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Review Article

REVIEW ARTICLE

Efficacy of perineural *vs* systemic dexamethasone to prolong analgesia after peripheral nerve block: a systematic review and meta-analysis

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Abstract

Perineural dexamethasone has gained popularity in regional anaesthesia to prolong the duration of analgesia, but its advantage over systemic administration is disputed. The objective of this meta-analysis was to compare the analgesic efficacy of both routes of administration during peripheral nerve block. The methodology followed the PRISMA statement guidelines. The primary outcome was the duration of analgesia analysed according to the type of local anaesthetic administered (bupivacaine or ropivacaine). Secondary outcomes included cumulative opioid consumption in morphine i.v. equivalents, pain scores, and complication rates (neurological complications, infection, or hyperglycaemia). Eleven controlled trials, including 914 patients, were identified. The duration of analgesia was significantly increased with perineural dexamethasone *vs* systemic dexamethasone by a mean difference of 3 h [95% confidence interval (CI): 1.4, 4.5 h; $P=0.0001$]. Subgroup analysis revealed that the duration of analgesia was increased by 21% with bupivacaine (mean difference: 4.0 h; 95% CI: 2.8, 5.2 h; $P<0.00001$) and 12% with ropivacaine (mean difference: 2.0 h; 95% CI: −0.5, 4.5 h; $P=0.11$). The quality of evidence for our primary outcome was moderate according to the GRADE system. There were no significant differences in other secondary outcomes. No neurological complications or infections were reported. Glucose concentrations were not increased when dexamethasone was injected systemically, but this outcome was reported by only two trials. There is, therefore, moderate evidence that perineural dexamethasone combined with bupivacaine, but not ropivacaine, slightly prolongs the duration of analgesia, without an impact on other pain-related outcomes, when compared with systemic dexamethasone. Injection of perineural dexamethasone should be cautiously balanced in light of the off-label indication for this route of administration.

Key words: analgesia; anesthetics, local; dexamethasone; nerve block; pain, postoperative

Multiple adjuncts to local anaesthetics, such as neostigmine, tramadol, or clonidine, have been examined for their potential to prolong analgesia after regional nerve blocks, but with disappointing results.[1] Perineural dexamethasone was first explored clinically >12 yr ago,[2] followed by a myriad of clinical trials. Recently, a meta-analysis concluded that perineural dexamethasone, compared with placebo, prolonged the duration of analgesia by >8 h, when combined with long-acting local anaesthetics, suggesting that patients could benefit from a pain-free postoperative night.[3] The mechanism of action for this

prolongation of block is not fully understood, but suggested possibilities include decreased nociceptive C-fibre activity via a direct effect on glucocorticoid receptors,[4] a direct effect on inhibitory potassium channels,[5] a local vasoconstrictive effect,[6] or a systemic anti-inflammatory effect.[7]

Despite the evident clinical benefit, perineural dexamethasone remains an off-label route of administration. An alternative choice of dexamethasone i.v. has likewise been explored, which at moderate doses offers the potential for a systemic anti-inflammatory effect.[8] In a randomized controlled trial, Desmet and colleagues[9] explored both routes of administration and concluded that they offer an equivalent prolongation of analgesia. This early conclusion has been disputed in subsequent trials,[3 10 11] with some authors concluding that additional rigorous assessment of both routes of administration was warranted.[12]

The objectives of this meta-analysis were to compare the analgesic efficacy and side-effects of perineural *vs* systemic dexamethasone administration as an adjunct to local anaesthetic for peripheral nerve block in adult patients.

Methods

Literature search and inclusion criteria

This investigation followed the recommended process described in the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) statement.[13] The authors

