

Effect of high-dose preoperative methylprednisolone on recovery after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial

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Editor's key points

- There is considerable interest in the effects of steroids in the perioperative period.
- There is already evidence of beneficial effects on pain and nausea, although not in this patient population.
- Using predefined criteria, this study comprehensively assessed the postoperative effects of i.v. methylprednisolone (MP) on function and pain.
- There was no improvement in functional discharge criteria using MP, although pain control was better.

Background. High-dose glucocorticoid may reduce postsurgical pain and improve recovery. We hypothesized that 125 mg methylprednisolone (MP) would reduce time to meet functional discharge criteria after total hip arthroplasty (THA).

Methods. Forty-eight patients undergoing unilateral THA under spinal anaesthesia were consecutively included in this randomized, double-blind, placebo-controlled trial receiving preoperative i.v. MP or saline. All patients received a standardized, multimodal analgesic regime with paracetamol, celecoxib, and gabapentin. The primary outcome was time to meet well-defined functional discharge criteria. Secondary outcomes were handgrip strength and endurance, pain, nausea, vomiting, fatigue, sleep quality, and rescue analgesic-, antiemetic-, and hypnotic medicine requirements. The inflammatory response measured by C-reactive protein (CRP) and actual length of stay were also registered. Discharge criteria were assessed twice daily (at 09:00 and 14:00 h) until discharge. Other outcomes were assessed at 2, 4, 6, 8, and 24 h after operation, and also in a questionnaire from postoperative day (POD) 1–4.

Results. Time to meet discharge criteria was [median (IQR) (95% CI), MP vs placebo]: 23.5 (23.3–23.7) (17.8–43.8) vs 23.5 (23.0–23.8) (20.0–46.8) h, the mean difference (95% CI) being –1.3 (–4.7 to 2.2) h, $P=0.65$. Overall pain for the first 24 h after surgery was significantly reduced in the MP vs the placebo group ($P<0.01$), as was CRP at 24 h ($P<0.0001$). No other between-group differences were observed. No drug-related complications were observed at follow-up on POD30.

Conclusions. MP 125 mg i.v. before surgery added to a multimodal oral analgesic regime did not reduce time to meet functional discharge criteria after THA, but improved analgesia for the first 24 h.

Keywords: arthroplasty, replacement, hip; glucocorticoids; methylprednisolone; pain, postoperative

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Inflammatory components are part of the surgical stress response¹ that may affect postoperative recovery.^{2,3} In particular, the level of pain, fatigue, dizziness, nausea and vomiting (PONV), muscle weakness, and sleep quality may all be affected, increasing the need for hospitalization.^{4–6} By reducing the surgical injury-provoked inflammatory response, glucocorticoids may improve early postoperative recovery.^{7–9}

Dexamethasone 4–8 mg represents a well-documented recommendation for PONV prophylaxis,¹⁰ and there is a probability that higher doses of glucocorticoids may reduce

pain¹¹ and fatigue.¹² In orthopaedic joint replacement surgery, a single preoperative dose of dexamethasone 40 mg i.v. has been shown to decrease dynamic pain and to suppress the inflammatory response measured by C-reactive protein (CRP) after total hip arthroplasty (THA).¹³ Likewise, a single preoperative dose of methylprednisolone (MP) 125 mg i.v. has been shown to improve analgesia, reduce opioid requirements, CRP, PONV, and fatigue after total knee arthroplasty (TKA).¹⁴ In non-procedure-specific orthopaedic surgery, a single dose of MP 125 mg i.v.

administered to patients with moderate to severe pain 1 day after surgery was as effective as ketorolac 30 mg i.v. in reducing acute pain, and opioid requirement compared with both placebo and ketorolac.¹⁵

Despite the promising data so far, more procedure-specific studies are warranted on the effects of glucocorticoids on immediate postoperative recovery,¹⁶ in particular studies that closely assess different aspects of recovery. Also, evaluation of the effect of different multimodal analgesic regimes and combinations are generally needed.¹⁷ The aim of this trial was therefore to assess the effect of a single preoperative dose of MP 125 mg i.v. on postoperative recovery in patients undergoing THA, the primary outcome being time to meet well-defined functional discharge criteria. We hypothesized that 125 mg MP i.v. would reduce time to meet these criteria.

