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Systematic Review and Meta-Analysis

Transversus Abdominis Plane Block to Alleviate Postoperative Pain in Children: A Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

Background: Transversus abdominis plane (TAP) block has been applied as one of multimodal approaches to alleviate postoperative pain in children. The aim of this meta-analysis was to determine the effect of TAP block on postoperative pain management for children who underwent surgery.

Methods: The randomized controlled trials (RCTs) which evaluated the analgesia effect of TAP block in children who underwent surgery were searched on the databases of Medline, Embase, the Cochrane Controlled Trials Register and Google Scholar. The RCTs which compared the analgesic effect of TAP block group with control group (placebo or "no treatment") in children were included. Postoperative opioid consumption (48 hours) was considered as the primary outcomes. The secondary outcomes included the number of children needed postoperative opioid analgesia rescue, the time to first analgesic administration (hours) and pain score. The risk ratios (RR), weighted mean differences (WMDs), and their corresponding 95% confidence intervals (95% CIs) were calculated for both dichotomous and continuous outcomes.

Results: Five RCT trials with 257 children met our criteria and were included in the analysis. Compared with the control group, TAP block reduced the 48 hours morphine consumption by 0.03 mg/kg (95% CI -0.05 to -0.00, P=0.03, 159 children in 3 RCTs). Besides, the non-significant reductions were shown in the number of children needed postoperative opioid analgesia rescue (217 children in 4 RCTs) and time to first analgesic administration (hours, 184 children in 3 RCTs).

Conclusions: TAP block is one of the safe and effective multimodal-approaches to alleviate postoperative pain in children. Specially, when the TAP block was used, it can significantly reduce the opioid consumption, which may avoid the occurrence of dose-dependent side effects of opioid drugs.

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Although a number of efforts have been made on the management of postoperative pain in children over the last decades, many children still suffer from the acute and significant pain after surgery (1, 2). Sufficient postoperative pain control in children is benefit for the surgical stress relief and postoperative recovery (3, 4). Nowadays, multimodal pain management approaches including both pharmacological and non- pharmacological strategies have been applied to improve postoperative analgesia in children (5, 6). As a part of the multimodal analgesia approach, local or regional anesthesia technique has been considered as an effective analgesic strategy for children (7, 8).

As one of the multimodal analgesia strategies for the postoperative pain management, transversus abdominis plane (TAP) block, which includes the infiltration of local anaesthetic in the plane between the internal oblique and transversus abdominis muscles, has increasingly drawn clinicians' attention over the last decade (9-11). TAP block has been reported by Rafi at first time as early as 2001 (12), and in 2007 ultrasound was reported to use as guidance during the TAP block (13). A group of reviews and meta- analyses have investigated the analgesic effects of TAP block in various adult surgeries, such as laparoscopic surgery (14), hysterectomy (15) and caesarean delivery (16). However, there are few reviews on the analgesic outcomes for postoperative pain in children, and it remains to determine whether TAP block can improve the postoperative pain management in children.

The primary objective of the present meta-analysis was to examine whether there was a significant difference in opioid consumption between TAP block and non-TAP block treated children. The secondary aim involved the evaluation of difference in number of children needed postoperative opioid analgesia rescue, the time to first analgesic administration and the postoperative pain score.

METHODS

Literature Search Strategy

This meta- analysis was prepared according to the PRISMA statement (17) and the recommendations of the Cochrane Collaboration. Two authors (Ji-Bin Xing and Xiao-Yun Li) performed a through literature search of published reports for randomized controlled trials (RCTs) that evaluated the effects of TAP block on postoperative pain in children through the Medline, Embase, the Cochrane Controlled Trials Register and Google Scholar. The search was restricted to articles in the English language and up to July 9, 2014. The phrases "transversus abdominis plane block", "TAP block" and "field block" were respectively used in pairwise combination with text word "children". Articles ahead of publication were included during the search. Ji- Bin Xing and Xiao-Yun Li also read the titles and abstracts of the potential relevant trials to exclude irrelevant researches.

