British Journal of Anaesthesia **113** (3): 375–90 (2014)
Advance Access publication 6 June 2014 · doi:10.1093/bja/aeu156

BJA

Regional anaesthesia to improve pain outcomes in paediatric surgical patients: a qualitative systematic review of randomized controlled trials

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Editor's key points

- The authors performed a systematic review to evaluate randomized clinical trials that examined the effect of regional anaesthesia on postoperative pain outcome in paediatric patients.
- Currently, only a few regional anaesthesia techniques have been shown to reduce postoperative pain, and these only in a limited number of surgical procedures.

Summary. The development of analgesic interventions in paediatric surgical patients is often limited by the inherent difficulties of conducting large randomized clinical trials to test interventions in those patients. Regional anaesthesia is a valid strategy to improve postoperative pain in the adult surgical population, but the effects of regional anaesthesia on postoperative pain outcomes in paediatric patients are currently not well defined. The main objective of the current review was to systematically evaluate the use of regional anaesthesia techniques to minimize postoperative pain in paediatric patients. A systematic search was performed to identify randomized controlled trials that evaluated the effects of the regional anaesthesia techniques on postoperative pain outcomes in paediatric surgical patients' procedures. Seventy-three studies on 5125 paediatric patients were evaluated. Only few surgical procedures had more than one small randomized controlled trial favouring the use of regional anaesthesia to minimize postoperative pain (ophthalmological surgery, cleft lip repair, inguinal hernia, and urological procedures). Additional evidence is required to support the use of specific regional anaesthesia techniques to improve postoperative pain for several surgical procedures (craniectomy, adenotonsillectomy, appendectomy, cardiac surgery, umbilical hernia repair, upper and lower extremity) in paediatric patients. Currently, only a very limited number of regional anaesthesia techniques have demonstrated significant improvement on postoperative pain outcomes for a restricted number of surgical procedures. More studies are needed in order to establish regional anaesthesia as a valid strategy to improve analgesia in the paediatric surgical population.

Keywords: paediatric; regional block

Optimal postoperative pain control remains a goal to be achieved in the surgical population.[1 2] For paediatric patients having surgery, the development and implementation of analgesic techniques are often delayed by the inherent difficulties of conducting a large randomized clinical trial in that patient population.[3 4] In order to circumvent those difficulties, a large multi-institutional collaboration group has generated observational data to provide evidence for the use of regional anaesthesia in children.[5 6] Nevertheless, observational studies often contain systematic bias that are often difficult to control even with rigorous statistical methods.[7 8]

In 1963, Taylor and colleagues[9] described the use of a regional anaesthesia technique (retrobulbar block) to prevent the development of oculo-cardiac reflex in children compared with systemic atropine. Since then, several clinical studies have evaluated the use of regional blocks not only to minimize systemic drug effects but also to improve postoperative analgesia in the paediatric population with varying benefits. Currently, it is not well defined which regional blocks provide the greater rates of optimal postoperative pain control in children undergoing different surgical procedures. In addition, the rates of regional anaesthesia complications reported by clinical studies have yet to be systematically studied in the same population.

The main objective of the current review was to evaluate systematically the use of regional anaesthesia techniques to minimize postoperative pain in paediatric patients undergoing different surgical procedures. We also sought to examine complications associated with the use of regional anaesthesia in the same population.

Methods

We performed a qualitative systematic review following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA).[10]

Systematic search

Published reports of randomized trials evaluating the effects of regional anaesthesia blocks on surgical postoperative pain in

paediatric patients were searched using the National Library of Medicine's Pubmed database, the Cochrane Database of Systematic Reviews, and Google Scholar inclusive to May 21, 2013. Free text and MeSH terms 'blocks', 'pain', 'regional' 'postoperative', 'surgery ', 'analgesia', and 'opioid' were used individually and in various combinations. No language restriction was used. The search was limited to human subjects younger than 18 yr of age. An attempt to identify additional studies not found by the primary search methods was made by reviewing the reference lists from identified studies. No search was performed for unpublished studies. This initial search yielded 775 randomized clinical trials.

Selection of included studies

The study's inclusion and exclusion criteria were determined before the systematic search. Two authors (G.S.D.O. and K.S.) independently evaluated the abstract and results of the 775 articles obtained by the initial search. Articles that were clearly not relevant based on our inclusion and exclusion criteria were excluded at this phase. Disagreements on inclusion of the articles were resolved by discussion among the evaluators. If an agreement could not be reached, the dispute was resolved with the help of a third investigator (S.S.). The third investigator was blinded regarding evaluation of the first two authors.

Inclusion and exclusion criteria

We included randomized controlled trials that compared perioperative regional blocks with local anaesthetics and a control group in paediatric patients undergoing surgical procedures. Studies containing a concurrent use of an alternative multimodal analgesia regimen were excluded if a direct comparison between a regional anaesthesia technique and control could not be established. Studies that provided a direct comparison between two different regional anaesthetic techniques, two different local anaesthetics and/or comparisons involving a block adjunct were included. Included studies had to report at least on pain scores or opioid consumption as postoperative pain outcomes. No minimum sample size was required for inclusion in the meta-analysis (Fig. 1) .

Validity scoring

Two authors (G.S.D.O. and K.S.) independently read the included reports and assessed their methodological validity using a modified Jadad five-point quality scale.[11] The scale evaluates the study for the following: randomization, double-blind evaluation, concealment of study group to evaluator, valid randomization method, and completeness of data at follow-up. Discrepancies in rating of the trials were resolved by discussion among the evaluators. If an agreement could not be reached, the dispute was resolved with the help of a third investigator (S.S.). As only randomized trials were included in the analysis, the minimum possible score of an included trial was 1 and the maximum was 5. Trials were not excluded from the evaluation based on quality assessment scores.