Methods

Patients and design

The trial was approved by the regional ethics committee, the Danish Medicines Agency, and the Danish Data Protection Agency, and was registered at www.clinicaltrials.gov (reg. no. NCT00968903). Oral and written informed consent was obtained from all patients, and the study was carried out in accordance with the principles of the Helsinki Declarations. The CONSORT recommendations for reporting randomized, controlled clinical trials were followed.¹⁸

Patients scheduled for elective, unilateral, primary THA by one of the three orthopaedic surgeons at Hvidovre University Hospital, Copenhagen, Denmark, aged >18 yr, and familiar with the Danish language, were consecutively screened for inclusion in the study from April 2010 to January 2011. Exclusion criteria were history of alcohol or medical abuse, allergies to MP, daily use of glucocorticoids or strong opioids (morphine, fentanyl, hydromorphone, ketobemidone, methadone, nicomorphine, oxycodone, and meperidine), fertile women, history of severe heart disease (NYHA >2) or renal failure, active peptic ulcer disease, diabetic neuropathy, rheumatoid arthritis, and neurological or psychiatric diseases, potentially influencing pain perception.

The design was a single-centre, prospective, randomized, double-blind, placebo-controlled trial.

Randomization, study intervention, and blinding

Forty-eight included patients were randomly assigned to two groups of 24. A random allocation sequence concealed in 48 consecutively numbered, opaque, sealed envelopes, determining active treatment or placebo, was computer-generated by a project nurse not otherwise involved in the trial. No stratification or block randomization was made. The envelopes were opened on the morning of surgery, and the trial drug was prepared by a senior anaesthetist not otherwise involved in data collection.

The active treatment group received a single-dose of MP, 125 mg (2 ml) i.v. (Solu-Medrol®; Pfizer, Ballerup, Denmark) and the placebo group a single-dose of isotonic saline (2

ml) i.v. The test solution was administered just before performing the spinal anaesthesia.

All trial participants, care providers, and data collectors were blinded to allocation.

Outcome measures and assessments

The primary outcome was time to meet well-defined functional discharge criteria (discharge readiness). Secondary outcomes were handgrip strength and handgrip endurance (fatigue resistance), pain, nausea, vomiting, fatigue, sleep quality, and rescue analgesic-, antiemetic-, and hypnotic medicine requirements; finally, we evaluated the inflammatory response measured by the CRP and actual length of stay (LOS).

The functional discharge criteria were independent ability to get dressed, to get in and out of bed, to sit and rise from a chair/toilet, independence in personal care, and mobilization with crutches. In addition, sufficient oral pain treatment [visual analogue scale (VAS) <50 mm during activity] was a prerequisite. Discharge criteria were assessed twice daily at 09:00 and 14:00 h until discharge.⁵ Time to meet discharge criteria was calculated as the time from end of surgery till discharge criteria were met.

Handgrip strength and handgrip endurance were assessed using a digital hand dynamometer (SH5003, SAEHAN Corporation, Masan, Korea) before operation and 24 h after surgery. After standardized verbal instructions and a number of sub-maximal preconditioning trials, the patients performed five maximal handgrips—separated by 60 s pauses—with their dominant (writing) hand. Handgrips were performed seated in a standard position with hip and knee joint angles of 90°, the upper arm vertically aligned and slightly abducted to avoid upper body contact, the elbow flexed to 90°, and the forearm and hand in the neutral position. No lower arm–thigh or feet–floor contact was allowed, and strong verbal encouragement was provided during the 5 s contractions. The highest value of the five maximal handgrips was used to express handgrip strength in Newtons (N) (the dynamometer measured force in kilograms, which was multiplied with the acceleration of gravity = 9.82 m s⁻²). After having performed the maximal handgrips (and a 2 min pause), the patients finished the handgrip protocol by performing a final maximal handgrip, with the instruction to maintain a maximal grip for as long as possible. The time taken (in seconds) for the force to decrease to 50% of the previously established maximal handgrip strength was defined as handgrip endurance.⁴

Pain was assessed at rest (supine), upon 45° passive hip flexion with straight leg, upon ambulation with a walking aid (5 m), and upon rising from a chair using the 100 mm VAS (0, no pain, and 100, worst pain imaginable) before operation, and 2, 4, 6, 8, and 24 h after operation, and also in a questionnaire twice daily (in the evening before going to bed and in the morning when getting up) from the evening on the first postoperative day (POD) 1 to POD4. Nausea was assessed using a four-point numeric rating scale (NRS; 0, none; 1, slight; 2, moderate; 3, severe), vomiting by the

number of episodes (since last recording), and fatigue using a 10-point NRS (1, fit; 10, fatigued)¹⁹ at the same time points as above. Sleep quality was assessed using the 100 mm VAS (0, best conceivable sleep; 100, worst conceivable sleep).²⁰

