BJA

British Journal of Anaesthesia, ■ (■): 1–9 (2017)

doi: 10.1016/j.bja.2017.11.073
Advance Access Publication Date: xxx
Clinical Investigation

CLINICAL INVESTIGATION

Intravenous dexamethasone fails to prolong psoas compartment block when assessed by objective pinprick sensory testing: a prospective, randomized, dose-dependent, placebo-controlled equivalency trial

J. D. Turner[1,*], S. W. Dobson[1], R. S. Weller[1], G. B. Russell[2] and D. S. Henshaw[1]

[1]Department of Anesthesiology, Wake Forest School of Medicine, Winston-Salem, NC 27157-1009, USA and [2]Department of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC 27157-1009, USA

*Corresponding author. E-mail: jturner@wakehealth.edu

Abstract

Background: Recent studies have concluded that i.v. dexamethasone can prolong the duration of peripheral nerve blockade. We hypothesized that a 4 mg dose would equally prolong the duration of psoas compartment blocks (PCBs) when compared with 8 mg, and that both doses would prolong the duration when compared with placebo.
Methods: This was a prospective, randomized, placebo-controlled, dose-dependent, equivalency trial with 115 patients undergoing total hip arthroplasty. The patients received a PCB. Subsequently, 15 patients received i.v. normal saline (placebo), 50 patients received i.v. dexamethasone 4 mg, and 50 patients received i.v. dexamethasone 8 mg. The primary outcome was the duration in hours of PCB, determined by serial pinprick assessments. Secondary outcomes included pain scores, time to first analgesic, and opioid consumption. An intention-to-treat-analysis (ITA) and per-protocol analysis (PPA) were performed.
Results: The ITA showed that block duration in the 4 and 8 mg groups was equivalent [mean (standard deviation), 18.5 h (8.0) *vs* 18.1 h (7.1)]. However, neither group differed from placebo [19.6 h (6.7), (4 mg *vs* placebo), $P=0.97$; (8 mg *vs* placebo), $P=0.77$)]. Postoperative pain scores and opioid consumption were not different between groups. Time to first analgesic was not different between the 4 and 8 mg groups, or the 4 mg and placebo groups. The 8 mg group, however, had a longer time to first analgesic (median of 533 *vs* 432 min, $P=0.047$) when compared with placebo, although the significance was not observed in the PPA ($P=0.058$).
Conclusions: I.V. dexamethasone did not prolong PCB when duration was objectively assessed, or decrease total opioid consumption. However, dexamethasone 8 mg prolonged the time to first analgesic.
Clinical trial registration: NCT 02464176.

Keywords: analgesia; dexamethasone; nerve block

Editorial decision: September 13, 2017; **Accepted:** September 13, 2017

Editor's key points

- There is interest in using adjuvant agents, including dexamethasone, to prolong regional analgesia.
- This double-blind study objectively assessed the effect of intravenous dexamethasone on psoas compartment block.
- Dexamethasone 8 mg had a limited effect on time to first analgesia, but none on block duration.
- Objective measures of block duration may be a reliable assessment technique.
- The role of dexamethasone in regional anaesthesia requires further study.

Peripheral nerve blocks (PNBs) utilizing local anaesthetic medications are a mainstay in regional anaesthesia for providing postoperative analgesia. Whilst clinicians may choose to place a perineural catheter in order to extend the duration of analgesia, this technique requires additional skills, time, and resources beyond that which are typically required for a single-injection procedure. For these reasons, a significant amount of research has been devoted to identifying ways to prolong the duration of analgesia provided by a single-injection PNB. One area of focus has been the addition of adjuvant medications to the local anaesthetic. Medications that have been previously investigated include clonidine, buprenorphine, tramadol, midazolam, and neostigmine.[1]

Recently, dexamethasone, a glucocorticoid with minimal mineralocorticoid effect, has also garnered significant interest as a potential adjuvant analgesic medication. Several studies have concluded that it may be capable of prolonging the duration of PNB when administered perineurally (off-label use) along with local anaesthetics.[2–4] These investigations followed the finding that i.v. administered dexamethasone could improve the overall quality of recovery and decrease opioid consumption in certain surgical populations.[5] Interestingly, it has since been suggested that i.v. dexamethasone may also prolong the duration of PNB when administered in doses ranging from 2.5 to 10 mg.[6–14] However, this effect has not been consistently reproducible.[15]

