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#### CLINICAL INVESTIGATION

# High-dose versus low-dose local anaesthetic for transversus abdominis plane block post-Caesarean delivery analgesia: a meta-analysis

S. C. Ng<sup>1,\*</sup>, A. S. Habib<sup>2</sup>, S. Sodha<sup>1</sup>, B. Carvalho<sup>3</sup> and P. Sultan<sup>1</sup>

<sup>1</sup>Department of Anaesthesia, University College London Hospital, London, UK, <sup>2</sup>Department of Anesthesiology, Duke University School of Medicine, Durham, NC, USA and <sup>3</sup>Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, USA

\*Corresponding author. E-mail: sucheenng@gmail.com

### **Abstract**

Background: The optimal local-anaesthetic (LA) dose for transversus-abdominis-plane (TAP) block is unclear. In this meta-analysis, we aimed to determine whether TAP blocks for Caesarean delivery (CD) with low-dose (LD) LA demonstrated non-inferiority in terms of analgesic efficacy, compared with high-dose (HD) LA.

Methods: A literature search was performed for randomized controlled trials examining the analgesic efficacy of TAP blocks vs control after CD. The different dosing used in these studies was classified as HD or LD (bupivacaine equivalents >50 or  $\leq$ 50 mg per block side, respectively). The pooled results of each dose group vs control were indirectly compared using the Q test. The primary outcome was 24 h opioid consumption. Secondary outcomes included 6 and 24 h post-operative pain scores, time to first analgesia, 6 h opioid consumption, opioid-related side-effects, and maternal satisfaction.

Results: Fourteen studies consisting of 770 women (389 TAP and 381 control) were included. Compared with controls, the 24 h opioid consumption (milligram morphine equivalents) was lower in HD [mean difference (MD) 95% confidence interval (CI) -22.41 (-38.56, -6.26); P=0.007;  $I^2=93\%$ ] and LD [MD 95% CI -16.29 (-29.74, -2.84); P=0.02;  $I^2=98\%$ ] TAP groups. However, no differences were demonstrated between the HD and LD groups (P=0.57). There were also no differences between the HD and LD groups for the 6 h opioid consumption, time to first analgesia, 6 and 24 h pain scores, post-operative nausea and vomiting, pruritus, and maternal satisfaction.

Conclusions: The LD TAP blocks for CD provide analgesia and opioid-sparing effects comparable with the HD blocks. This suggests that lower doses can be used to reduce LA toxicity risk without compromising the analgesic efficacy.

Keywords: anaesthetic; local; analgesia; Caesarean section; pain management

#### Key points

- The authors systematically reviewed the literature regarding the analgesic efficacy of high-dose and lowdose transversus-abdominis-plane (TAP) blocks after Caesarean delivery.
- In the 14 studies considered (770 patients), both highand low-dose approaches appeared effective in reducing 24 h morphine consumption, but there was no apparent difference between the high- and low-dose techniques in this, or other, outcome measures.
- The authors suggest that the data support the use of low-dose TAP blocks, potentially reducing the risk of systemic local-anaesthetic toxicity.

The transversus abdominis plane (TAP) block was first described by  $\mathrm{Rafi}^1$  in 2001. After a Caesarean delivery (CD), TAP blocks have been shown to play a valuable role in providing adjunctive analgesia for patients who are undergoing CD with spinal anaesthesia without intrathecal morphine (ITM),  $^{2-5}$  and provide analgesic benefit to patients undergoing CD with general anaesthesia.  $^{4,6,7}$ 

During pregnancy, enhanced sensitivity to local anaesthetics (LAs) as a result of altered physiology may increase the risk of LA systemic toxicity (LAST). <sup>8,9</sup> Even when the recommended maximal allowable LA doses are adhered to, the minimum toxic plasma concentrations can still be exceeded. <sup>8</sup> There have been several published cases of tonic—clonic convulsions in women receiving TAP block for CD. <sup>9–11</sup> However, utilising lower doses may compromise the analgesic efficacy of the block. The optimum dosing strategy balancing analgesic efficacy and LAST remains unclear.