The total amount of sufentanil (μg) administered in the post-anaesthesia care unit (PACU) was registered. Furthermore, cumulated amounts of morphine (mg) and ondansetron (mg)—and if zolpidem was administered the previous night (yes/no)—were recorded 24 h after surgery and from POD1 to 4. Systemic inflammation was measured by CRP in venous blood before operation and 24 h after surgical incision. Actual LOS was counted as the number of postoperative nights in hospital, until discharge. Complications were registered during hospitalization and in a telephone interview on day 30. Also, readmissions and the reasons were registered. All data collection was performed by one of the two investigators.

Anaesthesia, surgery, and analgesia

Anaesthesia, surgical technique, and postoperative analgesia were standardized as also previously described in a similar study (with the same set up, anaesthesia, surgical procedure, and analgesia).²¹ Included patients were operated as number 1 or 2 each day. Surgery was performed under lumbar spinal anaesthesia with 12.5 mg isobaric bupivacaine (0.5%) and optional sedation with propofol ($1\text{--}5\text{ mg kg}^{-1}\text{ h}^{-1}$). Cefuroxime 1.5 g and tranexamic acid 1 g were administered i.v. before operation.²¹ Intraoperative fluid therapy was standardized and consisted of saline 0.9% $5\text{ ml kg}^{-1}\text{ h}^{-1}$ and colloid (Voluven®; Fresenius Kabi AB, Uppsala, Sweden) $7.5\text{ ml kg}^{-1}\text{ h}^{-1}$.²² Rivaroxaban (Xarelto, 10 mg) for thromboprophylaxis was administered after operation (starting 6–8 h after surgery) once daily and until discharge only. THA was performed using a posterior approach without the use of minimal invasive surgical techniques. Drains were not used.²¹ Prostheses were Bimetric-stems with Ringloc-cups or Magnum-cups (Biomet-Merck Inc., Warsaw, IN, USA). A multimodal oral analgesic regime consisting of slow-release paracetamol 2 g, celecoxib 400 mg, and gabapentin 600 mg was instituted 1–2 h before operation without any other premedication. Thereafter, celecoxib 200 mg and slow-release paracetamol 2 g was administered 12 hourly (7 a.m. and 10 p.m.) and gabapentin 300 mg (at 7 a.m.) and 600 mg (at 10 p.m.) up to and including POD6, after which the patient's general practitioner handled further pain management.²¹ Rescue analgesics (administered if VAS >50 mm at rest) consisted of sufentanil 5–10 μg i.v. in the PACU and subsequently of oral morphine 10 mg at the surgical ward. PONV was treated with ondansetron 4 mg and sleep disturbances with zolpidem 5 mg. Patients followed a routine, well-defined, fast-track rehabilitation regime, and were discharged directly to their homes.⁵

Statistical analysis

The estimated sample size for the primary outcome was calculated based on the results from a pilot study ($n=12$),

