The ALOHA trial: (intra-articular local anaesthetic in hip arthroscopy)—a three-arm randomized trial comparing pre-emptive, high- and low-dose intra-articular local anaesthetic in hip arthroscopy

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ABSTRACT

Pain after hip arthroscopy is variable and can be severe despite multimodal analgesia. Intra-articular local anaesthetic (IALA) may reduce acute postoperative pain after hip arthroscopy. However, neither its optimum dose nor timing of administration have been systematically evaluated. In 132 patients, a double-blinded, three-arm randomized controlled trial comparing IALA used during hip arthroscopy was conducted comparing 100 mg ropivacaine given at the end of the procedure (Group L, low dose), 200 mg ropivacaine at the end of the procedure (Group H, high dose) and 100 mg of ropivacaine given at the beginning and end of the procedure (Group P, pre-emptive). There were no statistically significant differences between the three groups for Numerical Rating Scale-11 pain scores in the recovery room [mean (standard deviation): Group L—2.2 (1.9); Group H—2.3 (2.1); Group P—2.7 (2.5); lowest P = 0.6], or post-recovery room Visual Analogue Scale pain scores at 2, 4 and 6 h.

There were also no significant differences in antiemetic usage and requirement for rescue fascia iliaca blockade between the three groups. Compared to a single 100 mg dose of ropivacaine at the end of the procedure, we were unable to demonstrate any advantage of either a higher dose IALA or a pre-emptive dose IALA when multimodal analgesia is used.

INTRODUCTION

Acute pain at rest following hip arthroscopy varies greatly and can be severe, requiring total intraoperative and recovery room IV morphine doses of up to 0.3 mg/kg IV morphine, despite multimodal systemic analgesic therapy [1]. Pre-emptive regional analgesic techniques offer superior analgesia but carry with them significant risks of falls, delayed mobilization and neuropraxia [2–4]. Fascia iliaca blockade (FIB) has been shown to be a useful analgesic adjunct and required as a rescue analgesic in approximately 3–4% of cases [5]. Although the precise cause and determinants of severe early postoperative pain after hip arthroscopy is unknown, the use of high pressure intra-articular fluid, femoral ostectomy and labral repairs have been associated with higher postoperative pain [1].

Intra-articular local anaesthetic (IALA) for hip arthroscopy has been shown to be of analgesic benefit in some small studies [6, 7]. Local anaesthetic (LA) agents have been shown to confer pre-emptive analgesic effects; however, no comparative literature exists regarding the optimal dose and timing of IALA administration [8]. We hypothesized that pre-emptive as well as higher dosage of postoperative administration IALA, would have improved analgesic efficacy and postoperative opioid usage in patients undergoing therapeutic hip arthroscopy.
METHODS

This study was approved by our institution’s Human Research and Ethics committee (Melbourne Health HREC, approval #2013.195) and registered under the Australian and New Zealand Clinical Trials Register (ACTRN #12614001121651). We conducted this study as per CONSORT recommendations (see Fig. 1). All patients provided written informed consent to be included in the trial. Inclusion criteria were age >18 years, and planned therapeutic hip arthroscopy for procedures on the ligamentum teres, labrum or femoroacetabular impingement. Patients were excluded if there were contraindications to any of the perioperative drugs in the study protocol. The primary study outcome measure was assessment of postoperative pain: (i) assessment in the recovery room, by median 11-point Numerical Rating Scale-11 (NRS-11) assessments of pain, and (ii) assessment in the postoperative ward, by Visual Analogue Scale (VAS) assessments of pain measured at 1.5, 2, 4 and 6 h postoperatively at rest. Secondary outcome measures included highest and lowest recovery room NRS-11 at rest, recovery room analgesic and anti-emetic usage, total 24 h postoperative opioid analgesic and anti-emetic use. Patients performed their preoperative VAS assessment at rest in the supine position whilst in the pre-anaesthesia bay. Recovery room NRS-11 assessments were made every 5–10 min depending on frequency of titrated IV morphine bolus requirements, until the patient’s NRS-11 was <5 or until analgesia was defined as satisfactory by the patient, at which time they were discharged to the ward.