Whilst studies have explored TAP blocks in the non-obstetric population and suggested similar efficacy between lower doses and higher doses of LA,  $^{12-15}$  few studies have directly compared post-CD analgesic outcomes after low-dose (LD) and high-dose (HD) LA for TAP blocks.  $^{16,17}$  Singh and colleagues  $^{16}$  concluded that in the presence of ITM, neither HD nor LD LA TAP decreased pain scores at 24 h, whilst another study demonstrated that LD LA TAP provided similar analgesia effects compared with a higher-dose LA.  $^{17}$ 

This meta-analysis aimed to determine whether TAP blocks for CD with LD LA demonstrated non-inferiority in terms of analgesic efficacy, compared with HD LA. The primary outcome of the study was 24 h opioid (in milligram morphine equivalents) usage postoperatively.

#### **Methods**

For this meta-analysis, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations were followed. As there is no universally accepted definition for HD or LD LA doses for TAP blocks, we assigned the various doses used in different studies to the HD and LD groups as bupivacaine equivalents >50 and  $\leq$ 50 mg per block side, respectively. This cut-off value was chosen to reflect the dosing strategy of bupivacaine 0.25%, 20 ml per side that is commonly administered in the clinical setting and in published research, to represent a lower-dose TAP block.

A literature search was performed without language restriction on October 20, 2015 and repeated on April 7, 2016. Searches were performed in PubMed (1966–April 2016); US

National Library of Medicine, MEDLINE (1966–April 2016); Cochrane Central Register of Controlled Trials, CENTRAL (1996–April 2016); Cumulative Index to Nursing and Allied Health Literature, CINAHL (1983–April 2016); and Excerpta Medica Database, EMBASE (1947–April 2016). The literature search was carried out with the following search terms: transverse abdominis, transversus abdominis, transversus abdominis plane block, TAP, TAP block; combined with Cesarean, Caesarean, C-section, Cesarean delivery, Caesarean delivery (Supplementary Appendix 1).

We identified randomized controlled trials comparing either HD or LD (or both) single-shot TAP blocks compared with control (no block, placebo block) for postoperative CD analgesia. Studies were included if TAP blocks were performed in the intraoperative period carried out by either landmarkbased or ultrasound-guided (USG) techniques, and patients underwent either elective or emergency CD (or both) under spinal or general anaesthesia. Studies were excluded if they utilized catheter-based TAP blocks, did not use similar analgesic adjuvants or long-acting intrathecal opioids within study groups (e.g. intrathecal morphine in control group, but not TAP group), and if TAP blocks were compared with other regional block techniques (excluding spinal anaesthesia). Letters, abstracts, case reports, reviews, comments, editorials, cadaveric studies, animal studies, and studies in a language that the authors were unable to translate were also excluded. A consensus amongst all authors was sought to finalize the list of studies to be included in the meta-analysis. Bibliographies of included studies and relevant review papers were also manually searched to capture any other relevant studies that met the inclusion criteria that may not have been identified in the original database search. We also searched for and reviewed published abstracts, and where appropriate, the authors were contacted.

The risk of bias for included studies was assessed using the Cochrane Risk of Bias tool. <sup>19</sup> The quality of included articles was also evaluated using the Jadad score. <sup>20</sup> Data extraction was independently carried out by at least two individuals (S.C.N. and S.S.). A standardized collection form was used for data extraction. Any relevant outcome data common to more than one paper were used for analysis. Discrepancies were resolved by re-examining the original manuscript. When any uncertainty arose, all authors were consulted and a consensus achieved. Where data were reported in a clear graphical format, the reviewers extracted the data from the graphs. If the source data were unclear, attempts were made to contact the authors.

The primary outcome was difference in cumulative 24 h opioid consumption (in milligram morphine equivalents) between the HD and LD TAP block groups. Secondary outcomes included 6 h opioid consumption; time to first analgesic request; 24 h postoperative pain scores at rest and on movement using pain rating scales; 6 h postoperative pain scores at rest and on movement using pain rating scales; opioid-related side-effects (nausea, vomiting, and pruritus); and patient satisfaction. In order to standardize analysis, opioids were converted to i.v. morphine equivalents (tramadol:morphine 10:1<sup>21</sup> and morphine oral:i.v. 2:1<sup>22</sup>), and LA agents were converted to bupivacaine equivalents based on previously published ratios (ropivacaine:bupivacaine 1:0.6<sup>23</sup> and levobupivacaine:bupivacaine 1:1<sup>24</sup>). Pain reported as visual, verbal, or numerical rating scales was converted to a 0- to 100-point scale (where 0=no pain and 100=worst pain imaginable).

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