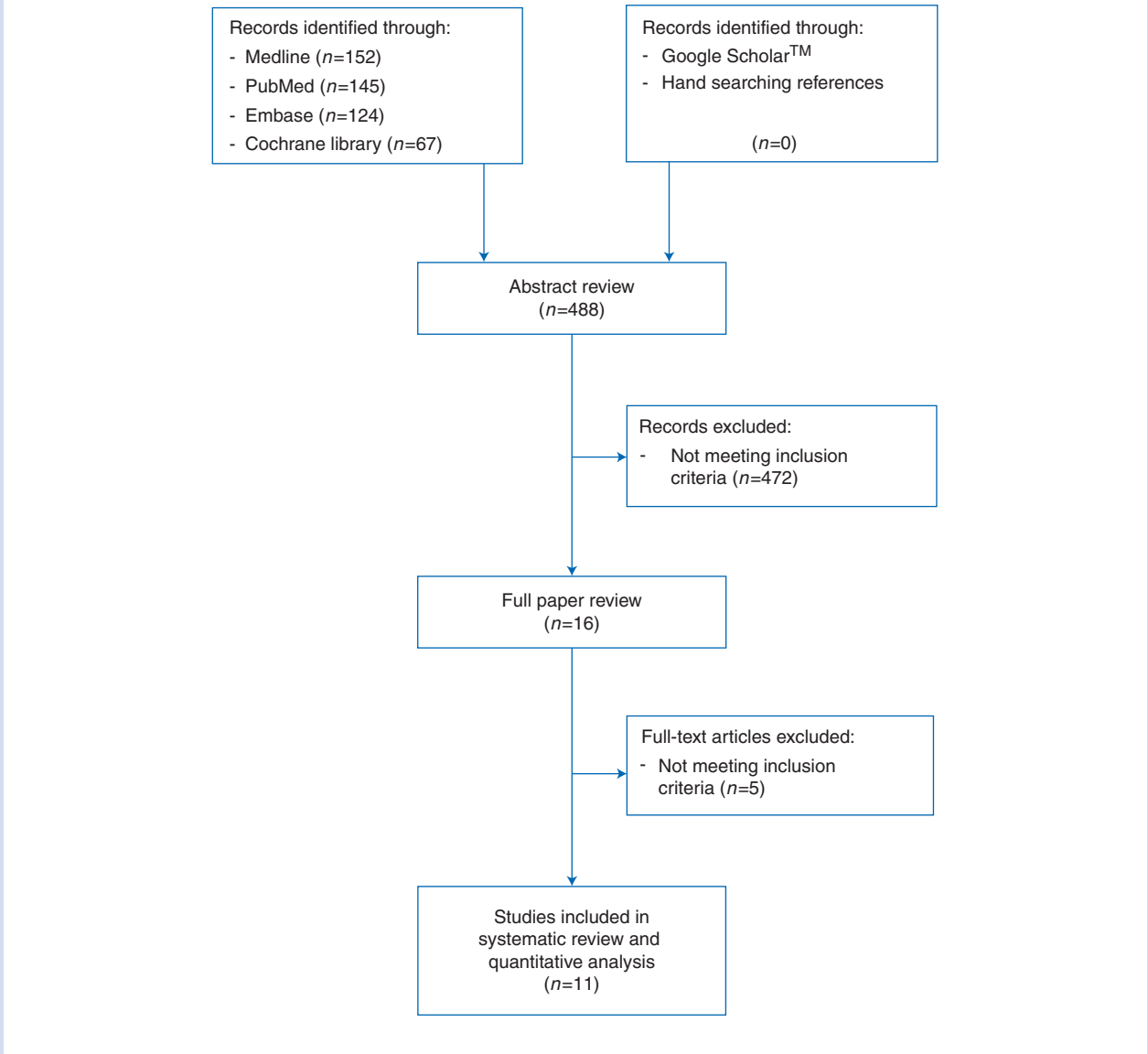

Fig 1 PRISMA flow diagram showing literature search results. Eleven randomized controlled trials were included in the analysis.

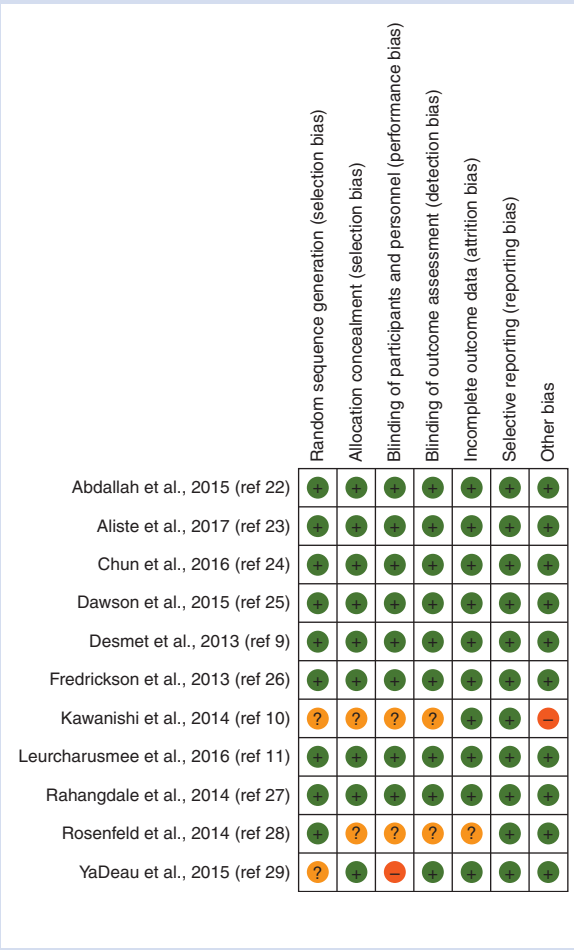

Fig 2 Cochrane collaboration risk of bias summary: evaluation of bias risk items for each included study. Green circle, low risk of bias; red circle, high risk of bias; yellow circle, unclear risk of bias.