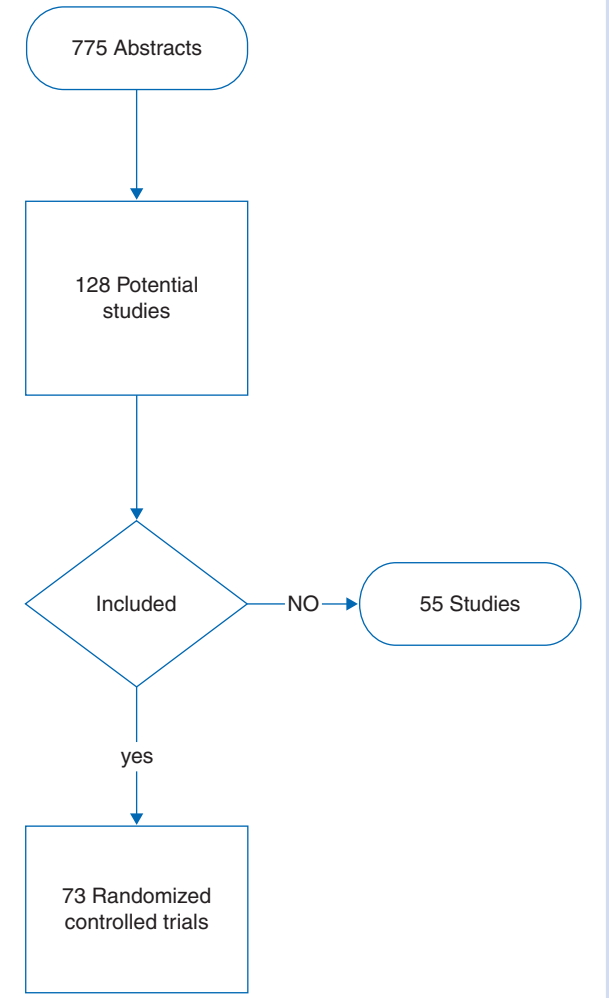

Fig 1 Flow chart outlining retrieved, excluded, and evaluated randomized controlled trials.

Data extraction

Two authors (G.S.D.O. and K.S.) independently evaluated the full manuscripts of all included trials and performed data extraction using a data collection form specifically developed for this review.

Discrepancies were resolved by discussion between the two investigators (G.S.D.O. and K.S.). If an agreement could not be reached between the two investigators, the decision was made by a third investigator (S.S.). Data extracted from trials included the local anaesthetic type and dose, nerve block type, sample size, number of subjects in treatment groups, follow-up period, type of surgery, early pain scores ($\leq$4 h) and late pain scores (24 h) at rest, cumulative opioid consumption, time to rescue analgesic administration (min), and adverse events.

Definition of relevant outcome data

Primary outcomes

Early acute postoperative pain scores at rest (4 h after operation); late acute postoperative pain scores (24 h after

operation); and cumulative opioid consumption (24 h) in the postoperative period.

Secondary outcomes

The time to first analgesic administration (min); adverse events including: postoperative hypotension, nerve damage, and local anaesthetic toxicity.

Meta-analyses

Since the study comparisons were clinically heterogeneous and/or the number of studies with homogenous comparisons were small (≤three studies), a qualitative description of outcomes was considered more appropriate to evaluate the included studies. We, therefore, did not evaluate the presence of publication bias as we did in our previous studies.[12–14]

Results

We evaluated 73 studies on 5125 paediatric patients. The median [inter-quartile range (IQR)] for the Jadad score of included studies was 3 (2–4). The median (IQR) of subjects receiving a regional anaesthetic technique was 29 (20–42). The characteristics of included studies are presented in Table 1.[15–88]

Craniectomy

One study evaluated the effect of a skull block with bupivacaine compared with the control on postoperative pain outcomes.[15] Pain scores and analgesic requirements were greater in the control group compared with the nerve block group. In addition, the authors reported a greater but not statistically significant rate of focal neurological infarction in the control group compared with the skull block group, odds ratio (95% confidence interval) of 3.2 (0.6–18.4).

Ophthalmological surgery

Five studies have examined the effect of regional anaesthesia techniques on postoperative analgesia outcomes in paediatric patients undergoing ophthalmological surgery.[16–20] Only one study reported on the performance of the retrobulbar block with no improvement in postoperative pain outcomes compared with the control.[16] Two studies evaluated the use of peribulbar block in children undergoing ophthalmic surgery.[17 18] Both studies reported lower analgesic requirements and lower postoperative pain scores in the peribulbar block group compared with the control. Two studies examined the effect of the subtenon block on postoperative analgesia outcomes in paediatric patients undergoing ophthalmic surgery.[19 20] Both studies reported lower analgesic requirements and lower postoperative pain scores in the subtenon block group compared with the control group.

Otologic surgery

Three studies evaluated the effect of nerve blocks on postoperative analgesia in paediatric patients undergoing otologic surgery.[21–23] Two studies examined the sole use of the great auricular nerve block[21 22] and one study examined the block of both the great auricular and occipital nerve.[23] None of the included studies demonstrated an advantage of the nerve block compared with the control with regard to postoperative pain, analgesic consumption, or both.

Tonsillectomy

Only one study evaluated the use of regional anaesthesia (bilateral glossopharyngeal block) to improve analgesia for adenotonsillectomy surgery.[24] The authors detected an improvement in postoperative pain scores and longer analgesia duration in the group who received a glossopharyngeal nerve block compared with the control. The authors did not report on the development of complications related to the performance of the block.

Cleft palate repair

Two studies evaluated the use of peripheral nerve blocks on cleft palate repair.[25 26] In one study, the authors found that a palatal block (blocking of naso palatine, greater, and lesser palatine nerves) improved postoperative pain scores.[25] Another study examined the addition of dexmedetomidine to bupivacaine on the duration of postoperative analgesia in patients receiving greater palatine nerve block for cleft palate repair.[26] The authors demonstrated that the group who received bupivacaine alone had greater pain scores and requested rescue analgesia sooner compared with the group who received bupivacaine and dexmedetomidine as a block adjunct.