One hundred and thirty-two adult patients were recruited from a single surgeon’s practice and randomly

Fig. 1. ALOHA consort diagram.
allocated to one of three groups of intra-articular injection: (i) low-dose LA (Group L—100 mg ropivacaine at end of the procedure), (ii) high-dose LA (Group H—200 mg ropivacaine at end of the procedure) and (iii) pre-emptive LA (Group P—100 mg ropivacaine just prior to and at end of the procedure).

Random permuted block sizes of 9, 12 and 15 were used to achieve balanced group sizes whilst minimizing excessive runs of single group allocations. A web-based randomization program (Sealed Envelope Ltd, London, UK) was used by a team member not involved with assessment of any patient outcome measures to allocate each patient’s treatment group. After randomization, IALA or placebo saline syringe orders were then allocated in a sealed envelope prior to the day of surgery. On the day of surgery, the scrub scout nurse prepared IALA/placebo syringes in the preparation room, separate from the operating room and out of sight from other team members, and did not share knowledge of syringe contents. Syringes were prepared under sterile conditions and as per the opened envelope instructions: Group L—pre-emptive syringe 20 ml normal saline/postoperative syringe 20 ml 0.5% ropivacaine (100 mg); Group H—pre-emptive syringe 20 ml normal saline/postoperative syringe 20 ml 1% ropivacaine (200 mg); Group P—pre-emptive syringe 20 ml 0.5% ropivacaine (100 mg)/postoperative syringe 20 ml 0.5% ropivacaine (100 mg). Pain assessments were performed by the recovery room nursing staff and postoperative ward staff, all of whom were blinded to the patients’ group allocation.

Intraoperative anaesthesia and analgesia was standardized to spontaneous ventilation sevofoflurane/oxygen:air (50:50%) laryngeal mask anaesthesia, induction with 1–2 mg/kg IV propofol and 10–15 μg/kg IV alfentanil, and administration of 1 mg/kg IV tramadol, 0.05 μg/kg IV morphone, 40 mg IV parecoxib and 1 g IV paracetamol from the start of the procedure. All patients received 8 mg dexamethasone and 1 mg granisetron IV as preventative antiemetics. Hip arthroscopy was performed in the lateral decubitus position and surgical traction was applied with a McCarthy Hip Distractor (Innomed, Inc, Savannah, GA, USA). Intra-articular access was facilitated with an arthroscopic infusion of Ringer’s Lactate at constant pressures of 40 mmHg. Ligamentum Teres tears were debrided, and synovitis treated with synovecmctomy, with the aid of a radiofrequency ablation probe (Vulcan Efflex Ablator Probe, Smith and Nephew, Andover, MA, USA). Labral tears were treated with circumferential suture anchor refixation (Natotack Flex, Stryker, Sunnyvale, CA, USA). Femoral and acetabular ostectomy was performed under fluoroscopic guidance. Surgery duration was defined as the time from application of traction to the time when last wound dressings were applied.

Pre-emptive injection (LA or placebo) was administered upon portal placement under fluoroscopic control, whilst LA administered at the end of the procedure was given via the arthroscopic portal just before arthroscopic portal removal.

The study recovery room protocol for postoperative analgesia offered subjects (i) IV morphine 1 mg (if NRS-11 < 7)—2 mg (if NRS-11 7 or above) every 5–10 min, titrated up to 0.2 mg/kg for clinical review or until dose limiting side effects such as sedation or nausea and vomiting occurred, simultaneously with IV tramadol 50 mg every 15 min, up to a total theatre and recovery room dose not exceeding 200 mg. Breakthrough antiemetics offered were cyclizine 50 mg IV (one dose) and droperidol 10 mg/kg (one dose).