Eligibility Criteria

After the initial literature search, two authors (Ji-Bin Xing and Xiao-Yun Li) independently inspected the abstracts and results of the obtained articles. The inclusive article must be RCTs, which compared TAP block with control group (placebo or no treatment) in children. Sample size and surgical procedure were not limited. Furthermore, the RCTs used both ultrasound and landmark guidance for TAP block were included.

Quality Assessment

Modified Jadad criteria score was imported to independently appraise the quality of the study by two authors (Ji-Bin Xing and Xiao-Yun Li) (18). Divergence and disagreements during the evaluation were resolved through the discussion between Ji-Bin Xing and Xiao-Yun Li. Moreover, if the two authors could not come to an agreement, a third author (Xiang Li) would help to make a decision. Besides, the assessment score was not considered as the exclusion and weight criteria.

Data Extraction

To avoid transcription errors, the full texts of the included studies were assessed independently by Ji-Bin Xing and Xiao-Yun Li. The divergence during the assessment was resolved by the discussion between Ji-Bin Xing and Xiao-Yun Li, or made a decision by a third evaluator (Xiang

Li) when a consensus on the article assessment could not be reached by them. Sample size, age range of patients, number of children in TAP block and control group, surgery type, TAP block procedure, postoperative analgesia strategy and primary/secondary outcomes were extracted from the included articles. Postoperative opioid consumption was considered as primary outcomes. The secondary outcomes (if available) included the number of children needed postoperative opioid analgesia rescue, the time to first analgesic administration (hours) and pain scores. Dichotomous data on the number of children needed postoperative opioid analgesia rescue were extracted and converted to incidence rate. Continuous data such as cumulative opioid consumption were recorded using mean and standard deviation, and the data presented only as median and range were calculated to means and standard deviation according to the previous described formula (19).

Meta-Analyses

The extracted data were recorded and rechecked by Ji-Bin Xing and Xiao-Yun Li. Review Manager 5 (Cochrane Library, Oxford, UK) was applied as the meta-analytic techniques. The risk ratios (RR), weighted mean differences (WMDs), and their corresponding 95% confidence intervals (95% CIs) were calculated for both dichotomous and continuous outcomes. The I^2 statistic was used to measure the heterogeneity, and heterogeneity was considered significant if $P<0.05$ or $I^2>50\%$ (20). The selection of fixed effects model or random effects model was based on the heterogeneity. Statistical significance was determined when the 95% CIs did not include the value of 1.0 for the RRs or 0 for the WMDs.

RESULTS

Search Results

Through the systematic literature search, we obtained a total of 124 records. Figure 1 showed the flow diagram for the study identification and selection process. After reading and evaluating the titles, abstracts and full texts, 5 studies with 257 children ultimately met our inclusion criteria (21- 25). The characteristics and outcomes of each included studies were summarized in table.

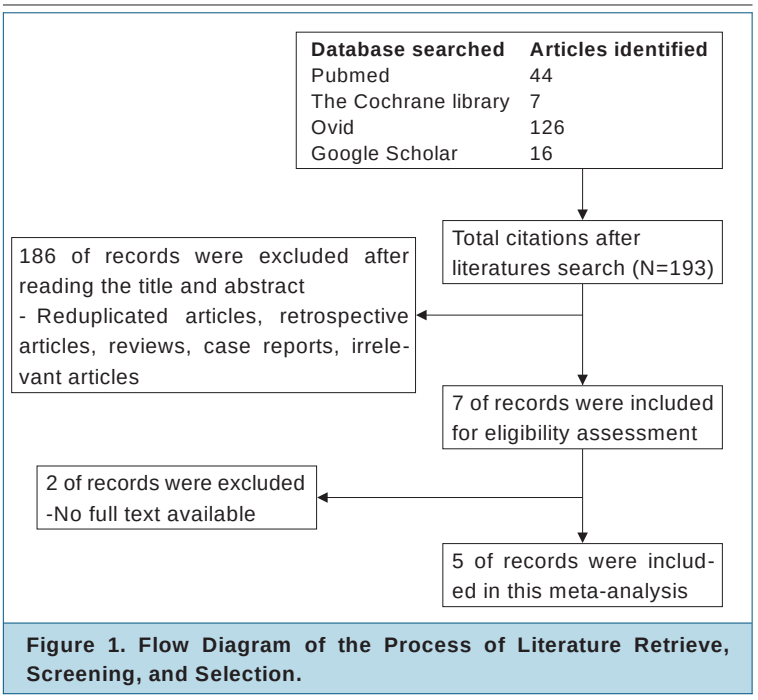

Figure 1. Flow Diagram of the Process of Literature Retrieve, Screening, and Selection.

