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Single High-Dose Systemic Methylprednisolone Administered Preoperatively Improves Pain Control and Sleep Quality After Total Hip Arthroplasty: A Double-Blind, Randomized Controlled Trial

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ABSTRACT

Background: This study was performed to evaluate the efficacy of preoperative high-dose methylprednisolone on pain levels and sleep quality following primary total hip arthroplasty.
Material and methods: A double-blind, randomized controlled trial was performed in adults underdoing total hip arthroplasty. A computer-generated, permuted-block randomization scheme with a 1:1 ratio between the intervention (125 mg methylprednisolone) and control groups (normal saline) was utilized. Patients underwent a similar preoperative and postoperative protocol. Pain was assessed using the visual analog scale (VAS). Sleep quality was assessed at the 2-week postoperative visit using the Pittsburgh Sleep Quality Index (PSQI).
Results: With a total of 70 patients, 35 patients were included in the intervention and placebo groups. Hospital stay was significantly shorter in the intervention group (1.5 ± 0.7 vs 2.0 ± 0.5 days, $P = .03$). Preoperative pain levels were similar between groups, while satisfactory pain control was achieved in a significantly larger number of patients in the intervention group (18 vs 8 patients, $P = .009$). The intervention group was significantly more likely to have a good sleep quality than the placebo groups (74% vs 31%, $P = .001$). No significant differences were found between preoperative and postoperative blood sugar levels. We did not observe any cases of early postoperative wound complication, infection, or deep vein thrombosis among our patients.
Conclusion: In this randomized controlled trial, preoperative administration of 125 mg of methylprednisolone was found to improve pain control, as measured by VAS, 24 hours after surgery, and sleep quality, as measured by PSQI, 2 weeks following surgery.

Introduction

Modern techniques and approaches have expanded the indications of total hip arthroplasty (THA), while providing a swift recovery with minimal complications for the majority of patients. Postoperative care has also transitioned from exclusively inpatient to outpatient, ambulatory THA in many cases, reducing the cost of care and enhancing the patient's quality of life [1]. Postoperative pain is challenging to manage and may delay patient's rehabilitation if not controlled. The short- and long-term risks associated with opioids have driven the surgeons to choose alternative, opioid-sparing pain management in the postoperative period [2]. Postoperative pain is multifactorial, and the activation of stress response pathways aggravates the pain caused by direct tissue injury, causing nausea and vomiting, poor sleep quality, and delayed rehabilitation [3].

Activation of inflammatory cascades and neuroendocrine responses seems to be closely related to postoperative pain and recovery. Consequently, corticosteroids have been proposed to enhance postoperative recovery and decrease pain levels [1,4]. In a systematic review, Yue et al. reported that the high-dose systemic

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steroid was effective in reducing postoperative nausea, vomiting, and pain after THA and total knee arthroplasty (TKA) [5]. The anti-inflammatory effects of high-dose systemic corticosteroids by reducing the physiological response to inflammatory signaling pathways (including interleukin-6 and C-reactive protein) are responsible for this effect [4]. Moreover, corticosteroids exert their anti-inflammatory effects by preventing the accumulation of inflammatory cells in the area of inflammation, inhibiting phagocytosis and the release of enzymes responsible for inflammation, and inhibiting the production and release of chemical mediators of inflammation [6]. Controversy still exists on the degree of pain control and the effects of corticosteroids on sleep quality after THA and TKA [1–3]. Lunn et al. did not find preoperative methylprednisolone to improve sleep quality although pain intensity was improved [7]. Other studies have found that pain levels and fatigue during walking were improved with preoperative methylprednisolone, but the sleep quality was unchanged [7–9]. Other studies have suggested that by suppressing stress responses, corticosteroids may help with postoperative sleep quality. There are also concerns regarding possible complications and risks associated with corticosteroids, including the risk of infection, blood glucose control, and systemic complications that may limit their application [10]. Other areas of controversy include the preferred corticosteroid and the optimal dosage, which are critical to minimize the possible side effects [8,9,11].

Therefore, this double-blind, randomized controlled trial (RCT) was performed to evaluate the efficacy of preoperative high-dose methylprednisolone on pain levels and sleep quality following primary THA. We hypothesized that patients who receive preoperative methylprednisolone will have lower pain levels at 24 hours after surgery and a higher sleep quality measured at 2 weeks postoperatively but higher fasting blood sugar (FBS) levels.