searched electronic databases, including the following: Medline (until January 2017), PubMed (until January 2017), Excerpta Medica database, Embase (until January 2017), and the Cochrane Central Register of Controlled Clinical Trials (until January 2017), and applied the following population search terms: Anaesthetic technique OR Anesthetic technique OR Anaesthesia conduction OR Anesthesia conduction OR Local anaesthetics OR Local anesthetics OR Nerve block OR Peripheral nerve block OR Regional anaesthesia OR Regional anesthesia. These search results were combined with Dexamethasone OR Glucocorticoids OR Steroids. Results were further limited by combining with Clinical trials OR Random allocation OR Therapeutic use. The following words were searched as keywords: Anaesth*, Anesth*, Nerve*, Dexamethas*, Glucocort*, Steroid*, Clinical*, Random*, Trial*. The results of this search strategy were limited to randomized controlled trials and humans. No age or language limits were placed on the search. Finally, the references of all articles retrieved from the search were manually scrutinized for any relevant trials not identified using the strategy described above, and Google Scholar™ was examined for any additional publications.

Population

The meta-analysis addresses male and female patients undergoing any surgical operation with a regional nerve block.

Intervention and comparator

Only trials comparing perineural dexamethasone and local anaesthetics with systemic (i.v. or i.m.) dexamethasone and perineural local anaesthetics alone for peripheral nerve block were included in the present meta-analysis.

Outcomes

The specific outcomes sought from each article were derived according to our standard approach, which we described in a previous meta-analysis on acute postoperative pain.[14] The primary outcome was the duration of analgesia or duration of sensory block, defined as the time interval between block performance or onset time of sensory block and the time of first analgesic request or initial pain report. Secondary acute pain-related outcomes were as follows: cumulative morphine i.v. consumption equivalent on postoperative day 1; any pain score recorded at rest and on movement in the early postoperative period (between 0 and 12 h after surgery) and on postoperative days 1 and 2; rates of postoperative nausea and vomiting within the first 24 h after surgery; and patient satisfaction. Secondary side-effect-related outcomes were rates of neurological complication, infection, and hyperglycaemia.

Trial characteristics

Extracted trial characteristics included the following: type of surgery; type of regional block; concentration and volume of local anaesthetics injected; dose of dexamethasone; and use and type of multimodal analgesia.

Rating of the studies

The quality of the research methodology of each randomized trial was assessed following the Cochrane Collaboration's Risk of Bias Tool for randomized controlled trials.[15] Two authors (A.J.-G. and K.R.K.) independently screened, reviewed, and scored the items for each trial using this method and extracted data for the analyses. Disagreements with scoring or extracted data were resolved through discussion with a third author (E.A.).

Data extraction

The source study text, tables, or graphs were used to extract the mean values, SD or SEM, 95% confidence intervals (CI), number of events, and total number of participants. The authors of trials that failed to report the sample size or results as a mean value and SD or SEM or 95% CI were requested twice by mail to give the missing or raw data. If no reply was obtained, the median and interquartile range were used for mean and SD approximations, as follows: the mean was estimated as equivalent to the median and the SD was approximated to be the interquartile range divided by 1.35.[16] All opioids were converted into equi-analgesic doses of morphine i.v. for analysis (morphine 10 mg i.v.=morphine 30 mg p.o.=hydromorphone 1.5 mg i.v.=hydromorphone 7.5 mg p.o.=pethidine 75 mg i.v.=oxycodone 20 mg p.o.=tramadol 100 mg i.v.).[17] Pain scores and patient satisfaction scores reported as visual, verbal, or numerical rating scales were converted to a standardized 0–10 analog scale for quantitative evaluations. Finally, we rated the