Recovery Room NRS-11 assessments were made every 5–10 min by the patient’s recovery room nurse verbally, requesting the patient’s rating of pain on an 11-point scale where ‘0’ described no pain at all, and ‘10’ defined as ‘worst pain possible’. Patients were discharged to the ward once their NRS-11 was <5 or until analgesia was defined as satisfactory by the patient. Postoperative VAS time points for pain assessment and the 24 h postoperative period were calculated from the time of application of surgical traction. Ward VAS assessments were performed by ward nursing staff, instructing patients to mark a single line across an uninterrupted horizontal 100 mm scale on a paper diagram where the extreme left- and right-hand ends of the scale were marked as ‘No Pain’ with smiling face schematic, and ‘Pain as Bad as it Possibly Could Be’ with crying face schematic, respectively.

Patients were offered rescue FIB if recovery room NRS-11 pain assessments were >5 despite maximum study protocol systemic analgesia, or if sedation, nausea or vomiting became rate-limiting factors to further administration of IV morphine. FIB was performed as originally described by Dalens with 20 ml of 0.5% ropivacaine [9]. Patients with an NRS persisting above 5 or who were still dissatisfied with their analgesia at this point were offered IV morphine via a Patient Controlled Analgesia device and ketamine infusion of 0.1–0.2 mg/kg/h, and were included in the intention-to-treat analysis. Once discharged to the ward patients were initially offered 2.5–5 mg oral oxycodeone as first-line analgesia, 50–100 mg oral tramadol as second-line analgesia and 2.5–5 mg intramuscular or subcutaneous morphine as third-line analgesia every 6 h. 1 mg IV bd granisetron and 50 mg IV tds cyclizine were offered as needed for nausea and vomiting. Opioid doses were expressed as IV morphine equivalents; for tramadol we
used the manufacturer’s recommended equipotency of 1 mg IV morphine = 10 mg IV tramadol; for oxycodone, 2 mg oral oxycodone = 1 mg IV morphine [10].

Statistical analysis
All calculations were performed using GraphPad Prism 5 (GraphPad Software, CA, USA) and G*Power 3.1 (University of Dusseldorf, Dusseldorf, Germany) statistical software with intention to treat analysis. With the exception of recovery room lowest NRS-11 scores, our data were deemed suitable for parametric testing by Shapiro–Wilk and Kogomorov–Smirnov normality testing and visual histogram appraisal. Categorical data were compared with $\chi^2$ testing, and continuous data analysed with one-way analysis of variance and Bonferroni multiple comparisons testing, with Bonferroni correction of P-values. (Recovery room NRS-11: highest, median and lowest NRS-11 values; Postoperative VAS: mean values at 1.5, 2, 4 and 6 h) between multiple pairs of groups.

Power calculation
Sample size was determined ‘a-priori’ with the use of G*Power V 3.1 (University of Dusseldorf, Dusseldorf, Germany). Morgenthaler et al. found an overall reduction in VAS at rest after hip arthroscopy of [mean (standard deviation, SD)] of 10 mm (18 mm) over a 20-h postoperative period when comparing the effect of LA Bupivacaine 50 mg against placebo. Assuming approximate LA potency of 1 mg Bupivacaine = 1.5–2 mg Ropivacaine, and a linear dose–response of relationship between LA dose and reduction in postoperative VAS, each 100 mg of IALA Ropivacaine reduces postoperative VAS by [mean (SD)] 10 mm (18 mm). With desired power of 0.8 the number of patients per arm required to demonstrate a mean VAS difference of 10 mm by two-tailed unpaired t-test at alpha of 0.05 was 17 patients. Sample sizes were more than doubled in our study to account for multiple comparisons.

RESULTS
Forty-four hip arthroscopies were performed in each group with similar demographics, premorbid comorbidities, length of surgery and surgical procedures performed (Fig. 1 and Table I). There were no acute complications from the use of IALA or rescue FIB. All patients were discharged home on the morning of postoperative day 1 with the use of crutches and oral analgesia.