Cleft lip repair

Five studies examined regional anaesthesia and its effects on postoperative analgesia in cleft lip repair procedures.[27–31] Three of these studies evaluated the effect of infraorbital nerve block compared with a control group.[27 29 31] In all three studies, the infraorbital nerve block was found to be superior in postoperative analgesia compared with the control group. One study reported that the addition of meperidine to bupivacaine for infraoral and infraorbital peripheral nerve blocks increased the duration of postoperative analgesia in cleft lip repair surgery compared with bupivacaine alone.[30] Another study examined if the addition of systemic fentanyl would improve the analgesic benefits of bilateral infraorbital nerve blocks, but the authors did not detect a difference in postoperative analgesia outcomes.[28]

Appendectomy

Three studies evaluated the effects of regional anaesthesia techniques on postoperative analgesia in children undergoing appendectomies.[32–34] One study looked at unilateral transversus abdominis plane (TAP) blocks for open appendectomy and concluded that the TAP block was superior to the control for postoperative pain control.[32] In contrast, a different study found no difference in postoperative pain control between TAP block and control in laparoscopic appendectomy cases.[33] One study examined somatic paravertebral block *vs* control in subjects undergoing open appendectomy.[34] The authors

Table 1 Summary of studies included in analysis

Authors	Year of publication	Procedures	Number treatment/ control	Block/intervention	Outcomes	Block complications	Modified Jadad score (1–5)[7]
Ahn and colleagues[15]	2008	Craniectomy	21/18	Preoperative skull block after anaesthesia induction with 0.25% 5–8 ml bupivacaine mixed with 20–40 mg methylprednisolone	Pain: scores lower in the skull block group at 15 and 25 min postop. PACU discharge quicker in the skull block group	Five focal infarctions developed in the conventional group postop and two in the skull block group	3
Ateş and colleagues[16]	1998	Ophthalmic	10/10/10	Retrobulbar block	Analgesia use: no difference up to 24 h Pain: the subconjunctival bupivacaine group had higher pain scores from 2 to 4 h postoperative	None related to the block	1
Deb and colleagues[17]	2001	Ophthalmic	25/25	Peribulbar block	Children in the block group had lower postoperative pain at all time points and lower analgesic requirement	None related to the block	1
Subramaniam and colleagues[18]	2003	Ophthalmic	42/43	Peribulbar block	Children in the block group had lower postoperative pain and lower analgesic requirement	None related to the block	3
Chhabra and colleagues[19]	2009	Ophthalmic	98/98	Subtenon block	Lower analgesic requirement and greater postoperative pain in the subtenon block	None reported	5
Ghai and colleagues[20]	2009	Ophthalmic	58/56	Subtenon block	Lower analgesic requirement and lower postoperative pain in the subtenon block	None related to the block	5
Voronov and colleagues[21]	2008	Otologic surgery	100/100	Auricular nerve block	Pain: no difference Analgesia use: no difference	None related to the block	3
Suresh and colleagues[22]	2002	Otologic surgery	20/20	Great auricular nerve block	Analgesia : no statistically difference in rescue analgesic requirement	None related to the block	3
Cregg and colleagues[23]	1995	Otologic surgery	21/22	Great auricular and occipital nerve block the great auricular and lesser occipital nerves	Pain: no significant difference Analgesia use: no difference	None related to the block	1
Mohamed and colleagues[24]	2009	Tonsillectomy	50/50	Bilateral glossopharyngeal nerve block	Pain: lower postoperative pain scores Analgesia use: longer analgesia duration	None related to the block	2
Jonnavithula and colleagues[25]	2010	Cleft palate repair	15/29	Palatal block (naso palatine, greater and lesser palatine nerves)	Pain: the block group had lower postoperative pain scores Analgesia use: lower need for rescue analgesia compared with placebo	None related to the block	3
Obayah and colleagues[26]	2010	Cleft palate repair	15/15	Greater palatine nerve block with dexmedetomidine	Analgesia use: the control group requested analgesia sooner Pain: the control group had significantly higher pain scores after 8 h	None related to the block	3

Takmaz and colleagues[27]	2009	Cleft lip repair	20/20	Bilateral infraorbital nerve block	Analgesia use: time to first requirement longer in the bupivacaine group. Total consumption of paracetamol was higher in the saline group. Tramadol was needed in all saline patients and no bupivacaine patients Pain: pain scores were four times higher in the saline group in the recovery room	None related to the block	3
Simion and colleagues[28]	2008	Cleft lip repair	23/23	Infraorbital nerve block+fentanyl	Analgesia use: time to first rescue medication was greater in the block group	None related to the block	3
Rajamani and colleagues[29]	2006	Cleft lip repair	41/41	Infraorbital nerve block	Analgesia use: less analgesia needed in the bupivacaine group per child Pain: pain scores were lower in the block group	None related to the block	5
Jonnavithula and colleagues[30]	2007	Cleft lip repair	20/20	Infraorbital nerve block with meperidine as an adjunct	Analgesia use: duration of analgesia was greater in the group who received meperidine as an adjunct	One patient from the control group alone had erythema on the cheek	2
Prabhu and colleagues[31]	1999	Cleft lip repair	15/15	Bilateral infraorbital nerve block	Analgesia use: all patients in the peri-incisional group required analgesics with only two in the infraorbital group in the first 24 h Pain: the block group had better pain relief for 8 h postoperative	Not stated	3
Carney and colleagues[32]	2010	Appendectomy	19/21	TAP block	Analgesia use: TAP block reduce morphine requirement. Time to first requirement of morphine was shorter in the control group	No difference	4
Sandeman and colleagues[33]	2011	Laparoscopic appendectomy	42/45	TAP block	Analgesia use: no difference Pain: pain scores were lower in the block group in the recovery room only	No difference	5
Splinter and colleagues[34]	2010	Appendectomy	18/18	Somatic paravertebral block	Analgesia use: the somatic group required less morphine and their time to first dose was significantly less	None related to the block	2
Chaudhary and colleagues[35]	2012	Cardiac	14/13	Parasternal intercostal block	Pain: scores were significantly lower in the block group Analgesia use: the control group had significantly greater opioid consumption	One child was excluded due to excessive bleeding in the block group	4
De Windt and colleagues[36]	2010	Minor hand surgery	30/30	Wrist block	Pain: the wrist block group had lower pain overall in the day hospital and recovery room Analgesia use: the time to first analgesic intake was longer in the opioid group	None related to the block	3
Trifa and colleagues[37]	2012	Forearm/hand surgery	30/30	Axillary block and clonidine as block adjunct	Pain: no difference	Not stated	5