Table 1 Trial characteristics

Reference	Group (*n*)	Local anaesthetic	Regional nerve block	Regional technique	Surgery	Other anaesthesia	Postoperative analgesia	Primary outcome
Abdallah *et al.* (2015)[22]	Perineural dexamethasone 8 mg (25), dexamethasone 8 mg i.v. (25)	Bupivacaine 0.5%, 30 ml	Supraclavicular brachial plexus block	Ultrasound	Distal upper limb surgery	I.V. sedation with propofol or midazolam	Fentanyl, paracetamol, codeine, oxycodone	Duration of analgesia
Aliste *et al.* (2017)[23]	Perineural dexamethasone 8 mg (75), dexamethasone 8 mg i.v. (75)	Lidocaine 1% plus bupivacaine 0.25% plus epinephrine 5 μg ml^{-1}, 30 ml	Axillary brachial plexus block	Ultrasound	Distal upper limb surgery	I.V. sedation with propofol	Not specified	Duration of motor block
Chun *et al.* (2016)[24]	Perineural dexamethasone 5 mg (50), dexamethasone 5 mg i.v. (49)	Ropivacaine 0.75%, 8 ml	Interscalene brachial plexus block	Ultrasound	Arthroscopic shoulder surgery	General anaesthesia	Ketorolac, tramadol	Duration of analgesia
Dawson *et al.* (2016)[25]	Perineural dexamethasone 8 mg (30), dexamethasone 8 mg i.v. (30)	Ropivacaine 0.75%, 20 ml	Ankle block	Ultrasound	Foot surgery	None	Paracetamol, oxycodone, tramadol	Duration of analgesia
Desmet *et al.* (2013)[9]	Perineural dexamethasone 10 mg (49), dexamethasone 10 mg i.v. (49)	Ropivacaine 0.5%, 30 ml	Interscalene brachial plexus block	Nerve stimulation	Arthroscopic shoulder surgery	General anaesthesia	Paracetamol, diclofenac, piritramide	Duration of analgesia
Fredrickson *et al.* (2013)[26]	Perineural dexamethasone 10 mg (33), dexamethasone 10 mg i.m. (33)	Bupivacaine 0.5%, 30 ml	Sciatic nerve block (popliteal approach) plus saphenous nerve block	Ultrasound	Ankle, hind- and midfoot surgery	General anaesthesia	I.V. morphine, paracetamol, diclofenac, tramadol	Proportion of patients reporting pain at 48 h
Fredrickson *et al.* (2013)[26]	Perineural dexamethasone 8 mg (28), dexamethasone 8 mg i.m. (32)	Bupivacaine 0.5%, 30 ml	Ankle block	Ultrasound	Forefoot surgery	General anaesthesia	I.V. morphine, paracetamol, diclofenac, tramadol	Proportion of patients reporting pain at 48 h
Kawanishi *et al.* (2014)[10]	Perineural dexamethasone 4 mg (12), dexamethasone 4 mg i.v. (10)	Ropivacaine 0.75%, 20 ml	Interscalene brachial plexus block	Ultrasound	Arthroscopic shoulder surgery	General anaesthesia	Flurbiprofen, loxoprofen	Duration of analgesia
Leurcharusmee *et al.* (2016)[11]	Perineural dexamethasone 5 mg (61), dexamethasone 5 mg i.v. (62)	Lidocaine 1% plus bupivacaine 0.25% plus epinephrine 2.5 μg ml^{-1}, 35 ml	Infraclavicular brachial plexus block	Ultrasound	Distal upper limb surgery	I.V. sedation with propofol	Not specified	Duration of motor block
Rahangdale *et al.* (2014)[27]	Perineural dexamethasone 8 mg (27), dexamethasone 8 mg i.v. (23)	Bupivacaine 0.5% plus epinephrine 3.3 μg ml^{-1}, 0.45 ml kg^{-1}	Sciatic nerve block (infragluteal approach)	Ultrasound	Ankle and foot surgery	I.V. sedation with propofol	Paracetamol, hydrocodone	Quality of recovery questionnaire (QoR-40) score
Rosenfeld *et al.* (2016)[28]	Perineural dexamethasone 8 mg (42), dexamethasone 8 mg i.v. (37)	Ropivacaine 0.5%, 28 ml	Interscalene brachial plexus block	Ultrasound	Arthroscopic and open shoulder surgery	General anaesthesia	Morphine, hydromorphone, hydrocodone, oxycodone, ketorolac	Duration of analgesia
YaDeau *et al.* (2016)[29]	Perineural dexamethasone 4 mg (28), dexamethasone 4 mg i.v. (27)	Bupivacaine 0.25%, 35 ml	Sciatic nerve block (popliteal approach, 25 ml) plus adductor canal block (10 ml)	Ultrasound	Ankle and foot surgery	Neuraxial anaesthesia plus i.v. sedation with propofol or midazolam	Paracetamol, meloxicam, pregabalin, oxycodone	Pain on movement at 24 h postoperative

quality of evidence for each outcome following the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group system.[18]