A total of 10 patients had incomplete VAS assessments over the 1.5–6 h postoperative study period (Fig. 1); 1 at all ward VAS time points; 4 at 2 h; 4 at 4 h; and 1 at 6 h. Overall, patients’ mean pain assessments appeared to be that of satisfactorily controlled pain with mean NRS-11 in all groups below 2.7 (Fig. 2). All mean VAS at 1.5 h, 2 h and 4 h were below 3.6, 3.1 and 2.2 respectively, with no significant difference between the three groups at any time.
However, both recovery room NRS-11 and postoperative VAS pain assessment ratings had large SDs, indicating the large variability of pain response in patients undergoing hip arthroscopy (Tables II and III).

Pain assessments are of the greatest magnitude in the recovery room and at the ward at 1.5 h postoperatively with the highest pain score of 3.5 (SD 3.0) and postoperative VAS at 1.5 h of 3.6 cm (SD 1.9 cm). Postoperative mean VAS approximately halved at the 6 h postoperative time point.

Four percent of patients received rescue FIB. Of the six patients receiving rescue FIB, all except 1 patient-reported much improved pain. This patient was then prescribed a 0.15 mg/kg/h ketamine infusion.

The overall intraoperative and recovery room mean opioid requirements where 0.23 mg/kg IV (SD 0.1) morphine equivalent analgesic doses whilst the remainder of the 24 h postoperative period had a much smaller need with only 0.09 mg/kg (SD 0.1). There were no significant differences between groups in opioid requirements (Group L = 0.22 mg/kg; Group H = 0.23 mg/kg; Group P = 0.24 mg/kg IV morphine equivalent analgesic doses) (Fig. 4).

There were no significant differences in antiemetic doses between groups with the largest difference between means in granisetron requirements being only 0.07 mg ($P = 0.6$) and the largest difference between means in cyclizine requirements being only 0.9 mg ($P = 0.9$) (Fig. 4).

**DISCUSSION**

Our double-blinded, three-arm randomized controlled trial comparing the analgesic efficacy of pre-emptive and different dosages of postoperative LA found no statistically or clinically significant difference between the three groups, in the primary outcome of postoperative recovery room and ward pain score outcomes, nor the secondary outcomes of opioid usage, antiemetic requirements or rescue FIB.

Whilst our study demonstrated no difference in pre-emptive or dosage of IALA, the use of IALA in hip arthroscopy has been demonstrated to be beneficial. Baker et al. [7] found that 25 mg postoperative IA bupivacaine had opioid sparing effects compared with the same dose infiltrated around portal insertion sites. Whilst Morgenthaler et al. [6] used 50 mg postoperative IA bupivacaine versus IA placebo to achieve a mean 20-h VAS superiority of 10 mm at rest.

In knee arthroscopy, the use of pre-emptive IA has mixed results. Tuncer et al. [11] demonstrated superior analgesia up to 6 h postoperatively when pre-emptive administration of 50 mg IA bupivacaine was used prior to surgery, when compared with postoperative dosing. Goodwin demonstrated variable short-term pre-emptive effects [12, 13], whilst Fagan et al. [14] did not demonstrate superiority.

A systematic review conducted by Kolaczko et al. [15] assessed 17 studies from 2008 to 2018 which found no differences in narcotic consumption, VAS score at discharge, time until discharge or incidence of complication based on pain control modality utilized. Furthermore, no statistically significant difference in PACU narcotic utilization, VAS pain scores at discharge, time to discharge or incidence of complications was found between perioperative pain regimens in hip arthroscopy.

In our study, several factors may account for the lack of any demonstrable effect with higher dose and pre-emptive administration of IALA. The overall mean pain assessment scores were moderate-to-low, hence the perioperative use of good multimodal analgesia may have masked any benefit.
Table II. Recovery room 11-point numerical rating scale assessments of pain

