The Journal of Arthroplasty 37 (2022) 1684–1687

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Practice Guidelines

Corticosteroids in Total Joint Arthroplasty: The Clinical Practice Guidelines of 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

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ARTICLE INFO

Article history:
Received 25 January 2022
Received in revised form
23 February 2022
Accepted 7 March 2022
Available online 31 March 2022

Keywords:
corticosteroid
dexamethasone
methylprednisolone
total joint arthroplasty
total knee arthroplasty
total hip arthroplasty

The American Association of Hip and Knee Surgeons (AAHKS), The American Academy of Orthopaedic Surgeons (AAOS), The Hip Society, The Knee Society, and The American Society of Regional Anesthesia and Pain Medicine (ASRA) have worked together to develop evidence-based guidelines on the use of corticosteroids in primary total joint arthroplasty (TJA). The purpose of these guidelines is to improve the treatment of primary TJA patients and reduce practice variation by promoting a multidisciplinary, evidence-based approach to the use of corticosteroids following primary TJA.

The combined clinical practice guidelines are meant to address common and important questions related to the efficacy and safety of corticosteroids in primary TJA. Utilizing the AAOS Clinical Practice Guidelines and Systematic Review Methodology, the committee members completed a systematic review and meta-analyses to support the clinical practice guidelines [1]. Direct meta-analyses were performed when the data allowed, but network meta-analyses were not performed. Network meta-analyses are limited in their ability to control for significant variation, particularly in the multimodal analgesic protocols utilized, and the time points outcomes were reported. The current clinical practice guidelines were based on the available evidence, so future updates may become necessary as additional literature becomes available with future research.

Guideline Question 1

For patients undergoing primary TJA, do perioperative corticosteroids affect postoperative pain, opioid consumption, nausea/vomiting, and/or complications?

Response/Recommendation 1A

Perioperative intravenous dexamethasone reduces postoperative pain, opioid consumption, and nausea/vomiting after primary TJA.

Strength of Recommendation 1A

Strong.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to https://doi.org/10.1016/j.arth.2022.03.043.

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https://doi.org/10.1016/j.arth.2022.03.043

Response/Recommendation 1B

There is insufficient evidence on whether intravenous dexamethasone increases the risk of complications after primary TJA, including periprosthetic joint infection and wound healing.

Strength of Recommendation 1B

Consensus.

Rationale

We reviewed sixteen studies that evaluated the impact of perioperative dexamethasone on outcomes after TJA [2–17]. Fourteen of the sixteen studies were assessed as high quality, and two studies were assessed as moderate quality of evidence. Due to heterogeneity in the dosage, the number of doses, frequency, and duration of treatment, a limited number of meta-analyses were performed.

All sixteen studies evaluated the effects of perioperative dexamethasone on postoperative pain. Eleven of the sixteen studies found that perioperative dexamethasone reduces postoperative pain [5–14,16]. Of the nine studies that looked at pain with activity, seven studies reported dexamethasone significantly reduced pain compared to placebo [6–8,10,11,13,16]. At 24 hours postoperatively, six studies found dexamethasone reduced postoperative pain compared to placebo [5,7,9,11–13] while an additional six studies found no difference at the same timepoint [2–4,8,10,14].

Fifteen studies evaluated opioid consumption within 72 hours after TJA [2–14]. Eleven studies found that administration of perioperative intravenous dexamethasone reduces postoperative opioid consumption [2,5–9,11–15] while the remaining four studies found no difference compared to placebo [3,4,10,16]. Five studies included in a direct meta-analysis with no heterogeneity ($I^2 = 0$) found that patients who received intravenous dexamethasone required significantly less opioids for breakthrough pain (0.44 relative risk [RR]; 95% confidence interval [CI] 0.28-0.68) [7,8,11,12,16].

Thirteen studies evaluated the incidence of postoperative nausea and vomiting among TJA patients who received intravenous dexamethasone [2,4–12,14–16]. Twelve of the thirteen studies found intravenous dexamethasone reduced postoperative nausea and vomiting [2,4–12,14,16]. Nine of these studies included in a direct meta-analysis with moderate heterogeneity ($I^2 = 48.3\%$) found that patients who received intravenous dexamethasone had significantly less nausea and vomiting postoperatively compared to placebo (0.43 RR; 95% CI 0.30-0.63) [4,6–8,10–12,15,16].

There was limited literature on complications after TJA with intravenous dexamethasone treatment. Only six studies evaluated complications with intravenous dexamethasone and found no difference compared to placebo in rates of superficial and deep infection, gastrointestinal hemorrhage, deep vein thrombosis (DVT), and intramuscular thrombosis [6,8,11,12,15,16]. Given the limitations of the current literature, it is the opinion of the workgroup that there is insufficient evidence on whether intravenous dexamethasone influences the risk of complications after primary TJA, in particular, periprosthetic joint infection and wound healing.

