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Multiple Low-Dose Dexamethasone Further Improves Clinical Outcomes Following Total Hip Arthroplasty

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ABSTRACT

Background: The recommended dose regimen of dexamethasone in total hip arthroplasty (THA) has not been determined. This study was performed to assess the effects of multiple low-dose dexamethasone on clinical outcomes after THA.
Methods: Two hundred ten patients undergoing THA received 3 doses of normal saline (Group A), 2 doses of intravenous dexamethasone and 1 dose of normal saline (Group B), or 3 doses of intravenous dexamethasone (Group C). The primary outcome was the visual analog scale (VAS) score for pain and nausea. The incidence of postoperative nausea and vomiting, use of analgesic and antiemetic rescue, C-reactive protein (CRP) level, range of motion, length of stay (LOS), and complications were also compared.
Results: The VAS score (dynamic pain and nausea) on postoperative day 1 was significantly lower in Groups C and B than Group A. On postoperative day 2, the VAS score (dynamic pain and nausea) was lower in Group C than Groups A and B. In Group C, patients had a lower incidence of postoperative nausea and vomiting and reduced use of analgesic and antiemetic rescue. The CRP level was lower in Group B than Group A. Group C had the lowest CRP level among all 3 groups. LOS was shorter in Group B than Group A, while Group C had an even shorter LOS than Group B. Range of motion was greater in Group C. No complications occurred in any group.
Conclusion: The 3-dose dexamethasone regimen can further relieve postoperative pain, ameliorate postoperative nausea, provide additional inflammatory control, enhance mobility, and shorten LOS following THA.

Total hip arthroplasty (THA) is reportedly the most efficacious procedure for advanced osteoarthritis and other hip diseases [1]. However, surgery-induced inflammation often contributes to moderate to severe postsurgical pain [2]. Furthermore, inflammatory components and the adoption of anesthetic and analgesic drugs commonly provoke postoperative nausea and vomiting (PONV), which is considered to be more distressing than postoperative pain [3,4]. Both pain and PONV can hamper early recovery and result in poor patient satisfaction [5,6]. Thus, decreasing postoperative inflammation, which subsequently ameliorates pain and moderates PONV, is of fundamental significance to improving clinical outcomes and lowering healthcare system costs [5,7].

Multimodal and perioperative approaches have been used for inflammation relief [8,9]. Glucocorticoids have powerful anti-inflammatory effects and are currently used in several surgical procedures, including THA [5,10,11]. According to previous studies, glucocorticoids not only meliorate PONV but also play a role in multimodal analgesic protocols in THA [10]. Nevertheless, the recommended dose regimen has not been determined because of clinical heterogeneity [5,7,10]. Additionally, concerns regarding treatment-related adverse effects have limited the use of glucocorticoids [10,12]. Our previous study demonstrated the clinical

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effect and safety of 2 low-dose perioperative dexamethasone regimens following THA [5]. However, the second dose was given within the first 3 hours postoperatively under consideration of the high incidence of PONV in the early postoperative period [5,7,11]. Whether it is necessary and safe to administer an additional dose after 24 hours remains unknown.

Consequently, we performed this study to clarify the clinical effect and safety of a multiple-dose dexamethasone regimen. We expected to determine (1) whether the multiple-dose regimen can provide additional pain relief, (2) whether this regimen can further ameliorate nausea and reduce PONV, (3) whether the additional dose of dexamethasone can further decrease inflammatory components, (4) whether this regimen can further shorten the length of stay (LOS) and improve range of motion (ROM), and (5) whether multiple-dose dexamethasone enhances the risk of treatment-related adverse effects.

Materials and Methods

Study Design

This prospective study protocol was approved by the institutional review board and registered in the International Clinical Trial Registry (ChiCTR-IOR-17011081). Informed consent for participation in this trial was obtained from each patient before surgery.

Patient Cohort

From April 2017 to September 2017, patients who were scheduled to undergo primary THA were screened for enrollment in this trial. The exclusion criteria were revisions, bilateral procedures, allergies to dexamethasone, administration of any glucocorticoids during the 3 months before surgery, administration of any strong opioids during the past 7 days, and the presence of rheumatoid disease, systemic lupus erythematosus, ankylosing spondylitis, serious cardiac or cerebrovascular problems, or severe liver or kidney function deficiency.