Postoperative Opioid Consumption (Up to 48 Hours)

Three studies reported the data concerning the opioid consumption during the 48 hours following surgery (21, 23, 25). The heterogeneity was not significant among these three articles ($I^2=43\%$, $P=0.17$), therefore the fixed effects model was appropriate to use. After pooling the data, we found that TAP block, compared with other control treatments, significantly reduced the 48 hours opioid (morphine) consumption by 0.03 mg/kg (Figure 2, 95% CI -0.05 to - 0.00, $P=0.03$).

Number of Children Needed Postoperative Opioid Analgesia Rescue

Four studies provided data concerning the numbers of children needed postoperative opioid analgesia rescue (22- 25). The study by Carney et al. (21) was excluded because all of the children received postoperative opioid analgesia which was not based on the postoperative pain level.

Different standards for measuring postoperative pain were employed in these studies. Rescue opioid analgesia was defined as the morphine usage when the face, legs, activity, cry and consolability (FLACC) scale score was ≥3 (23), modi-

Table. Summary of Studies Included in A 1

Study	Ages	N	Groups (N)	Procedures	TAP block technique	Type of anesthesia	Postoperative analgesia strategy	Primary/secondary outcomes	Modifed Jadad score
Lorenzo et al. (2014) (23)	0-6 years	32	1. TAP block (N=16) 2. Local infiltration (N=16)	Unilateral open pyeloplasty	Preoperative ultrasound guided TAP block with 0.4 ml/kg bupivacaine 0.25% with 1:200,000 epinephrine	Sevoflurane/fentanyl/propofol/rocuronium	0.05 mg/kg morphine + intravenously/0.5 mg/kg ketorolac as needed	Primary: Proportion of patients requiring 1 or more doses of rescue opioid administration for a FLACC score of 3 or higher; Secondary: Cumulative morphine requirements in the recovery room and pain score on arrival to the PACU and adverse events	4
Sahin et al. (2013) (24)	2-8 years	57	1. TAP block (N=29) 2. Local infiltration (N=28)	Unilateral inguinal hernia repair	Preoperative ultrasound guided TAP block with 0.5 ml/kg bupivacaine 0.25%	Sevoflurane/propofol/fentanyl	Oral paracetamol 15 mg/kg 4 hourly + intravenous morphine 0.05 mg/kg as rescue analgesic	Primary: Time to first analgesic; Secondary: The cumulative amount and number of doses of analgesic, pain scores and adverse effects in 24 postoperative hours	4
Sandeman et al. (2011) (25)	7-16 years	87	1. TAP block (N=42) 2. control (N=45)	Laparoscopic appendicectomy	Preoperative ultrasound guided TAP block with 0.5 ml/kg ropivacaine 0.2%	Succinylcholine/propofol/sevoflurane/fentanyl	PCA morphine	Primary: Proportion of subjects using >200 mg/kg morphine; Secondary: PCA morphine use, pain scores, time intervals to the first use of PCA and other analgesics, sedation scores, postoperative nausea or vomiting, and time to hospital discharge	4
Fredrickson et al. (2010) (22)	2-7 years	41	1. TAP block (N=21) 2. Control (N=20)	Inguinal surgery	Preoperative ultrasound guided TAP block with 0.3 ml/kg of a 50:50 mixture of lidocaine 1% and ropivacaine 1% with 1:200,000 epinephrine	Sevoflurane/fentanyl	Oral ibuprofen + intravenous morphine 50 µg/kg as needed	Analgesic consumption, parental satisfaction, and pain score	5
Carney et al. (2010) (21)	4-16 years	40	1. TAP block (N=19) 2. Control (N=21)	Open appendectomy	Preoperative TAP block with 2.5 ml/kg ropivacaine 0.75%	Sevoflurane/propofol	Patient- controlled/nurse- controlled morphine analgesia	Primary: 48-hour morphine consumption; Secondary: Time to first request for morphine, VAS scores, and side effects associated with morphine consumption	4