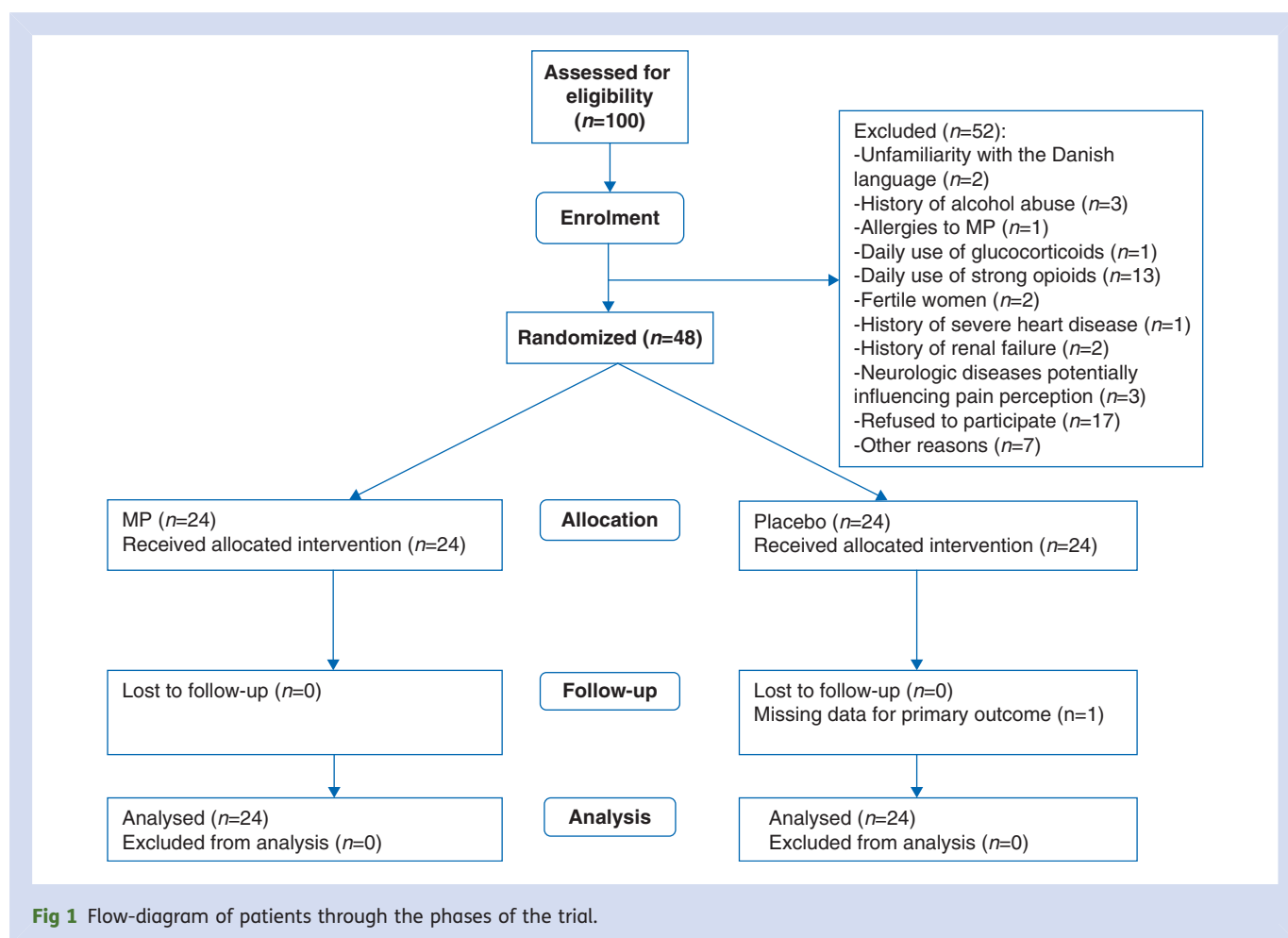
where time to meet well-defined functional discharge criteria after primary, unilateral THA at Hvidovre University Hospital was found to be 25.6 (6.7) h [mean (standard deviation, SD)]. A total of 48 patients would allow the detection of a 25% reduction in time (from 25.6 to 19.2 h) in the MP group compared with the placebo group, at a two-sided 5% significance level, with a power of 90%, allowing for a 5% drop-out rate.

Continuous numeric variables were assessed for the normality of distribution (Kolmogorov–Smirnov). Depending on whether variables were normally distributed (age, BMI, preoperative handgrip strength, preoperative sleep quality, preoperative haemoglobin, summarized pain upon ambulation and upon rise from chair the first 24 h after surgery, and CRP 24 h after surgery), they are presented as means with SD , and otherwise as medians with inter-quartile ranges (IQR) and 95% confidence intervals (95% CI). Between-group comparisons were made using unpaired t-tests and the Mann–Whitney rank-sum tests, when appropriate. Categorical variables are presented as counts with percentage, and between-group comparisons were made using the Fisher exact or χ^2 test, when appropriate. Continuous data with repeated measures (pain, fatigue, and sleep quality) were analysed using repeated measurement regression with random intercepts and first-order auto-correlation and presented as an overall Wald χ^2 test for differences in means between the groups. Also, composite pain (summarized pain) was calculated for each of the four pain assessments, by adding up pain scores from the different time points (2–24 h) and POD1–4. Outcomes for the first 24 h and outcomes thereafter (POD1–4) were analysed separately due to the different ways of data recording—investigator and questionnaire, respectively. Data analyses were conducted using SPSS for windows, version 12.0 (SPSS Inc., Chicago, IL, USA) and R for windows, version 2.11.1 (R Foundation for Statistical Computing, Vienna, Austria). $P<0.05$ was considered statistically significant.