In total, 210 consecutive patients were randomized into 3 study groups. Group A served as the control group and received three 2-mL doses of intravenous isotonic saline; Group B received two 10-mg doses of intravenous dexamethasone (2 mL; Tianjin Kingyork Group Co, Ltd, China) and one 2-mL dose of normal saline; and Group C received three 10-mg doses of intravenous dexamethasone. The first dose was administered by analgesists immediately prior to anesthesia induction, the second dose was administered by a nurse immediately upon the patient's return to the inpatient unit (3-4 hours after the first dose), and the third dose was given 24 hours after the first dose. The postoperative protocol was performed by nurses. A random-allocation sequence was used, in which the group assignments were concealed in opaque sealed envelopes and only opened before surgery. The analgesists and nurses were not involved in this trial. The patients, surgeons, data controller, and analyst were blinded.

Surgical Procedures

All patients who were planned to undergo general anesthesia were operated on in the lateral decubitus position with the standard posterolateral approach. We performed the operations without tourniquet application or vacuum wound drainage, and the prostheses were cementless cups and stems. All patients received infiltration of a local anesthetic in the perisurgical area [20 mL of ropivacaine (100 mg/10 mL) and 60 mL of normal saline] before wound closure. No nerve block or intravenous patient-controlled analgesia was utilized perioperatively.

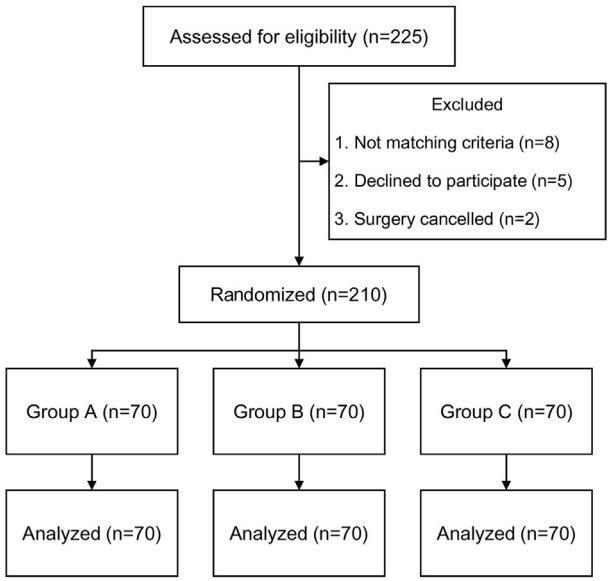

Fig. 1. Flow diagram of patients shows the study design.

Postoperative Care Protocol

A standardized clinical pathway was used for all patients during the hospital duration. Active ROM exercise and strength training were performed under the supervision and assistance of a physiotherapist, and the patients began walking with a walker on the first postoperative day (POD1).

Our protocol for relieving pain and PONV was the same for all patients. Postoperative pain treatment was performed with oral diclofenac at 50 mg every 12 hours, initiated about 3 hours after surgery. When the patients reported pain with a score of >6 on a 0 to 10-point visual analog scale (VAS), an intramuscular injection of pethidine hydrochloride (50 mg) was administered. Oral mosapride (5 mg three times daily, before each meal) was started 1 day before the operation and administered again when the patients resumed oral intake postoperatively. Nausea of at least a moderate level (VAS score of >4) and vomiting were treated with an intramuscular injection of metoclopramide (10 mg). No other analgesic or antiemetic drugs were used throughout the study period.

Table 1
Baseline Characteristics of the Study Population.

Demographics	Group A (n = 70)	Group B (n = 70)	Group C (n = 70)	*P* Value
Age (y)	57.5 ± 12.0	56.6 ± 10.5	55.6 ± 9.7	.575
Gender (M/F)	37/33	37/33	29/41	.295
Height (cm)	161.1 ± 6.9	160.2 ± 7.3	161.0 ± 7.0	.739
Weight (kg)	61.7 ± 8.8	60.0 ± 9.1	59.7 ± 9.4	.367
BMI (kg/m^2)	23.8 ± 3.4	23.3 ± 2.8	23.0 ± 3.0	.280
DDH-OA (n)	35	41	37	.585
ONFH (n)	22	19	22	.815
OA (n)	13	10	11	.782
ROM (°) (Flex)	91.2 ± 18.3	91.2 ± 17.2	93.4 ± 12.7	.666
ROM (°) (Ext)	0.7 ± 3.4	−0.1 ± 3.2	−0.6 ± 4.3	.091
ROM (°) (Abd)	24.3 ± 11.3	23.6 ± 11.1	22.2 ± 9.4	.504
Dynamic pain	5.2 ± 0.7	5.1 ± 0.7	5.3 ± 0.8	.654
Pain at rest	3.0 ± 0.8	3.0 ± 0.8	3.1 ± 0.7	.514

M/F, male/female; BMI, body mass index; DDH-OA, osteoarthritis secondary to developmental dysplasia of the hip; ONFH, osteonecrosis of the femoral head; OA, osteoarthritis; Flex, flexion; Ext, extension; Abd, abduction.