Material and methods

This was a randomized, double-blind clinical trial that was conducted at a referral university hospital in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. This RCT was registered in the Iranian Clinical Trial Registry database (IRCT#: IRCT20200118046174N3), after institutional review board approval was obtained (IR.TUMS.SINAHOSPITAL.REC.1399.040) from our institution. Patients older than 18 years who were candidates for a primary, elective THA were included in the study. Patients with a history of renal or liver disease, peptic ulcer disease, diabetic neuropathy, poorly controlled diabetes mellitus or hypertension, patients who had received corticosteroids in the past 3 months, as well as those younger than 18 years were excluded. Diabetic patients were counseled regarding the possible complications of corticosteroids and underwent a consult with endocrinology for preoperative and postoperative management. All patients gave written informed consent prior to enrollment and were included after a thorough discussion regarding our goals for the study, the randomized nature of the trial, the risks and benefits, and possible complications.

A computer-generated, permuted-block randomization scheme with a 1:1 ratio between the intervention and control groups was used to randomize patients. The allocation was concealed using sealed and opaque envelopes, numbered consecutively. An independent researcher who was not involved in other study procedures performed the randomization process. Patients received either methylprednisolone (125 mg, intravenous [IV]) in the intervention group or normal saline (2 mL, IV) as the control group after induction of anesthesia. The same researcher who randomized the patients was in charge of preparing the injections, and the patient and surgeon were blinded to the allocation and intervention.

Patients underwent a similar surgical procedure and postoperative care: All patients underwent general anesthesia for the procedure. Patients received antibiotics prior to incision, which was continued for 24 hours in all patients. All surgeries were performed by 2 authors, S.H.S. (via a direct anterior approach) and B.S. (via a direct lateral approach). All patients received multimodal pain management, including intraoperative and postoperative acetaminophen (1 g/12 h, IV), pregabalin (75 mg every 6 hours, oral), celecoxib (200 mg twice daily, oral), and a proton pump inhibitor. Deep vein thrombosis (DVT) prophylaxis was similar in all patients and included aspirin 80 mg twice daily for 30 days after surgery. Patients were admitted postoperatively, and physical therapy was initiated to start muscle strengthening and range-of-motion exercises on the day of surgery and weight-bearing as tolerated on postoperative day 1. Patients were discharged on postoperative day 1 or 2 depending on their pain and general condition, surgeon's preference, and patient's living conditions and distance from the hospital. FBS levels were measured on the day of surgery and the following day. Preoperative blood pressure was recorded at the time the patient was admitted and was rechecked before discharge.

Postoperative visits were done at 2, 6, 12, and 24 weeks postoperatively, and radiographs were taken at all visits. Pain was assessed using the visual analog scale (VAS), with a scale from 0 (no pain) to 10 (most severe pain imaginable) at all visits. Pain control was deemed satisfactory with a VAS score of 3 or lower, with the data being collected 24 hours after surgery. Sleep quality was assessed at the 2-week postoperative visit through the Pittsburgh Sleep Quality Index (PSQI), which is a validated self-rated questionnaire to measure the quality and patterns of sleep in adults. Good sleep quality was defined as a PSQI score of 5 or lower [12].

An a priori power analysis was performed, which showed that for a power of 80%, a two-tailed P value of 0.05, a medium effect size ($d = 0.7$), and equal allocation between groups, we would need a total of 68 patients to be adequately powered. The decision was made to recruit 70 patients, with 35 patients in each group.

Statistical analysis was performed with SPSS version 23.0 for Windows (IBM, Armonk, NY). Results are presented as mean ± standard deviation for quantitative variables and are summarized by frequency (percentage) for categorical variables. Continuous variables were compared using Student t-tests or Mann-Whitney test depending on whether the data were normally distributed or not. Comparisons between categorical variables were made using chi-square tests.

Results

Patient recruitment was completed in 9 months, and as shown in Figure 1, 35 patients were allocated to each group. The mean age was 44.5 years in the entire cohort, and females were predominant (41 patients). There were no significant differences in preoperative demographics and anthropometric variables between the intervention and placebo groups, as summarized in Table 1.

Intraoperatively, 11.4% and 17.1% of patients in the intervention and placebo groups, respectively, received a packed cell transfusion ($P = .79$). No significant differences were found between preoperative and postoperative FBS levels (Table 2). While preoperative systolic blood pressure was similar between groups ($P = .82$), patients receiving methylprednisolone had a higher mean postoperative systolic blood pressure measurements (135 vs 129 mmHg, $P = .01$). The time from surgery to walking independently was similar between intervention and placebo groups (1.1 ± 0.4 vs 1.1 ± 0.5 days, $P = .79$). However, the duration of hospital stay was significantly shorter in patients receiving methylprednisolone (1.5 ± 0.7 vs 2.0 ± 0.5 days, $P = .03$). Preoperatively, both groups had a very low rate of good sleep quality ($P = .55$). On the 2-week