Results

One hundred patients were assessed for eligibility in the trial, and 48 randomized patients all received their allocated intervention, and were included in an intention-to-treat analysis (Fig. 1). Regarding the primary outcome, data were missing in one patient for unknown reasons. Handgrip strength and endurance data were missing in further two patients due to severe dizziness, making testing impossible in one case, and because the investigator was absent in another case. Two post-discharge questionnaires were missing. Baseline patient characteristics and pre- and perioperative characteristics were similar in the two groups (Table 1).

Time to meet functional discharge criteria was: MP 23.5 (23.3–23.7) (17.8–43.8) h vs placebo 23.5 (23.0–23.8) (20.0–46.8) h, the mean difference (95% CI) being -1.3 (-4.7 to 2.2) h, $P=0.65$. No significant difference was observed in the number of patients who achieved discharge criteria at each time of measurement, $P=0.81$ [count (%), MP



vs placebo] being at 14:00 h on POD 0: 0 (0%) vs 0 (0%); at 09:00 h on POD 1: 20 (83.3%) vs 18 (78.3%); at 14:00 h on POD 1: 3 (12.5%) vs 3 (13.0%); and at 09:00 h on POD 2: 1 (4.2%) vs 2 (8.7%).

No significant differences were observed for handgrip strength 24 h after surgery [median (IQR) (95% CI), MP vs placebo]: 282 (228–385) (178–590) vs 314 (227–364) (148–495) N, the mean difference (95% CI) being 10 (–55 to 76) N, $P=0.90$ or for handgrip endurance: 21 (17–30) (4–76) vs 24 (18–33) (5–47) s, the mean difference (95% CI) being 0.7 (–7 to 9) s, $P=0.79$.

Overall pain for the first 24 h after surgery was reduced in the MP vs the placebo group for all four pain assessments (Fig. 2). Also, summarized pain scores were significantly lower for most assessments (ambulation $P=0.027$, rise from chair $P=0.001$, rest $P=0.047$, passive hip flexion $P=0.057$). No significant difference in overall pain was observed from POD1 to 4 (ambulation $P=0.85$, rise from chair $P=0.89$, rest $P=0.35$) or in summarized pain (ambulation $P=0.84$, rise from chair $P=0.40$, rest $P=0.93$).

No significant difference was observed in the number of patients having sufentanil in the PACU [count (%), MP vs placebo]: two patients (8.3) vs one patient (4.2), $P=1.0$. Also, no significant difference was observed in cumulated

consumption of morphine for the first 24 h after operation [median (IQR) (95% CI), MP vs placebo]: 10 (10–19) (0–25) vs 15 (5–25) (0–50) mg, the mean difference (95% CI) being –4 (–10 to 2) mg, $P=0.27$, or from POD1 to 4, $P=0.21$. The incidence of nausea and vomiting was low, without significant differences between the groups for the first 24 postoperative hours or from POD1 to 4 regarding the number of patients with nausea, episode(s) of vomiting, the number requiring ondansetron, or in combined nausea score (Table 2). No significant difference was observed between the groups in overall fatigue for the first 24 h after surgery ($P=0.83$) or from POD1 to 4 ($P=0.62$). Also, no significant difference in sleep quality was observed ($P=0.72$), and no significant difference in consumption of hypnotics between the groups throughout the study period ($P>0.30$) was observed. The CRP response 24 h after surgical incision was significantly lower in the MP group, compared with the placebo group [mean (SD), MP vs placebo]: 44.3 (16.8) vs 104.7 (39.2) mg litre⁻¹, the mean difference (95% CI) being –60.4 (–78.5 to –42.2) mg litre⁻¹, $P<0.0001$. No significant difference was observed in actual LOS [median (IQR) (95% CI), MP vs placebo]: 1 (1–2) (1–3) vs 1 (1–2) (1–2) nights, the mean difference (95% CI) being 0 (–0.3 to 0.3) nights, $P=0.76$.