Study or subgroup	TAP block group Mean	SD	Total	Control group Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Carney 2010	0.03	0.04	19	0.07	0.05	21	71.3%	-0.04 (-0.07, -0.01)
Lorenzo 2014	0.07	0.05	16	0.06	0.1	16	18.6%	0.01 (-0.04, 0.06)
Sandeman 2011	0.24	0.19	42	0.23	0.16	45	10.1%	0.01 (-0.06, 0.08)
Total (95% CI)			**77**			**82**	**100.0%**	**-0.03(-0.05, -0.00)**

Heterogeneity: Chi^2=3.53, df=2 (P=0.17); I^2=43%
Test for overall effect: Z=2.13 (P=0.03)

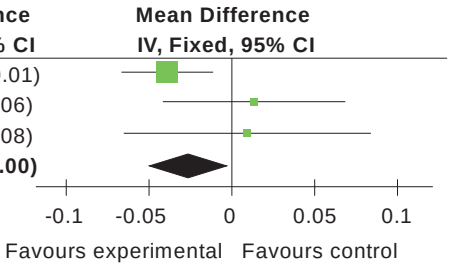

Figure 2. Forest plot Showing the 48 Hours Postoperative Opioid Consumption of Children with or without TAP Block.

Study or subgroup	TAP block group Events	Total	Control group Events	Total	Weight	Risk ratio M-H, random, 95% CI
Fredrickson 2010	8	21	4	20	16.1%	1.90 (0.68, 5.35)
Lorenzo 2014	13	16	6	16	22.9%	2.17 (1.10, 4.26)
Sahin 2013	16	29	28	28	30.1%	0.56 (0.40, 0.78)
Sandeman 2011	29	42	31	45	30.9%	1.00 (0.76, 1.33)
Total (95% CI)		**108**		**109**	**100.0%**	**1.11 (0.62, 1.98)**
Total events	66		69			

Heterogeneity: Tau^2=0.26; Chi^2=18.01, df=3 (P=0.0004); I^2=83%
Test for overall effect: Z=0.36 (P=0.72)

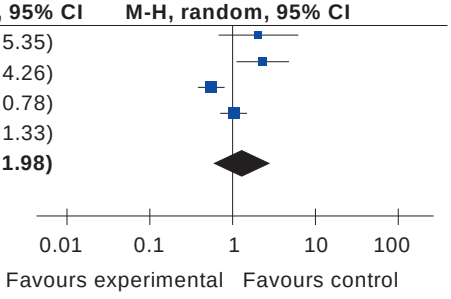

Figure 3. Forest Plot Showing the Number of Children Needed Post-Operative Opioid Analgesia Rescue in TAP block and Control Group.

Study or subgroup	TAP block Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, random, 95% CI
Carney 2010	1.83	1.12	21	0.28	0.095	19	34.5%	1.55 (1.07, 2.03)
Sahin 2013	17	6.8	29	4.7	0.1	28	32.8%	12.30 (9.76, 14.84)
Sandeman 2011	5.33	6.52	42	6	0.16	45	32.6%	-0.67 (-3.37, 2.03)
Total (95% CI)			**92**			**92**	**100.0%**	**4.36 (-2.13, 10.84)**

Heterogeneity: Tau^2=31.66, Chi^2=69.62, df=2 (P<0.00001); I^2=97%
Test for overall effect: Z=1.32 (P=0.19)

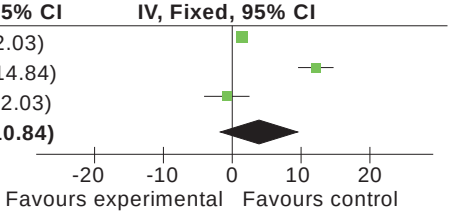

Figure 4. Forest Plot Showing the First Analgesic Administration Time (Hours) of Children with or without TAP Block.

fied Children's Hospital of Eastern Ontario Pain Scale (mCHEOPS) score was ⩾5 (24), the consumption of morphine was >200 μg/kg (25) or the numerical pain score (NPS) was >5 (22). After pooling these data, there was significant heterogeneity among the 4 studies (I^2=83% , P= 0.0004) and the random effect model was appropriate to use. The analysis of the aggregated data favored a reduction of children needed postoperative opioid analgesia in TAP group. However this reduction was not statistically significant (Figure 3, RR: 1.11, 95% CI 0.62, 1.98, P= 0.72). The further subgroup analysis was not performed because of the limited number of studies.