Continued

Table 1 *Continued*

Authors	Year of publication	Procedures	Number treatment/ control	Block/intervention	Outcomes	Block complications	Modified Jadad score (1–5)[7]
Altintas and colleagues[38]	2000	Hand/forearm	25/24	Axillary block preoperative and postoperative	Pain: higher pain scores cumulatively in the preoperative group Analgesia use: similar between the groups	Not stated	2
Ponde and Diwan[39]	2009	Radial club hands	25/25	Nerve stimulator *vs* ultrasound-guided infraclavicular block	Analgesia use: similar between the groups	No difference	3
De José María and colleagues[40]	2008	Upper limb	40/40	Supraclavicular block; infraclavicular block	Analgesia: no differences	No difference	1
Carre and colleagues[41]	2000	Upper limb	35/35	Single injection axillary; multiple fractionated doses	Analgesia: no differences	Not stated	2
Omar and colleagues[42]	2011	Hip surgery	20/20	Psoas compartment block and caudal block	Analgesia use: the caudal group had significantly greater doses of morphine administered	Urinary retention significantly greater in the caudal group	4
Kim and colleagues[43]	2011	Orthopaedic surgery of anterior or lateral thigh	32/32	Fascia iliaca compartment block	Pain: on arrival to PACU and 10 min later, the fascia group had significantly lower scores	No difference	3
Farid and colleagues[44]	2010	Reconstructive knee surgery	12/11	Femoral nerve block; fascia iliaca block	Analgesia use: no significant difference	Not stated	3
Oberndorfer and colleagues[45]	2007	Lower extremity	23/23	Ultrasound; nerve stimulator	Anaesthetic use: the US group had lower anaesthetic amount used. Duration of analgesia higher in the US group	Not stated	2
Rodrigues and colleagues[46]	2009	Congenital clubfoot	30/32/28/28	Caudal; sciatic and femoral nerve; sciatic and saphenous; sciatic with infiltrative anaesthesia of the medical incision	Analgesia use: no difference	No difference	3
Isaac and colleagues[47]	2006	Umbilical hernia repair	6/7	Rectus sheath block	Analgesia use: no difference Pain: no difference	None related to the block	2
Gurnaney and colleagues[48]	2011	Umbilical hernia repair	26/26	Rectus sheath block	Analgesia: no difference Pain: no difference	No difference	3
Naja and colleagues[49]	2005	Hernia repair	25/25	Paravertebral block	Pain: scores were lower in the paravertebral block Analgesic consumption was reduced in the paravertebral block	No difference	3
Jagannathan and colleagues[50]	2009	Unilateral groin surgery	25/23	Ilioinguinal block in addition to a caudal block	Pain: average pain score higher in the saline group. Hernia repair patients were the only group with significant differences in pain scores	No difference	4
Fredrickson and colleagues[51]	2010	Inguinal surgery	20/21	TAP block compared with ilioinguinal block	Pain: more patients reported pain in the TAP group Analgesia use: more patients required ibuprofen in the TAP group	Not stated	3

Disma and colleagues[52]	2009	Inguinal hernia repair	20/19/21	Ilioinguinal/iliohypogastric block; 0.125 levobupivacaine; 0.25 levobupivacaine; 0.375 levobupivacaine	Pain: scores higher in the 0.125 group than 0.25 or 0.375 at 15, 20, 25, and 30 min Analgesia use: time to first administration of analgesia higher in the 0.125 group	None related to the block	3
Weintraud and colleagues[53]	2009	Inguinal hernia repair	31/35	Landmark-based ilioinguinal nerve block; ultrasound-guided ilionguinal nerve block	Analgesia use: the landmark group needed more intraoperative analgesia	No difference	3
Trifa and colleagues[54]	2009	Unilateral hernia, hydrocelectomy, orchidopexy	36/36	Ilioinguinal-iliohypogastric nerve block; 1 mg ml^{-1} ropivacaine; 2 mg ml^{-1} ropivacaine	Analgesia use: more children in the 1 mg ml^{-1} group needed additional postoperative analgesia	No difference	5
Naja and colleagues[55]	2006	Hernia repair	39/40	Paravertebral block/ilio-inguinal nerve block	Analgesia use: lower in the paravertebral block group Pain: lower in the paravertebral block group	No difference	4
Kundra and colleagues[56]	2006	Unilateral hernia repair	34/34/34/30	Iliohypogastric nerve block at 1 cm inferiomedial to ASIS; iliohypogastric nerve block at 1–2 cm medial to ASIS; iliohypogastric nerve block at 2 cm superior-medial to ASIS; iliohypogastric nerve block at 2 cm superior-medial to ASIS	Pain: during first 8 h postoperative, pain scores were higher in the superior-medial group Analgesia use: the superior-medial group required more analgesia	Isolated incident of transient femoral nerve palsy in the inferiomedial group	2
Khosravi and colleagues[57]	2005	Herniotomy	30/30	Ilioinguinal/iliohypogastric nerve block	Pain: the i.v. tramadol group experienced less pain	None related to the block	3
Kaabachi and colleagues[58]	2005	Heriorrhaphy or orchidopexy	49/49	Ilioinguinal/iliohypogastric nerve block; ilioinguinal/iliohypogastric nerve block+clonidine	Analgesia use: no significant difference	Not stated	2
Willschke and colleagues[59]	2005	Inguinal hernia, orchidopexy, hydrocele	50/50	Fasical click method; ultrasound-guided ilioinquinal block	Analgesia use: the fascial click group needed more analgesia on skin incision and required less analgesics postoperative	No difference	2
Sasaoka and colleagues[60]	2005	Inguinal hernia repair	48/50	Ilioninguinal/iliohypogastric nerve block; ilioinguinal/iliohypogastric nerve block+genitofemoral block	Analgesia use: no significant difference	No difference	3
Tsuchiya and colleagues[61]	2004	Inguinal hernia repair	10/10/10	Ilioinguinal/iliohypogastric; ropivacaine; bupivacaine; lidocaine	Pain: postoperative pain was greater in the lidocaine group compared with the ropivacaine and/or bupivacaine groups	No difference	1
Ivani and colleagues[62]	2002	Inguinal	20/20	Caudal block and clonidine; ilioinguinal block and clonidine	Analgesia use: no difference	No difference	3
Lim and colleagues[63]	2002	Hernia repair	44/43	Ilioninguinal/iliohypogastric nerve block single shot; ilioinguinal/ iliohypogastric nerve block double shot	Analgesia: no significant difference in the rate of analgesia The presence of local anaesthetic in inguinal canal significantly higher in the double-shot group	Not stated	3