There are several potential explanations for the inconsistent findings related to the ability of i.v. dexamethasone to prolong PNB. One is that, to date, all studies have utilized a surrogate outcome to quantify block duration rather than objectively measuring it, likely because the latter is clinically cumbersome. To complicate matters further, the surrogate end point chosen has varied amongst studies. Whilst some studies have relied on quality of recovery surveys or patient-quantified block duration, other studies have used time to first analgesic request as an indicator of block duration. Unfortunately, many of these surrogate end points actually measure the duration of analgesia rather than the duration of the nerve blockade. Whilst both the duration of analgesia and the duration of the actual nerve blockade may be clinically relevant, it is important to recognize that an intervention may affect one without affecting the other. Another potential explanation is that both perineural and i.v. routes are often studied simultaneously, making it difficult to distinguish the effect of one route from the other. For this reason, some authors have suggested that perineural and systemic dexamethasone studies should be performed independently in order to better understand the effects of each on the duration of PNB.[16] Lastly, the dose of i.v. dexamethasone has varied between studies, and, to date, the optimal dose remains unknown.

Based on the results of previous studies, which demonstrated that 8 mg of i.v. dexamethasone effectively prolongs PNB, we investigated whether a 4 mg dose would be equally effective when using an objective end point of serial pinprick sensory testing to determine block duration.[6,13,14] We hypothesized that both 8 and 4 mg doses of i.v. dexamethasone would prolong the duration of a psoas compartment block (PCB) to an equivalent extent, and that both doses would prolong the duration when compared with placebo.

Methods

This was a double-blind, prospective, randomized, placebo-controlled, dose-dependent, equivalency trial performed at a single centre. We received Institutional Review Board approval before the initiation of the study, and it was prospectively registered at clinicaltrials.gov (NCT02464176). Written informed consent was obtained from all patients.

Patients, 18–90 yr of age, presenting to the Wake Forest Baptist Medical Center for primary elective total hip arthroplasty (THA), were eligible. Patients were excluded if they had contraindications to regional anaesthesia (allergy to amide local anaesthetics, coagulopathy, or infection in the area of the anticipated PCB), peripheral neurological dysfunction or neuropathy, insulin- and non-insulin-dependent diabetes mellitus, systemic corticosteroid use within 30 days of surgery, chronic opioid use (≥40 mg of oxycodone equivalents daily or any long-acting opioid), pregnancy, allergy or adverse reaction to dexamethasone (i.e. psychosis), or the inability to comprehend or reliably participate in the study.

The study was conducted from May 2015 to November 2016, and 115 participants were randomized into three groups. All patients received a PCB with 25 ml of bupivacaine (2.5 mg ml^{-1}) with 1:200 000 epinephrine. After block placement, Group 1 received i.v. normal saline (placebo=dexamethasone 0 mg), Group 2 received i.v. dexamethasone 4 mg, and Group 3 received i.v. dexamethasone 8 mg. Block randomization of patients occurred through the use of sequentially numbered opaque sealed envelopes where both the patient and the study investigators were blinded to the randomization. All i.v. study medications were prepared by a physician anaesthesiologist not involved in patient assessment, and given in equal volumes (2 ml) in syringes marked 'study drug' to preserve blinding.

Unless contraindicated, each patient received the following oral premedication for analgesia: acetaminophen 1 g, celecoxib 400 mg, and pregabalin 150 mg. Monitoring throughout the PCB procedure consisted of pulse oximetry, electrocardiogram, non-invasive blood pressure, and end-tidal carbon dioxide. After i.v. sedation with midazolam and fentanyl as needed, a nerve-stimulator-guided PCB was performed, as described by Capdevila and colleagues.[17] All blocks were performed with a 21 G insulated needle (Arrow StimuQuik; Teleflex Medical, Wayne, PA, USA) with an acceptable current for quadriceps motor response between 0.3 and 0.8 mA, and pulse width of 0.1 ms. After block placement, the i.v. study drug was administered. Block success was then confirmed in every patient by testing the anterior thigh at the midpoint between the inguinal crease and patella (L1–L3 dermatomes) for sensory change/loss at 15 and 30 min after block placement. If this was not possible because of clinical time constraints, block confirmation occurred in the post-anaesthesia recovery area