Table 1 Baseline patient characteristics and pre- and perioperative characteristics. Data are expressed as mean (sd), count (%), or median (IQR) where appropriate. However, data for age is expressed as mean (range). BMI, body mass index; ASA, American Society of Anesthesiologists physical status; NSAID, non-steroidal anti-inflammatory drugs; Weak opioid tramadol or codeine; CRP, C-reactive protein (detection level 6 mg litre⁻¹, ref. <10 mg litre⁻¹); Hb, haemoglobin (ref. male 8.1–10.3 mmol litre⁻¹, ref. female 7.1–9.3 mmol litre⁻¹); MP, methylprednisolone

Variable	MP (n=24)	Placebo (n=24)
Patient characteristics		
Age (yr)	66 (53–80)	66 (50–78)
Sex (male/female)	12/12 (50/50)	9/15 (38/62)
BMI (kg m ⁻²)	27 (4)	27 (5)
ASA (I/II/III)	11/13/0 (46/54/0)	9/14/1 (38/58/4)
Non-smokers	17 (71)	20 (83)
Preoperative data		
Handgrip strength (N)	332 (129)	315 (101)
Handgrip endurance (s)	23 (19–36)	24 (14–35)
Pain, VAS (0–100)		
At rest	18 (2–38)	17 (4–37)
Upon passive hip flexion	7 (0–32)	4 (0–20)
Upon ambulation	19 (11–34)	31 (9–61)
Upon rise from chair	20 (8–41)	29 (9–46)
Sleep quality		
Fatigue, NRS (1–10)	4 (3–5)	3 (2–5)
CRP (mg litre ⁻¹)	6 (6–6)	6 (6–6)
Hb (mmol litre ⁻¹)	8.8 (0.7)	8.5 (0.7)
Daily consumption of		
Paracetamol	13 (54)	17 (71)
NSAID	14 (58)	13 (54)
Weak opioid	4 (17)	3 (13)
Sleeping medicine	3 (13)	0 (0)
Perioperative data		
Duration of surgery (min)	48 (40–55)	45 (40–53)
Time for end of surgery (a.m.)	9.45 (9.30–10.00)	9.45 (9.30–11.00)
Bleeding intraoperatively (ml)	400 (256–530)	400 (200–550)
Prosthesis, Bimetric-stem +Ringloc-/Magnum-cup	21/3 (88/12)	21/3 (88/12)

No apparent complications, related to the study drug during hospitalization or on follow-up on POD 30, were observed. Especially, no superficial or deep infections occurred. One patient in the placebo group was re-operated due to dislocation of the THA on the first postoperative night, and one patient in the MP group was readmitted after discharge due to hip dislocation (closed reduction).

Discussion

This randomized, double-blind, placebo-controlled trial demonstrated that MP 125 mg i.v. before elective, unilateral,

primary THA did not reduce time to meet functional discharge criteria.

However, both pain and CRP response were reduced the first 24 h after surgery.

Pain, dizziness, and general muscle weakness have recently been suggested to be the main clinical reasons for being hospitalized the first days after THA and TKA.⁵ Glucocorticoids may reduce pain¹¹ and inflammatory-induced muscle weakening after surgery.⁴ Thus, time to meet functional discharge criteria could potentially be reduced with glucocorticoids. The (only) twice daily assessment of the discharge criteria may have impaired the possibility to demonstrate a potential difference between the groups, since time to meet discharge criteria (and actual LOS) was already short. However, the twice daily assessment is our daily clinical practice⁵ and a potential minor difference (less than the study was powered to demonstrate) might not be clinically relevant.

Overall and summarized pain were significantly reduced in the MP group compared with the placebo group, in agreement with that previously reported in THA after a single preoperative dose of dexamethasone 40 mg i.v., with decreased dynamic pain (standing up) at 24 h.¹³ Despite our detailed and prolonged assessment of pain upon ambulation, rise from a chair, rest, and upon passive hip flexion, we did not observe a prolonged analgesic effect. This was suggested by Romundstad and colleagues¹⁵ in non-procedure-specific orthopaedic surgery after administration of a single dose of MP 125 mg i.v. to patients with moderate to severe pain 1 day after surgery (reduced opioid consumption up to 72 h). In a previous study in THA patients, no additional effect of preoperative dexamethasone 8 mg was observed when combined with pregabalin 300 mg.²³ Thus, our study supports the conclusion that a certain amount of glucocorticoid is needed to reduce postoperative pain and opioid consumption.¹¹ We have previously shown a reduction in overall pain for the first 48 h after TKA with a single preoperative high dose of MP (125 mg i.v.),¹⁴ but the same dose in THA did not improve immediate postoperative analgesia to the same extent as seen in TKA,¹⁴ possibly due to lower pain scores with the multimodal analgesic regime after THA compared with TKA.