Continued

Table 1 *Continued*

Authors	Year of publication	Procedures	Number treatment/ control	Block/intervention	Outcomes	Block complications	Modified Jadad score (1–5)[7]
Splinter and colleagues[64]	1995	Hernia repair	96/104	Caudal block	Analgesia use: opioid use had no difference. Acetaminophen was used more in the local group Pain: no difference	No difference	3
Gunter and colleagues[65]	1999	Inguinal herniorrhaphy	20/15	Ilioinguinal–iliohypogastric nerve block	Analgesia use: the mean number of rescue doses greater the in control group Pain: time-weighted pain score greater in the control group	No difference	2
Tug and colleagues[66]	2011	Inguinal	35/35	Paravertebral block and caudal block	Analgesia use: more patients in the caudal group needed postoperative analgesia	Two patients had slight motor weakness in the caudal group	3
Breschan and colleagues[67]	2005	Inguinal hernia or orchidopexy	61/60/61	Caudal block with ropivacaine *vs* bupivacaine *vs* levobupivacaine	Analgesia: no differences	No difference	2
Bosenberg and colleagues[68]	2002	Inguinal	36/38/36	1 mg kg^{-1} ropivacaine; 2 mg kg^{-1} ropivacaine; 3 mg kg^{-1} ropivacaine	Pain: during first 4 h 1 mg kg^{-1} group had higher pain scores Analgesia use: total dose during first 4 h higher in the 1 mg kg^{-1} group	No difference	3
Senel and colleagues[69]	2001	Urogenital, rectal and lower abdominal surgery	20/20/20	Bupivacaine; bupivacaine with tramadol; tramadol	Analgesia use: more patients needed additional analgesia in the tramadol alone group than bupivacaine alone group. The tramadol alone group had short duration of analgesia	No difference	2
Da Conceicao and colleagues[70]	1999	Herniorrhaphy	40/40	Caudal block with bupivacaine *vs* ropivacaine	Pain: no difference Analgesia: no difference	No difference	3
O'Sullivan and colleagues[71]	2011	Circumcision	32/34	Dorsal penile nerve block by landmark *vs* dorsal penile nerve block by ultrasound	Analgesia use: no difference Pain: no difference	No difference	3
Naja and colleagues[72]	2011	Circumcision	30/30	Pudendal; dorsal	Pain: lower scores in the pudendal group during first 12 h Analgesia use: lower use in first 6 h in the pudendal group	Two minor haematomas in the dorsal group	3
Faraoni and colleagues[73]	2010	Circumcision	20/20	Penile nerve block by ultrasound *vs* penile nerve by landmark	Analgesia use: longer time to first administration of analgesia in the ultrasound group. Pain: higher in the landmark group at arrival and 30 min after in the PACU	Not stated	3
Margetts and colleagues[74]	2008	Circumcision	20/20	Caudal block with ketamine *vs* penile block	Analgesia use: time to first analgesia longer in the caudal group	None related to the block	3

Choi and colleagues[75]	2003	Circumcision	30/30	Topical eutectic mixture of local anaesthetic *vs* dorsal penile block	Pain: no difference Analgesia: the penile block resulted in longer analgesia	None related to the block	5
Howard and colleagues[76]	1999	Circumcision	31/29	Topical eutectic mixture of local anaesthetic *vs* dorsal penile block	Distress scores higher in the eutectic group	Not stated	4
Holliday and colleagues[77]	1999	Circumcision	10/19/19	Topical eutectic mixture of lidocaine *vs* dorsal penile block *vs* control	The control group had elevated behavioural scores compared with the penile group during and after circumcision	Two eutectic group patients had blistering	5
Hardwick-Smith and colleagues[78]	1998	Circumcision	20/20	Ring block	Ring block had less crying receiving the block. Two hours postoperative, there were no significant differences	No difference	2
Butler-O'Hara and colleagues[79]	1998	Circumcision	21/23	Topical eutectic mixture of local anaesthetic *vs* dorsal penile block	Pain: the eutectic group demonstrated more pain overall. Average pain scores were lower in the penile group	Three patients in the eutectic group had erythema. One patient in the penile group developed penile oedema	5
Lander and colleagues[80]	1997	Circumcision	12/15/13/14	Ring block; dorsal penile block; topical eutectic mixture of local anaesthetic	Pain: the ring block resulted in less crying and was effective through all stages of procedure	One newborn in the placebo group had a choking episode. One other placebo newborn had an episode of abnormal posture, apnoea, and choking	2
Serour and colleagues[81]	1996	Circumcision	122/128	Dorsal penile nerve block; GA+dorsal penile nerve block	Analgesia use: all the children given analgesics were from the general anaesthesia plus penile block group	None related to the block	2
Broadman and colleagues[82]	1987	Circumcision	25/25	Ring block	Analgesia use: the ring block group required less analgesia Pain: scores less at 15 min observation in the block group	No difference	4
Weksler and colleagues[83]	2005	Post-circumcision	50/50	Penile block *vs* caudal block	Analgesia use: no difference	Tachycardia in three patients in the penile group and six in the caudal group	4
Khalil and colleagues[84]	1999	Urological, lower abdominal, lower extremity	36/39	Caudal block with bupivacaine *vs* ropivacaine	No differences	Not stated	3
Seyedhejazi and colleagues[85]	2011	Hypospadias	44/41	Caudal block *vs* penile block	Analgesia use: the penile block group required more analgesia	No difference	2