Time to First Analgesic Administration (Hours)

Three studies provided data on the time to first analgesic administration (21, 24, 25). The random effect model was used as the significant heterogeneity among the 3 studies (I^2=97% , P< 0.00001). There was a non-significant trend toward increase of first analgesic administration time for children who had treated with the TAP block compared with those treated with no TAP block or placebo (Figure 4, 95% CI 4.36, -2.13, 10.84, P=0.19).

Postoperative Pain Score

The descriptions of postoperative pain score

were diverse from the reviewed studies. There were two studies applied visual analogue scale (VAS) to measure the postoperative pain (21, 25), and others used FLACC (23), NPS (22) and mCHEOPS (24) as the assessment of pain score. The inconsistency and heterogeneity in the post-operative pain severity precluded quantitative analysis. 3 RCTs demonstrated the reduction of pain scores after TAP block. In detail, 2 RCTs indicated that the post-operative pain scores were reduced after TAP block at all time points assessed (21, 24), while 1 RCT reported that the median pain scores but not scores at each time interval were reduced for the TAP group in the recovery ward (25).

DISCUSSION

The most primary finding of the current meta-analysis was the significant effect of TAP block in reduction of postoperative opioid consumption in children treated with a TAP block. Similar as adult, opioids remain an indispensable part of modern pain management strategy in children (26, 27). The reduction in postoperative opioid consumption suggested that the TAP block can relieve the pain in children after surgery. Furthermore, the reductions of pain scores in the included studies also support the analgesic effect of TAP block in children.

Usually, opioid analgesics are taken by children with the doses based on the age, sex, race, and pharmacogenetic factors. However, a number of dose- dependent side effects of opioid drugs such as nausea and vomiting still occur (28, 29). Thus, it is meaningful for the reduction of opioid analgesics consumption in children. Some researchers have suggested that minimizing the dose of opioid analgesics could reduce the side effects (30). The previous meta-analyses in adult have demonstrated the significant reduction of opioid usage in regional anesthesia treated adults group while comparing with placebo treated group, and the side effect of opioids such as nausea, sedation, and pruritus were reduced due to the lower opioid consumption (14, 31, 32). Thus, for children, we speculated that the treatment of TAP block may reduce the occurrence of side effect related with opioid analgesics through the decrease of opioid usage.

Although the significant reduction in the opioid consumption of children receiving TAP block was demonstrated, we were unable to find an obvious reduction in the number of children who needed postoperative opioid analgesia rescue. Meanwhile, we did not observe the significant difference in the time of first opioid analgesic requirement between TAP block and control group. As the first time of opioid usage are usually at the early stage after surgery (14, 21, 22, 25), we speculated that TAP block cannot fully alleviate the early postoperative pain. However, as the time passed, the analgesia effect of TAP block gradually played a role on the postoperative pain management. Thus, the preoperative administration of the TAP block seemed optimal to manage postoperative pain and reduce the opioid consumption. The early meta-analysis also preferred the preoperative administration of TAP block to the postoperative administration of the block on the management of early pain at rest and reduction of postoperative opioid consumption (14). Besides, as the opioid analgesics were usually applied according to the subjective pain measurement strategies, it was possible that the anxiety sensitivity, catastrophizing and parental responses may contribute to higher estimations of the children's pain intensity and stronger solicitousness of opioid analgesic, which created greater number of children needed postoperative opioid analgesia rescue than actual (33, 34).

