 to 0.68). Additionally, nine studies with moderate heterogeneity ($I^2 = 48.3\%$) demonstrated a significant reduction in postoperative nausea and vomiting when IV dexamethasone was administered compared to placebo (relative risk 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 reduced pain, opioid use, and PONV compared to a single dose.

In 2021, an update to the Problem, Research, Objective, Solutions, Presentation, Engagement, Close, Tracking guidelines focused on procedure-specific pain management for THA and recommended intraoperative IV dexamethasone (8 to 10 mg) [2]. The guidelines also included an analgesic regimen comprising preoperative or intraoperative paracetamol, cyclo-oxygenase-2-selective inhibitors or nonsteroidal anti-inflammatory drugs, and opioids as rescue analgesics postoperatively.

Subsequent to these publications, a comprehensive systematic review and meta-analysis involving 32 randomized controlled trials (RCTs) (involving 3,521 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 (visual analogue scale) 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 Grading of Recommendations, Assessment, Development, and Evaluation 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 corticosteroids in TJA [4–15]. There are two high-quality RCTs that included 1,060 primary THAs [4] and 485 TKAs [9], respectively, confirmed the safety and efficacy of IV corticosteroids 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 nonserious adverse events (primarily driven by differences in nausea, vomiting, and dizziness) was 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 to 48 hours was 37.9 mg (interquartile range 20.7 to 56.7) with single dose, 35.0 mg (range, 20.6 to 52.0) for repeated dose, and 43.0 mg (range, 28.7 to 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 doses exceeded the predefined minimal important difference of 10 mg (10.7 mg; range, 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 IV corticosteroids 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 to 7 found that neither *one or two* doses of *IV* dexamethasone demonstrated prolonged effects on overall pain or sleep quality and there was no *effect on overall* patient satisfaction [18]. Furthermore, the main study reported no difference in serious adverse events at 90-day follow-up on serious adverse events [9].

Both the studies by Steiness et al. and Gasbjerg et al. included patients who have 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 Perioperative Administration of Dexamethasone and Infection trial suggest these increases are minimal and unlikely to clinically impact outcomes in nonacute, 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 who have 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 corticosteroids 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 who have a low pain threshold or regular opioid use, compared to a dose of 0.3 mg/kg. This difference was not observed in patients who have a regular opioid use undergoing THA [5] or TKA [6] with a high pain threshold or no regular opioid use. Further studies are needed to validate these findings.

CRediT authorship contribution statement

Armita A. Abedi: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Javad Parvizi:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **Maher Halawa:** Writing – review & editing, Supervision, Methodology, Formal analysis, Data curation. **James A. Harty:** Writing – review & editing, Supervision, Conceptualization. **Hongyi Shao:** Writing – review & editing, Supervision, Data curation. **Abdullah S. Hammad:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization.

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