CRP level was reduced at 24 h in the MP group compared with the placebo group as shown in other studies.¹³ Suppression of the surgery-induced inflammatory response (CRP) may be a possible explanation for the observed analgesic benefit, since inflammatory mediators are involved in nociceptive processing.^{6–7} No difference between the groups was observed for handgrip strength or handgrip endurance. Previously, handgrip endurance (fatigue resistance) has been shown to be improved after treatment with COX-2 inhibitors.²⁴ On the other hand, surgery-induced inflammation has been shown to be related to reduced handgrip endurance.⁴ However, we performed measurements 24 h after surgery (due to the fast recovery and discharge) when compared with 2 and 4 days after operation,⁴ and 1 and 2 weeks after initiation of treatment with COX-2 inhibitors²⁴ in previous studies. PONV was a very limited clinical problem, and we

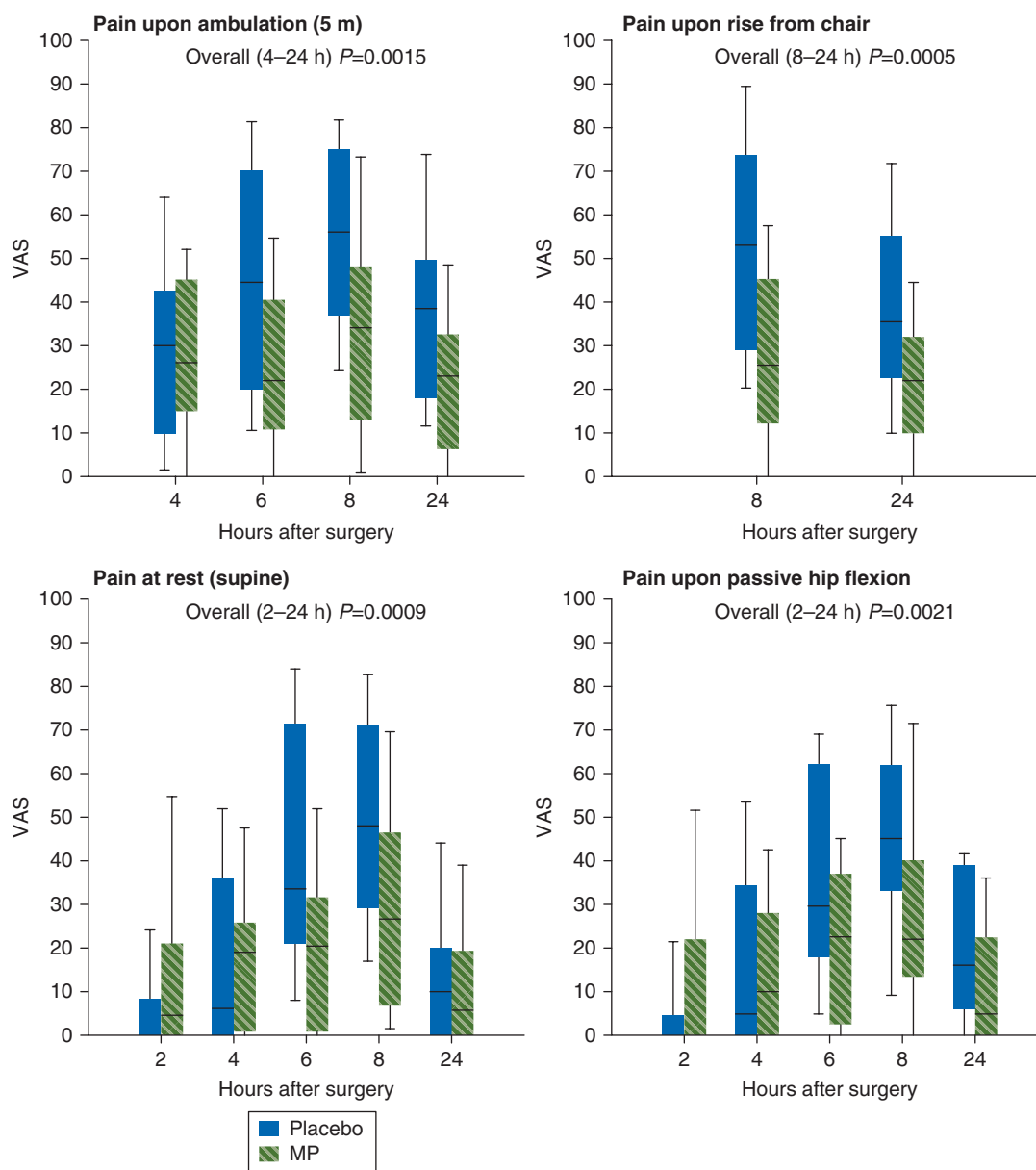


Fig 2 Pain for the first 24 h after THA. Horizontal lines indicate medians, boxes indicate IQRs, and whiskers indicate 5th–95th percentiles. Test for significant differences between the groups was analysed using repeated measurement regression with random intercepts and first-order auto-correlation, and presented as an overall Wald χ^2 test for differences in means between the groups.

did not observe any difference between the groups—despite the extensive literature supporting the efficacy of glucocorticoids as a PONV-prophylactic agent.¹⁰ The limited use of opioids in both groups might explain this low PONV incidence (and other opioid-related side-effects).

A strength of this study arises from the detailed assessment of outcomes by only two data collectors, resulting in few missing data and protocol violations, and from the standardized surgical, anaesthetic, and analgesic regime for all patients. The study might be under-powered to demonstrate potential differences between the groups for secondary

outcomes, and it was not powered regarding evaluation of safety aspects. However, the study was powered regarding evaluation of the primary outcome.