Guideline Question 2

For patients undergoing primary TJA, does the dose of perioperative corticosteroid affect postoperative pain, opioid consumption, nausea/vomiting, and/or complications?

Response/Recommendation

There is limited evidence to determine if there is a difference between high dose and low dose intravenous dexamethasone with regard to postoperative pain, opioid consumption, nausea/vomiting, or complications after primary TJA.

Strength of Recommendation

Limited.

Rationale

One high-quality study and one moderate-quality study evaluated the impact of dosing of perioperative intravenous dexamethasone on opioid consumption and pain after TJA [3,14]. Turner et al. compared 8 mg intravenous dexamethasone (eg high dose) vs 4 mg intravenous dexamethasone (eg low dose) following a psoas block prior to primary total hip arthroplasty (THA) [3]. The authors found no difference in postoperative pain or opioid consumption between the two different dexamethasone doses [3]. Kim et al. compared postoperative intravenous dexamethasone at 0.2 mg/kg vs 0.1 mg/kg for 24 hours after primary total knee arthroplasty (TKA) and found no difference in postoperative opioid consumption or postoperative pain at 2 days postoperatively [14]. Only Kim et al. evaluated postoperative nausea after TKA and found no difference between high- and low-dose intravenous dexamethasone [14]. While one high- and one moderate-quality study are sufficient to make a moderate recommendation, the workgroup downgraded the recommendation to limited as they believe that the data in these two studies alone are insufficient to make a definitive recommendation regarding the dose of corticosteroids that should be administered prior to primary TJA.

Guideline Question 3

For patients undergoing primary TJA, do additional doses of perioperative corticosteroid affect postoperative pain, opioid consumption, and/or nausea/vomiting?

Response/Recommendation

Multiple doses of perioperative intravenous dexamethasone lead to reduced pain, opioid consumption, and nausea/vomiting compared to a single dose of perioperative intravenous dexamethasone.

Strength of Recommendation

Strong.

Rationale

We reviewed three high-quality studies that compared multiple doses of intravenous dexamethasone to a single dose of dexamethasone [6,9,12]. Due to heterogeneity in the dosage, the number of doses, frequency, and duration of treatment, no meta-analyses were performed.

Xu et al. compared 3 doses (20 mg intraoperatively, and 10 mg on postoperative days 1 and 2) to a single dose (20 mg dose intraoperatively) [6]. Wu et al. compared two doses (10 mg intraoperatively and 10 mg 6 hours postoperatively) to a single dose of 10 mg intraoperatively [12]. Backes et al. also compared two doses of dexamethasone 10 mg prior to induction and 10 mg on postoperative day 1 with a single 10 mg dose before induction [9]. All

three studies reported decreased opioid consumption and pain in the early postoperative period compared to a single dose [6,9,12]. Two of the three studies reported decreased nausea at 24 hours postoperatively with multiple doses, while Xu et al. found no difference between multiple and single doses.

Since a multiple-dose regimen of dexamethasone provides an improved reduction in pain, opioid consumption, and nausea compared to a single dose, the workgroup evaluated the number of additional doses needed for improved effect. One high-quality study by Lei et al. compared two doses of intravenous dexamethasone (10 mg at induction and at 4 hours postoperatively) to three doses (10 mg at induction, 4 hours postoperatively, and 24 hours postoperatively) [8]. The authors found that patients who received three doses had decreased pain, opioid consumption, and nausea at 48 hours postoperatively compared to patients who received two doses [8]. Given there is only one study that compares multiple doses, the workgroup does not feel that there is enough evidence to make a definitive recommendation regarding the number of doses (eg two, three, or more) that should be given postoperatively. However, the evidence does support that multiple doses of intravenous dexamethasone can help further reduce postoperative pain, opioid consumption, and nausea after primary TJA compared to a single dose.

Guideline Question 4

For patients undergoing primary TJA, are there contraindications to perioperative corticosteroid use?

Response/Recommendation

Perioperative corticosteroids may lead to increased postoperative blood glucose levels and should be used with caution in patients with diabetes mellitus.

Strength of Recommendation

Consensus.

Rationale

There are no studies in the literature that directly address contraindications to perioperative corticosteroid use in primary TJA. There is a concern utilizing corticosteroids in patients with diabetes mellitus, as this may lead to an increase in postoperative blood glucose levels. The long-term medical consequences of uncontrolled diabetes are well understood, but the short-term effects of transient increases in blood glucose remain unknown in both diabetic and nondiabetic patients. With regard to complications specific to TJA, Kheir et al. found that postoperative blood glucose levels on postoperative day 1 predict the risk of periprosthetic joint infection with a linear increase in the risk of PJI for blood glucose levels beyond 115 mg/dL [18]. The authors report that the optimal blood glucose threshold to reduce the risk of PJI is 137 mg/dL.