Continued

Table 1 *Continued*

Authors	Year of publication	Procedures	Number treatment/control	Block/intervention	Outcomes	Block complications	Modified Jadad score (1–5)[7]
Chhibber and colleagues[86]	1997	Hypospadias repair	30/36/32	Penile block before *vs* after operation *vs* both	Pain: 3 and 12 h postoperative pain better in the before and after group than either one alone Analgesia use: by 12 h, the before and after surgery group required less analgesia	Not stated	3
Tripi and colleagues[87]	2005	Ureteroneocystostomy	15/18	Caudal block with bupivacaine+epinephrine *vs* caudal block with bupivacaine+epinephrine+clonidine	Analgesia: the mean duration of caudal analgesia was higher in the clonidine group. The clonidine group also required less postoperative opioids	No difference	5
Tirotta and colleagues[88]	2009	Open heart surgery	35/37	Continuous incisional infusion 0.25% levobupivacaine or bupivacaine *vs* control	Analgesia: postoperative morphine consumption was decreased in the local anaesthetic group	None stated	4

concluded that somatic paravertebral block was superior to control in postoperative analgesia after open appendectomy.

Cardiac

One study examined the effect of parasternal intercostal blocks in paediatric patients undergoing cardiac surgery.[35] The authors found that the subjects who received a parasternal intercostal block had shorter time to extubation, lower pain scores, and lower fentanyl requirements at 24 h compared with the control.

Another study evaluated the use of a continuous incisional infusion of 0.25% bupivacaine compared with saline for open heart surgery.[88] The authors detected an opioid-sparing effect of the local anaesthetic compared with saline.

Upper extremity

Six studies have evaluated peripheral nerve block in paediatric patients for procedures involving the upper extremities.[36–41] One study examined the wrist block for minor hand surgery and demonstrated an improvement on analgesia outcomes in subjects who received the wrist block compared with the control.[36] Trifa and colleagues[37] did not detect a benefit of the perineural addition of clonidine for an axillary block compared with the control on postoperative pain outcomes. One study evaluated the time of the axillary block performance (preoperative *vs* postoperative) on pain outcomes in forearm or hand surgery.[38] The authors concluded that presurgical block was not superior to post-surgical block.

One investigation compared the use of nerve stimulation to ultrasound guidance for infraclavicular blocks in patients undergoing surgery for radial club hands.[39] The authors did not detect a benefit of the ultrasound compared with nerve stimulator technique on postoperative pain outcomes. Another study did not find a benefit on analgesia outcome when the infraclavicular and supraclavicular approaches were compared.[40] Carre and colleagues[41] did not detect a benefit on the number of injections of an axillary nerve block on postoperative pain outcomes.

Hip and pelvis

Only one study examined a regional anaesthesia technique in children for hip or pelvic surgeries.[42] Omar and colleagues[42] compared postoperative analgesic effects of psoas compartment block *vs* a caudal block in paediatric patients undergoing hip reduction/osteotomies. They found that the children in the caudal group used more morphine in 24 h after operation and needed rescue analgesia sooner than the psoas compartment block group. In addition, the caudal group was more likely to develop urinary retention.

Lower extremity

Five studies evaluated peripheral nerve block for children undergoing lower extremity surgical procedures, including the thigh, knee, and foot.[43–46] For procedures involving the anterior and lateral thigh, Kim and colleagues[43] found that patients who received a fascia iliaca compartment block had

significantly lower pain scores on arrival to the post-anaesthesia care unit (PACU) compared with the control. Another study compared the femoral nerve block with the fascia iliac block in reconstructive knee surgery.[44] The authors found no difference in pain scores or postoperative morphine consumption between the two regional blocks.

Oberndorfer and colleagues[45] examined ultrasound-guided *vs* nerve stimulator-guided sciatic and femoral nerve blocks in children. They concluded that ultrasound-guided sciatic and femoral nerve blocks in the paediatric population had a longer duration of analgesia when compared with the nerve stimulator technique. The prolonged sensory block was also achieved with less volume of local anaesthetic.

One study, in a suboptimal design, compared the caudal block *vs* sciatic and femoral nerve block *vs* sciatic and saphenous nerve block *vs* sciatic with infiltrative anaesthesia along medial incision for club foot surgery.[46] The four groups did not differ with regard to total consumption of postoperative morphine.

Umbilical hernia

Two studies examined the effect of the rectus sheath blocks compared with the control in analgesic efficiency after operation for umbilical hernia repair surgery. Both studies found no statistically significant difference in postoperative opioid consumption between the two groups.[47 48]

Inguinal hernia and groin

Several studies examine the role of regional anaesthesia techniques on postoperative pain outcomes in the paediatric population for inguinal and groin procedures.[49–70]

Three investigations examined the paravertebral block for inguinal procedures in children.[49 55 66] Naja and colleagues[49] compared paravertebral block with a control group and demonstrated improved postoperative analgesia outcomes in the paravertebral block group. The same author then examined the ilioinguinal nerve blocks when compared with paravertebral blocks in similar surgeries.[55] Consumption of analgesics was significantly greater in the ilioinguinal nerve block group during the first 36 h after operation, and pain scores were significantly less in the paravertebral group. Another research group compared the caudal *vs* paravertebral blocks in children undergoing inguinal hernia procedures.[66] The paravertebral group needed significantly less rescue analgesia when compared with the caudal group.

Several investigations have evaluated the caudal block for inguinal hernia surgery. Splinter and colleagues[64] compared the caudal block with a control for hernia repair procedures. They found no difference in postoperative pain scores and overall opioid consumption between the two groups; however, the control group did require more acetaminophen when compared with the caudal group. Another study compared caudal block and ilioinguinal–iliohypogastric nerve blocks with clonidine for inguinal surgery in children.[62] The investigators found no difference in pain scores, time to recovery, and need for rescue analgesia between the two techniques.