|                      |         |         |         |
|----------------------|---------|---------|---------|
|                      | Group L | Group H | Group P |
| Highest NRS-11       | Mean    | 2.9     | 3.1     | 3.5     |
| Bonferroni multiple corrections corrected P-values | SD      | 2.5     | 2.8     | 3.0     |
|                      | One-way ANOVA | P = 0.11 |         |         |         |
|                      | versus Group H | 0.37   | versus Group P | 1.0   | versus Group L | 0.13   |
| Lowest NRS-11        | Mean    | 1.4     | 1.6     | 2.2     |
| Bonferroni multiple corrections corrected P-values | SD      | 1.5     | 1.9     | 2.1     |
|                      | One-way ANOVA | P = 0.03 |         |         |         |
|                      | versus Group H | 1.0   | versus Group P | 0.16  | versus Group L | *0.03  |
| Median NRS-11        | Mean    | 2.2     | 2.3     | 2.7     |
| Bonferroni multiple corrections corrected P-values | SD      | 1.9     | 2.1     | 2.5     |
|                      | One-way ANOVA | P = 0.09 |         |         |         |
|                      | versus Group H | 0.54  | versus Group P | 1.0   | versus Group L | 0.09   |

Group H, high-dose ropivacaine group, 200 mg IALA at end of operation; Group L, low-dose ropivacaine group, 100 mg IALA at end of operation; Group P, pre-emptive ropivacaine group, 100 mg ropivacaine prior to start of operation and 100 mg at end of operation.

Table III. Postoperative visual analogue scale assessments of pain

|                      |         |         |         |
|----------------------|---------|---------|---------|
|                      | Group L | Group H | Group P |
| VAS 1.5 h (cm)       | Mean    | 3.3     | 3.1     | 3.6     |
| Bonferroni multiple corrections corrected P-values | SD      | 1.8     | 16      | 19      |
|                      | One-way ANOVA | P = 0.33 |         |         |         |
|                      | versus Group H | 1.0   | versus Group P | 0.93  | versus Group L | 0.44  |
| VAS 2 h (cm)         | Mean    | 2.9     | 2.6     | 3.1     |
| Bonferroni multiple corrections corrected P-values | SD      | 1.4     | 1.7     | 1.7     |
|                      | One-way ANOVA | P = 0.59 |         |         |         |
|                      | versus Group H | 1/0   | versus Group P | 1.0   | versus Group L | 0.92  |
| VAS 4 h (cm)         | Mean    | 2.0     | 2.0     | 2.2     |
| Bonferroni multiple corrections corrected P-values | SD      | 1.4     | 1.3     | 1.8     |
|                      | One-way ANOVA | P = 0.28 |         |         |         |
|                      | versus Group H | 0.37  | versus Group P | 1.0   | versus Group L | 0.6   |
| VAS 6 h (cm)         | Mean    | 1.6     | 1.9     | 1.8     |
| Bonferroni multiple corrections corrected P-values | SD      | 1.8     | 1.4     | 1.5     |
|                      | One-way ANOVA | P = 0.08 |         |         |         |
|                      | versus Group H | 0.08  | versus Group P | 0.46  | versus Group L | 1.0   |
in IALA dosing or timing. Our postoperative pain scores were similar to other published studies [1, 16].

We did not include a placebo arm in our study, therefore we cannot exclude the possibility that any dose of IALA may lack significant efficacy when used in conjunction with systemic multimodal analgesia.

We did not assess VAS on weight-bearing or movement of the hip joint postoperatively; the greater pain experienced under these circumstances may have demonstrated a pre-emptive or dose-dependent IALA effect. Morgenthaler’s positive study findings included a larger effect size when assessment of pain on movement was used; however, his team also demonstrated a statistically significant effect on pain at rest. IALA may have an effect on intra-articular sources of pain however may not have an effect on periarticular structures. Periarticular LA infiltration appeared to be effective for postoperative pain in hip arthroscopy in one retrospective study [17].

Although our sample size was larger than most previous studies on IALA, the possibility of a type 2 error still exists. The further increase in statistical power afforded by our higher sample size, however, adds strength to the existing literature that under a variety of surgical, patient and concomitant multimodal analgesic contexts, the additive effect of IALA may be limited.

CONCLUSIONS

The dosage of intra-articular LA at the end of hip arthroscopy and the use of pre-emptive intra-articular LA at the start of the operation, made no difference in postoperative pain, analgesic or antiemetic requirements. If intra-articular LA is to be used in hip arthroscopy, we recommend a single dose of 100 mg ropivacaine postoperatively.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

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