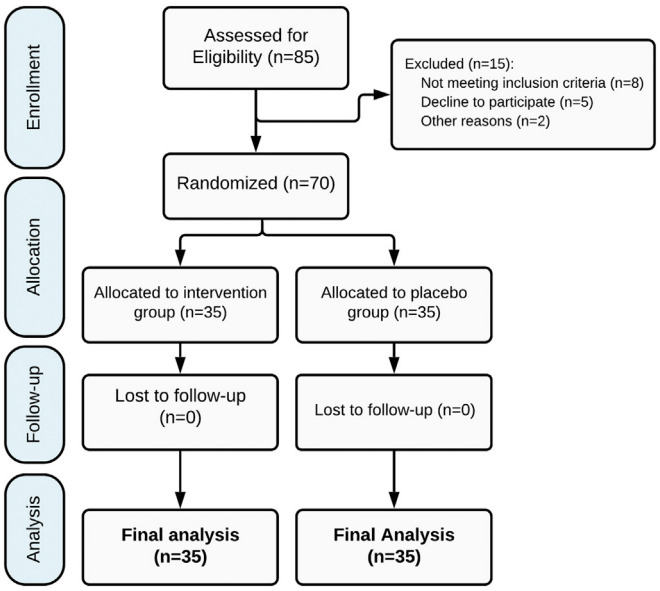

Figure 1. CONSORT diagram for patient selection and enrollment in this study.

postoperative visit, the intervention group was significantly more likely to have a good sleep quality than the placebo groups (74% vs 31%, $P = .001$). Preoperative pain levels were similar between groups, while satisfactory pain control was achieved in a significantly larger number of patients in the intervention group (18 vs 8 patients, $P = .009$). We did not observe any cases of early postoperative wound complication, infection, or DVT among our patients.

Discussion

Postoperative pain and sleep quality are important aspects of patient satisfaction and could directly and indirectly influence the outcomes of THA [1,3]. Owing to their modulation of inflammatory pathways, corticosteroids have been used to improve postoperative nausea and vomiting, pain, and sleep quality [4,6]. Controversy still exists owing to the risks associated with corticosteroid use, which may include hyperglycemia (especially in diabetic patients), increase in blood pressure, and infection [6,13,14]. This RCT was conducted to elucidate the effects of single high-dose methylprednisolone administered preoperatively on postoperative pain and sleep quality in adults undergoing THA.

Preoperative corticosteroids have been shown to reduce postoperative pain levels and improve sleep quality in an array of surgeries. In a systematic review, Sauerland et al. reviewed all randomized clinical trials of corticosteroid use in trauma and elective surgeries and found that a perioperative single-shot administration of high-dose corticosteroids was not associated with adverse outcomes [10]. Furthermore, in patients with multiple fractures, the risk of pulmonary complications was lower with corticosteroids. Corticosteroids exert their anti-inflammatory action by manipulating several cytokine pathways [4,6,13,14]. A previous RCT found decreased levels of interleukin-6 after surgery in THA patients who received methylprednisolone preoperatively, which may explain the beneficial effects on pain control, nausea, and vomiting. Interestingly, this decrease was not associated with an increase in thrombogenic markers [15].

We found that single-dose systemic methylprednisolone administered preoperatively decreased pain levels 24 hours after surgery compared with placebo. Evidence is conflicting regarding pain control with systemic steroids although the heterogeneity of studies in the administered drug and its dosage may play a role in this. Sculco et al. reported insignificant changes in pain levels after THA in patients who received preoperative hydrocortisone although total administered patient-controlled anesthesia was significantly less in the intervention group [15]. Other studies have found improved pain control with the use of systemic steroids at different time points [3,7–9,15–18].

With the exponential increase in the use of fast-track hip-recovery programs and ambulatory THA, the duration of hospital stay is an important factor in reducing the cost of THA and facilitating earlier patient rehabilitation and return to activities of daily living [2,5,17]. While the evidence is once again conflicting, several studies have shown beneficial effects of preoperative systemic steroids in reducing the hospital stay after THA and TKA [8]. Although all our patients underwent inpatient THA and were admitted for at least 24 hours, we did observe a significant decrease in the duration of hospital stay in patients who received preoperative systemic methylprednisolone.

Sleep quality following surgery is an important determinant of patient satisfaction and overall well-being and is affected by several surgical and nonsurgical factors [3]. To the best of our knowledge, this is the first study to report changes in sleep quality, as measured by a validated patient-reported measure, with preoperative systemic corticosteroids. We found that while the majority of patients (74%) who received preoperative methylprednisolone had a good sleep quality, defined as a PSQI ≤5, less than a third of patients in the placebo group had a good sleep quality. This is an important finding since decreased sleep quality and sleep disturbances are

Table 1
Baseline characteristics of the study population.