Multiple studies have examined different drug dosing for caudal blocks in children. Bosenberg and colleagues[68] looked at caudal blocks for inguinal surgery using the same volume of either 1, 2, or 3 mg ml^{-1} of ropivacaine. The authors concluded that 2 mg ml^{-1} ropivacaine provided superior postoperative analgesia compared with 1 mg ml^{-1}, and less incident of motor block compared with 3 mg ml^{-1} ropivacaine. Two studies compared bupivacaine with ropivacaine for caudal blocks in paediatric patients undergoing inguinal surgery.[67 70] Both showed no differences in analgesia between the two groups, but did find less motor block in the ropivacaine group compared with bupivacaine. The study of Breschan and colleagues[67] also compared levobupivacaine, which also did not differ in analgesia, with bupivacaine or ropivacaine. Senel and colleagues[69] studied the bupivacaine–tramadol combination caudal when compared with bupivacaine alone and tramadol alone for inguinal surgery. The authors found that analgesia time was superior in the bupivacaine and tramadol caudal group. The tramadol alone caudal group required more analgesia after operation and had higher pain scores at 4 and 6 h after operation compared with the groups with bupivacaine in the caudal block.

Three studies examined the ilioinguinal–iliohypogastric nerve blocks when compared with the control for groin surgeries in children.[50 57 65] Two studies concluded that postoperative pain outcomes were improved with the ilioinguinal–iliohypogastric blocks.[50 67] One study found that patients in an i.v. tramadol group experienced less pain at the second and third postoperative days.[60]

Another study compared ilioinguinal blocks with TAP blocks for postoperative analgesia in children for inguinal surgery.[51] Patients receiving TAP blocks were more likely to report pain and required more rescue analgesia when compared with the ilioinguinal block group.

Multiple different techniques have been evaluated with regard to ilioinguinal–iliohypogastric nerve blocks in paediatric patients undergoing groin surgery. It has been shown that an ultrasound-guided approach to ilioinguinal nerve block compared with landmark approach allows for lower need of intraoperative analgesia.[53] Another study looked at a single-shot *vs* double-shot ilioinguinal–iliohypogastric nerve block technique but did not find benefits on postoperative analgesic outcomes between the techniques.[63] The fascial click method proved to be inferior compared with ultrasound-guided ilioinguinal–iliohypogastric blocks for groin surgery in paediatric patients.[59] Intraoperative and postoperative analgesia requirements were significantly lower with the ultrasound-guided approach. Kundra and colleagues[56] examined the effect of needle insertion site on ilioinguinal–iliohypogastric nerve blocks in children undergoing groin surgery. The authors found that all four different insertion sites could be used to successfully achieve analgesia, and that all the insertion sites had lower pain scores and less opioid requirements compared with the control. There was one isolated incident of transient femoral nerve palsy in the inferomedial group.

Four articles examine the effect of local anaesthetic dosing on pain outcomes of the ilioinguinal–iliohypogastric nerve

blocks in children undergoing groin surgery.[52 54 58 61] Trifa and colleagues[54] found that a more efficient block is achieved when using a high-concentration/low-volume dose of ropivacaine when compared with high-volume/low-concentration that resulted in less need for postoperative analgesics. One study looked at three different concentrations of levobupivacaine in ilioinguinal–iliohypogastric blocks for paediatric patients undergoing ambulatory surgery.[52] The investigators found that pain scores were higher in the 0.125% group when compared with 0.25% or 0.375% at 15, 20, 25, and 30 min after operation. A comparison of ropivacaine, bupivacaine, and lidocaine for ilioinguinal nerve block in children for ambulatory surgery detected that pain scores were lower in the ropivacaine and bupivacaine groups when compared with the lidocaine group.[61] One study evaluated the addition of clonidine to bupivacaine for ilioinguinal–iliohypogastric nerve blocks in paediatric patients undergoing groin surgery.[58] This study found no difference in postoperative pain outcomes between the two groups.

Circumcision

Two trials compared penile blocks with caudal blocks in children with regard to postoperative pain outcomes.[74 83] One study found a statistical significance difference in the time to first analgesic requirement favouring the caudal group over the control group when the caudal block was performed with 0.25% bupivacaine and 0.5 mg kg^{-1} of ketamine.[74] Another study did not show a significant difference in analgesia between the penile block and caudal block.[83]

Two studies compared the penile ring block with the control, and found that the ring block was superior for postoperative analgesic outcomes.[78 82] One study compared the penile ring block with dorsal penile nerve block with eutectic mixture of local anaesthetic (EMLA) cream and placebo.[80] The authors found that all three treatment groups were superior to placebo, with the most effective being the ring block.

Four studies compared EMLA cream with dorsal penile nerve blocks in paediatric patients undergoing circumcision.[76 77 79] Three of these studies were done in newborns and found that the dorsal nerve penile block was superior to EMLA cream or placebo in postoperative pain outcomes.[76 77 79]

Two studies compared ultrasound-guided and the landmark-based approaches for dorsal penile nerve blocks in patients undergoing circumcision.[71 73] The study of O'Sullivan and colleagues[71] found no differences in opioid consumption between the two groups, but the ultrasound-guided technique required longer times to be performed compared with the landmark-based approach. In contrast, the study by Faraoni and colleagues[73] demonstrated that the ultrasound-guided dorsal penile nerve block was associated with decreased pain scores on arrival to PACU and 30 min after, and also longer time until rescue analgesia was needed compared with the landmark-based approach. The ultrasound-guided method was also associated with a longer duration of the procedure.

A study compared the dorsal penile nerve blocks alone with dorsal penile nerve blocks and general anaesthesia.[81] The authors found that only the patients from the penile nerve block and general anaesthesia group required additional analgesia in the PACU. PACU time and incidence of nausea and vomiting were also significantly higher in the block and general anaesthesia group. Another group looked at pudendal blocks *vs* penile nerve blocks for circumcision procedures.[83] The authors show that the pudendal block group had significantly lower postoperative pain scores and fewer postoperative analgesic use compared with the dorsal penile nerve block group at 0 and 6 h.

Other urological procedures

One study investigated the effect of different local anaesthetics (ropivacaine *vs* bupivacaine) on pain outcomes for caudal blocks in children undergoing ambulatory surgical procedures.[84] No difference in postoperative analgesia outcomes was detected between the study groups. Two investigations evaluated the use of a regional anaesthesia for hypospadias procedures.[85 86] One study found the caudal block to be superior compared with a penile block with regard to the need for postoperative rescue analgesia.[85] Another study examined the effect of the penile block timing for hypospadias repair in children.[86] They found that a penile block performed before and at the conclusion of surgery provided better postoperative pain control at 3 and 12 h postoperative when compared with either a single penile block before surgery or at the conclusion of surgery.