Decisions on the indication for perioperative administration of high-dose glucocorticoid in THA are likely to depend on future safety studies,¹¹ especially since the potential analgesic improvement is relatively short-lived. Furthermore, as previously demonstrated, the acute outcome after THA is satisfactory with a multimodal analgesic regime, consisting of slow-release paracetamol, celecoxib, and gabapentin.²¹ The focus should be to before operation identify those THA

Table 2 Nausea, vomiting, and consumption of ondansetron. Data are expressed as count (%) or median (IQR) where appropriate. Combined nausea scores were calculated by adding up nausea scores (none/slight/moderate/severe=0–3) from the assessments in the periods: 0–24 (2, 4, 6, 8, and 24) h; and POD1–4 (twice daily, morning and evening). Outcomes for the first 24 postoperative hours and outcomes thereafter (POD1–4) were analysed separately due to the different ways of assessments—by an investigator and in questionnaire, respectively. Test for significant differences between the groups were done with the Mann–Whitney rank-sum test (continuous data) and the Fisher exact test (categorical data). MP, methylprednisolone; POD, postoperative day

Variable	MP (n=24)	Placebo (n=24)	P-value
No. of patients with nausea (slight/moderate/severe)			
2 h	2/0/0 (8.3/0/0)	2/0/0 (8.3/0/0)	—
4 h	1/1/0 (4.2/4.2/0)	1/0/0 (4.2/0/0)	—
6 h	0/1/0 (0/4.2/0)	2/0/0 (8.3/0/0)	—
8 h	3/1/0 (12.5/4.2/0)	4/1/1 (16.7/4.2/4.2)	—
24 h	0/1/0 (0/4.2/0)	4/1/1 (16.7/4.2/4.2)	—
Combined nausea score			
0–24 h	0 (0–0.75)	0 (0–1)	0.11
POD1–4	0.5 (0–2)	0 (0–2)	0.86
No. of patients with episode(s) of vomiting			
0–24 h	3 (12.5)	4 (16.7)	1.00
POD1–4	1 (4.2)	4 (16.7)	0.19
No. of patients requiring ondansetron (range 4–8 mg)			
0–24 h	1 (4.2)	3 (12.5)	0.35
POD1–4	0 (0)	0 (0)	1.00

patients at risk of developing more severe postoperative pain and impaired recovery.

In conclusion, a preoperative single dose of MP 125 mg i.v.—added to a multimodal oral analgesic regime—did not reduce time to meet functional discharge criteria after THA, despite improved analgesia for the first 24 postoperative hours.

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Declaration of interest

None declared.

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