Of the 16 studies included in this clinical practice guideline evaluating dexamethasone, four studies excluded all patients with diabetes mellitus regardless of the type of diabetes or their hemoglobin A1c (HbA1c) [2–4,17]. Three studies excluded patients with poorly controlled diabetes, defined as a HbA1c > 7.5% [9,10,14]. One additional study excluded all type I diabetics, as well as patients with HbA1c > 7% [13]. Given patients with diabetes mellitus were excluded from a majority of the included studies in this clinical practice guideline, there is not enough evidence to make an evidence-based recommendation on the use of corticosteroids in patients with diabetes mellitus. However, it is the opinion of the workgroup that corticosteroids should be used with caution in patients with both types I and type II diabetes mellitus due to the aforementioned risks of both medical and TJA specific complications, including PJI and wound complications. The authors recommend providers consider postoperative blood glucose monitoring in patients with diabetes mellitus that receive intravenous dexamethasone. The timing, dose, number of doses, and frequency of doses should be individualized to each patient based on their type of diabetes and their HbA1c.

Areas for Future Research

The best available evidence on corticosteroids in primary TJA includes high-quality data; however, there remain many limitations in the formulation of this clinical practice guideline. A majority of studies published on the use of corticosteroids in TJA evaluate intravenous dexamethasone. While there are other intravenous corticosteroids that have been studied in TJA, including methylprednisolone and hydrocortisone, this literature is limited by a small number of studies and inconsistent reporting of outcome measures between studies [19–25]. Unfortunately, this limits the ability to draw any conclusion on their efficacy. It is unclear if there are any differences in efficacy or side effect profiles between intravenous dexamethasone and other intravenous corticosteroids. Further research should compare the various corticosteroids in TJA.

The contraindications and risks associated with corticosteroid use in TJA remain unknown. Many studies evaluating dexamethasone in TJA exclude patients with diabetes mellitus for concern of affecting their blood glucose levels. However, no studies to date have directly studied any potential implication of administering dexamethasone to TJA patients with diabetes mellitus. As a result, the workgroup recommends corticosteroids be used cautiously in this population. Future research is warranted to investigate if it is safe to use corticosteroids in patients with diabetes mellitus, and if so, at what dose and how many doses. These patients will require longer follow-up than the perioperative period to see if corticosteroids administered to patients with diabetes mellitus may further increase their already elevated risk for PJI. In addition, it is unclear if corticosteroids used in TJA are associated with an increased risk of other medical complications that have not been previously reported in the literature, such as avascular necrosis or adrenal-related complications. Future research is required to investigate whether corticosteroids, the dose, or the number of doses increase the risks of these medical complications.

It is clear that intravenous dexamethasone administered in the perioperative period reduces postoperative pain, opioid consumption, and nausea after primary TJA especially when multiple doses are given. However, there is significant heterogeneity in the number of doses, dosage, and frequency of corticosteroids administered in the current literature. For example, in this clinical practice guideline, the dose of intravenous dexamethasone administered perioperatively ranged from 4 mg to 20 mg, which may have very different efficacies and the risk of complications. Further research is needed to determine the optimal dose of corticosteroids, the number of doses, timing, and duration of corticosteroid treatment to optimize their clinical effects while minimizing risks associated with their use. In addition, with the shift to outpatient TJA, further research should investigate whether there is any clinical utility to providing patients who leave the same day of surgery with a single dose or multiple doses of oral steroids after discharge.

Peer Review Process

Following the committee's formulation of the Clinical Practice Guideline draft, it underwent a peer review by the board of

directors from AAHKS, ASRA, and the Hip and Knee Societies. The AAOS Evidence-Based Quality and Value Committee reviewed the Clinical Practice Guideline draft for endorsement. Additionally, the publication of the systematic review and meta-analysis on opioids in primary hip and knee arthroplasties that supported the formulation of the Clinical Practice Guideline has undergone peer review for publication.

Disclosure Requirement

All authors or contributors to the Clinical Practice Guideline have provided a disclosure statement in accordance with the publicly available AAOS Orthopedic Disclosure Program. All authors and contributors attest none of the disclosures present are relevant to the Clinical Practice Guidelines. In accordance with the AAOS Clinical Practice Guidelines and Systematic Review Methodology, all authors and contributors attest none of the current disclosures are relevant to the Clinical Practice Guidelines, and no prior relevant financial conflict was within a year of initiating work on the guideline.

FDA Clearance Statement

According to the FDA, it is the prescribing physician's responsibility to ascertain the FDA clearance status for all medications prior to use in a clinical setting.

Acknowledgments

We would like to thank AAHKS for providing the funding and administrative support. We would like to thank Jayson Murray, Nicole Nelson, and Francisco Casambre from the AAOS Department of Research, Quality, and Scientific Affairs for their assistance with the analysis and guidance. Lastly, we thank the leadership of the AAHKS, AAOS, ASRA, and the Hip and Knee societies for help with organizational support.

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