Tripi and colleagues[87] examined if caudal blocks with bupivacaine and epinephrine provided better postoperative pain *vs* bupivacaine, epinephrine, and clonidine in children undergoing ureteroneocystostomies.

Discussion

The most important finding of the current investigation was the lack of sufficient clinical trials to support the use of regional anaesthesia techniques in order to reduce postoperative pain for the vast majority of paediatric procedures. In contrast, no significant morbidity was attributed to regional anaesthesia techniques in more than 5000 patients examined in the current investigation. Since regional anaesthesia has been shown to be a valid strategy to improve postoperative pain outcomes in the adult population,[89–91] our review calls for the large need to further examine the effect of regional anaesthesia techniques on postoperative pain outcomes in paediatric patients.

We could only find enough evidence to support or refute the use of regional anaesthesia in order to improve analgesia in very limited circumstances. Among the strongest evidence to support the use of regional anaesthesia were paravertebral blocks for inguinal surgery (two studies), infraorbital blocks for cleft lip repair (five studies), and ring blocks (three studies) for circumcisions. Even for those types of blocks where more than one study was available, group comparisons were quite heterogeneous which limited our ability to provide a quantitative analysis. For example, the two studies supporting the use of paravertebral block for hernia repairs were performed using ultrasound guidance by the same authors, but they utilized different local anaesthetic solutions.[49 55]

Despite the paucity of studies to support the use of specific regional anaesthesia techniques in children, few studies have actually demonstrated lack of benefit. Among the strongest evidence for lack of regional anaesthesia benefit is the use of auricular block for otologic surgery (three studies). In several conditions such as the skull block for craniectomies or the glossopharyngeal block for adenotonsillectomy surgery, only one very small single-centred randomized trial suggested potential benefits which further warranted the need for additional studies.

It was interesting to note that even for established regional techniques such as the caudal block, the evidence for procedure-specific indications is not currently well defined. For inguinal surgeries, one study demonstrated mixed results when the caudal block was compared with the control.[64] For circumcisions, the caudal block demonstrated conflicting results on analgesia outcomes when compared with the penile block.[74 83] Since it has been recommended that analgesic interventions should be procedure-specific, more clinical trials evaluating the caudal block for specific procedures are needed.[92–94]

The use of ilioinguinal block to mitigate postoperative pain in children after hernia repair also resulted in conflicting results.[50 55 57] Nevertheless, several studies have focused on the evaluation of different techniques,[53 56 59 63] use of different local anaesthetic solutions,[52 54 61] or even the use of block adjuncts.[58] It still remains to be determined if the ilioinguinal block is effective to minimize postoperative pain after hernia repair. Future studies should further examine the efficacy of the ilioinguinal block to minimize postoperative pain in children.

Several trials evaluated the use of perineural drug adjuncts to augment the analgesic effects of local anaesthetics. We noted that, in some circumstances, perineural adjuncts were used, despite the lack of studies that demonstrated beneficial analgesic when local anaesthetics were used alone. For example, one study did not detect beneficial analgesic effects of clonidine when added to ropivacaine for axillary block.[37] Ketamine has been found to augment caudal block analgesia, but its safety has been previously questioned.[95–97] The safety of perineural adjuncts has been also questioned in the adult population.[98 99] We believe that it is more important to establish the efficacy of each specific block first than to evaluate adjuncts with limited data on safety.

The use of ultrasound compared with nerve stimulator/landmark techniques to improve postoperative analgesia in paediatric patients generated conflicting results. Even for the same nerve block such as the penile block for circumcision, two studies revealed contradictory results.[71 73] Although the use of ultrasound for regional anaesthesia demonstrated a higher success rate and a lower risk for an accidental vascular puncture compared with nerve stimulator guidance in the adult population, the benefits on analgesic outcomes were small.[100]

With the exception of the study of Carney and colleagues,[32] the studies included in the current systematic review did not include a 'sham block' but frequently used no interventions. McGuirk and colleagues[101] have developed a grading scale in order to classify studies regarding the risks of a sham block. Based on our current review, the risks associated with the majority of regional anaesthesia techniques in children should not be an impediment to the use of a sham block. In contrast, Waisel and Truog[102] suggested that placebo controls should only be used in non-vulnerable patient populations.

It is likely that barriers to perform randomized control trials in children have contributed to the lack of regional anaesthesia studies in paediatric patients, especially when comparing with the adult population.[103–106] Barriers to paediatric research contribute to create equity problems in child health.[107] Commonly cited barriers include: difficult recruitment, lack of funding, and ethical concerns.[108] Those barriers have also contributed to poor design of randomized controlled trial in children and a high rate of biases in paediatric clinical trials.[109]

Our review should only be interpreted in the context of its limitations. Since the comparisons were quite heterogeneous (different drugs, adjuncts, or both) and the number of studies for the same surgical procedure was small, we did not perform a quantitative analysis and limited our review to a qualitative evaluation. We could not quantitatively evaluate the presence of publication bias and it is possible that the negative studies evaluating analgesic outcomes after regional anaesthesia in paediatrics were never published. We also did not examine if variations on the block technique affected the pain outcomes, unless the evaluation of the technique was the primary objective of the study.

In summary, we performed a systematic review to evaluate the effect of regional anaesthesia techniques on postoperative pain outcomes in paediatric patients. Currently, only a very limited number of regional anaesthesia techniques for a restricted number of surgical procedures have demonstrated significant improvements on postoperative pain outcomes. More studies are warranted in order to establish regional anaesthesia as an optimal strategy to improve analgesia in paediatric surgical patients.

Authors' contributions

S.S.: study design, study conduct, and manuscript preparation; K.S.: study conduct and manuscript preparation; B.W.: study conduct and manuscript preparation; G.S.D.O.: study design, study conduct, data analysis, and manuscript preparation.

Declaration of interest

None declared.

Funding

This study was supported by the Department of Anesthesiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.

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Handling editor: J. G. Hardman