Variable	Intervention group (n = 35)	Placebo group (n = 35)	*P* value
Male gender	17 (48.6)	12 (34.3)	.225
Mean age, y	44.3 ± 15.2	44.6 ± 16.7	.941
Mean weight, kg	73.4 ± 10.7	73.3 ± 10.4	.973
Education level			.271
Illiterate	1 (2.9)	0 (0.0)	
Primary	7 (20.0)	11 (31.4)	
High school diploma	18 (51.4)	20 (57.1)	
Academic degree	9 (25.7)	4 (11.4)	

Table 2
Pre operative and postoperative variables compared between the intervention and placebo groups.

Variables	Intervention group (n = 35)	Placebo group (n = 35)	*P* value
Fasting blood sugar, mg/dL			
Preoperative	117.4 ± 10.3	119.0 ± 11.0	.54
Postoperative	123.0 ± 11.40	122.6 ± 11.4	.89
Systolic blood pressure, mmHg			
Preoperative	129 ± 11	129 ± 10	.82
Postoperative	**134 ± 11**	**128 ± 9**	**.01**
Good sleep quality (PSQI ≤5)			
Preoperative	1 (2.9)	2 (5.7)	.55
Postoperative	**26 (74.3)**	**11 (31.4)**	**.001**
Preoperative pain			1.0
Poor	20 (57.1)	20 (57.1)	
Fair	15 (42.9)	15 (42.9)	
Good	0 (0.0)	0 (0.0)	
Excellent	0 (0.0)	0 (0.0)	
Postoperative pain control			**.009**
Poor (VAS > 4)	**17 (48.5)**	**27 (77.1)**	
Satisfactory (VAS ≤ 3)	**18 (51.5)**	**8 (22.9)**	

Significant comparisons are indicated in bold.

important determinants of pain perception, rehabilitation compliance, and overall satisfaction, and several approaches have been used to improve sleep quality after THA [19].

There are concerns regarding the risk of wound dehiscence, infection, and DVT with systemic steroid use, particularly in patients with comorbidities [4,10,14]. We did not find an increase in the complication rate although our sample size might not be large enough to detect a change in uncommon outcomes. Previous trials of systemic steroids in joint arthroplasty have also not found an increase in deep infection and DVT incidence. Several studies have reported increased postoperative blood glucose levels in patients who received systemic steroids [5,11,18]. We did not find such a difference, which may be due to the fact that we excluded diabetics who had poor glucose control. However, we found higher systolic blood pressure measurements in the intervention group on postoperative day 1 although none of the patients in either group required adding medications to control the blood pressure.

We acknowledge several limitations to our study. First, the mean age of the patients included in this study (44.3 ± 15.2 years) is less than that of the overall THA patients, which has 2 main reasons: Older patients are more likely to have comorbidities excluding them from this study. Also, we typically treat older and high-risk patients at our referral facility where intensive care is available. Second, our sample size was limited due to the difficulties of designing and implementing randomized trials. While we were adequately powered to detect differences in PSQI and pain levels, we may have been underpowered to detect any differences in the infection rate, considering the low incidence of infections. Furthermore, we did not assess functional outcomes as our main goal was to assess short-term risks and benefits. Also, surgeon preferences may play a role in the duration of hospitalization, which we could not control. Finally, we did not control for underlying patient comorbidities and pathologies, which may be important determinants of postoperative pain and sleep quality control. Strengths of this study include its randomized controlled nature, a priori power analysis, and using a validated scoring system to measure sleep quality.

Conclusions

In conclusion, in a double-blind, RCT in adult patients undergoing THA, 125 mg of methylprednisolone administered preoperatively was found to improve pain control, as measured by VAS 24 hours after surgery, and sleep quality, as measured by PSQI 2 weeks following surgery. FBS changes were similar in the intervention and placebo groups, while postoperative systolic blood pressure was higher in the intervention group. No case of infection was observed during the study period.

Ethics approval and consent to participate

This RCT was registered in the Iranian Clinical Trial Registry database (IRCT#: IRCT20200118046174N3), after institutional review board approval was obtained (IR.TUMS.SINAHOSPITAL.REC.1399.040) from the Tehran University of Medical Sciences.

Consent for publication

The study protocol was throgouhly explained to patients. All included patients agreed with and signed a written informed consent (in Farsi).

Availability of data and materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

S.H.S., B.S., and M.R.G. contributed to study design and conceptualization. S.H.S., M.G., and M.R.G. collected data. S.H.S., B.S., and S.B. performed data analysis. B.S., M.G., and S.B. drafted the manuscript. All authors revised the manuscript and have read and approved the final version of the manuscript.

Trial registration

This RCT was registered in the Iranian Clinical Trial Registry database (IRCT#: IRCT20200118046174N3), Registered 03/01/2021, https://fa.irct.ir/trial/52568.

Conflicts of interest

The authors declare that there are no conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.03.006

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