The safety remains to be one of the barriers to performing TAP block to ameliorate postoperative pain in children. In 2009, Suresh and Chan (35) published a procedural guidance for the performance of TAP block in children, which ensured that this block technique could be safely performed for children. Long et al. (36) performed a multicenter safety analysis of 1994 cases from the Pediatric Regional Anesthesia Network (PRAN) Database, and they reported a minor incidence (0.3%) of complications related with TAP block in more than 1900 children. Furthermore, the complications in their study usually did not result in the serious consequence (36). Besides, as the local anaesthetic toxicity is the most likely serious adverse event for children, the optimal dose was also the assurance of safety. Sola et al. reported a minor dose

of 0.2 ml/kg of 0.2% levobupivacaine which could provide efficient perioperative analgesia in most of children experienced herniorrhaphy. In a word, the anxiousness of safety should not be a major barrier to the application of TAP block in children.

This present study was limited by the small size of included RCTs and the significant heterogeneity during the analyzing of primary and secondary outcomes. There were only five RCT trials with 257 children included in our meta-analysis, and some outcomes were missing in the included studies, such as the effect of TAP block on the incidence of postoperative side effect and the pain scores at different time point after surgery. Besides, multiple factors included the various surgery kinds, doses of local anaesthetic and evaluation method for postoperative pain, contributed to the significant heterogeneity. Limited to the small size of included trials, it was difficult to perform the subgroup analyses. Furthermore, the different control groups in each trial would be considered: three of the studies compared TAP block with another regional field infiltration (22-24), while the remaining two studies used placebo as control (21, 25). Future studies could compare the pain score, local anaesthetic side effects and volume of anaesthetic during surgery to further investigate the effect of TAP block.

In summary, we have detected the reduction of opioid consumption when the TAP block was performed on children. And in order to obtain better analgesic effect, the TAP block may be performed at the preoperative period. TAP block constitutes one of safe and effective multimodal approaches for postoperative pain management in children.

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No other conflicts of interest declared.

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Appendix

Search strategy

Pubmed

(TAP block[Text Word]) OR (transversus abdominis plane block*) OR ("TAP block"[Text Word]) AND (block[All Fields])) OR ((bier[All Fields]) AND (block [All Fields])) OR Ropivacaine OR Lidocaine OR Bupivacaine OR Tetracaine OR Mepivacaine OR Prilocaine OR levobupivacaine OR (("Anesthetics, Local" [MeSH]) OR ("Anesthetics, Local"[Pharmacological Action]) OR ("Anesthesia, Local"[MeSH])) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR single- blind method[mh] OR double blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR "clinical trial"[tw] OR ((singl* [tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask* [tw] OR blind*[tw])) OR placebos [mh] OR placebo* [tw] OR random*[tw] OR comparative study[pt] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animals[mh] NOT humans[mh]) AND ("Children" [MeSH] OR "kid" [text word] OR ("child" [text word]))

Embase

(transversus abdominis plane block/TAP block") and (regional anesthesia / or nerve block/ or local anesthesia/ or anesthetic agent/) or (((an?esthesia adj3 (conduction or regional)) or (block* adj3) or (Ropivacain* or Lidocain* or Bupivacain* or Tetracaine or Mepivacaine or Prilocaine or levobupivacaine)).ti,ab.) AND ((randomized- controlled- trial/ or randomization/ or controlled- study/ or multicenter- study/ or phase-3-clinical-trial/ or phase-4-clinical-trial/ or double- blind- procedure/ or single- blind- procedure/ or (random* or cross?over* or factorial* or placebo* or volunteer* or ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*))).ti,ab.) not (animals not (humans and animals)).sh.) AND (children/ or child/ or kid/)

Cochrane Controlled Trials Register

(MeSH descriptor Anesthesia, Conduction explode all trees) OR (MeSH descriptor Nerve Block explode all trees) OR ((regional anaesthesia) or (regional anesthesia)) OR ((conduction anesthesia)) OR (transversus abdominis plane block) OR (TAP block*) OR ropivacaine OR lidocaine OR bupivacaine OR tetracaine OR mepivacaine OR prilocaine OR levobupivacaine OR MeSH descriptor Anesthetics, Local explode all trees OR MeSH descriptor Anesthesia, Local explode all trees AND Children or child or kid AND (hyperalgesia OR allodynia OR MeSH descriptor Pain, Postoperative explode all trees) AND (postoperative pain OR preventive analg OR pre-emptive analg* OR preemptive analg*)

Exported only clinical trials