Statistical analysis

Meta-analyses were performed with the assistance of Review Manager software (RevMan version 5.3.5; The Cochrane Collaboration 2014, The Nordic Cochrane Centre, Copenhagen, Denmark). This software estimates the weighted mean differences for continuous data and risk ratio for categorical data between groups, with an overall estimate of the pooled effect. A meta-analysis was conducted only if two or more trials reported the outcome of interest. The coefficient I^2 was used to evaluate heterogeneity with predetermined thresholds for low (25–49%), moderate (50–74%), and high (>75%) levels.[19] A random-effects model was applied in the event of moderate or high heterogeneity; otherwise, a fixed-effects model was used. Our primary outcome, duration of analgesia, was analysed in subgroups according to the type of local anaesthetic (bupivacaine or ropivacaine) to account for heterogeneity. The likelihood of publication bias was assessed by drawing a funnel plot of the standard error of the mean difference in duration of the analgesia (*y*-axis) as a function of the mean difference in duration of analgesia (*x*-axis) and confirmed with Duval and Tweedie's trim and fill test.[20] This assessment was performed using Comprehensive Meta-analysis Version 2 software (Biostat, Englewood, NJ, USA). Finally, a trial sequential analysis was executed on the duration of analgesia combined with bupivacaine or ropivacaine to confirm whether firm evidence was reached or not (TSA software version 0.9.5.5 Beta; Copenhagen Trial Unit, Center for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark).[21] Results are presented as the mean difference or relative risk (RR) with 95% confidence interval (CI). A two-sided *P*-value <0.05 was considered significant.

Results

Of the 488 trials identified from the literature search strategy, 11 met the inclusion criteria, representing a total of 914 patients (Fig. 1).[9–11 22–29]

According to our assessment using the Cochrane Collaboration Risk of Bias tool (Fig. 2), the majority of trials had a low risk of bias. Attempts were made to contact the authors of seven studies,[9 10 22 25–28] and five provided the additional data requested.[9 22 25 27 28] Data were approximated from the median and range in three trials.[10 24 26]

Table 1 presents the trial characteristics. All trials combined dexamethasone with long-acting local anaesthetics (bupivacaine or ropivacaine) except one that used a sequential injection of dexamethasone first followed by ropivacaine, without needle tip repositioning between injections.[9] All trials administered systemic dexamethasone i.v. except one that used the i.m. route.[26] Studied doses of dexamethasone were 4,[10 29] 5,[11 24] 8,[22 23 25–28] and 10 mg.[9 26] One publication presented the results of two randomized controlled trials[26]; of note, all patients in these two trials received an additional dose of i.v. dexamethasone 8 mg at the end of surgery.[26]

Upper limb blocks included interscalene, axillary, supraclavicular, and infraclavicular brachial plexus blocks.[9–11 22–24 28] Lower limb block sites were the adductor canal, sciatic nerve, and ankle.[25–27 29] With the exception of one trial where the authors used a nerve stimulator for block localization,[9] all blocks were performed under ultrasound guidance. Regional block was combined with general anaesthesia in five trials[9 10 24 26 28] and with neuraxial anaesthesia in one.[29]

The duration of analgesia was significantly increased by an average of 17% when dexamethasone was injected perineurally *vs* systemically (mean difference: 3.0 h; 95% CI: 1.4, 4.5 h; $P=0.0001$; Fig. 3). Subgroup analysis revealed that the mean duration of analgesia with bupivacaine and systemic dexamethasone was 22.1 h (95% CI: 15.9, 28.3 h), whereas it was 26.8 h with bupivacaine and perineural dexamethasone (95% CI: 19.4, 34.1 h), representing an increase of 21% (mean difference: 4.0 h; 95% CI: 2.8, 5.2 h; $P<0.00001$). With ropivacaine, the mean duration of analgesia with systemic and perineural dexamethasone was 17.4 h (95% CI: 8.3, 26.6 h) and 19.5 h (95% CI: 9.8, 29.2 h) respectively, representing an increase of 12% that did not reach statistical significance (mean difference: 2.0 h; 95% CI: −0.5, 4.5 h; $P=0.11$). There was no subgroup difference ($P=0.16$). The

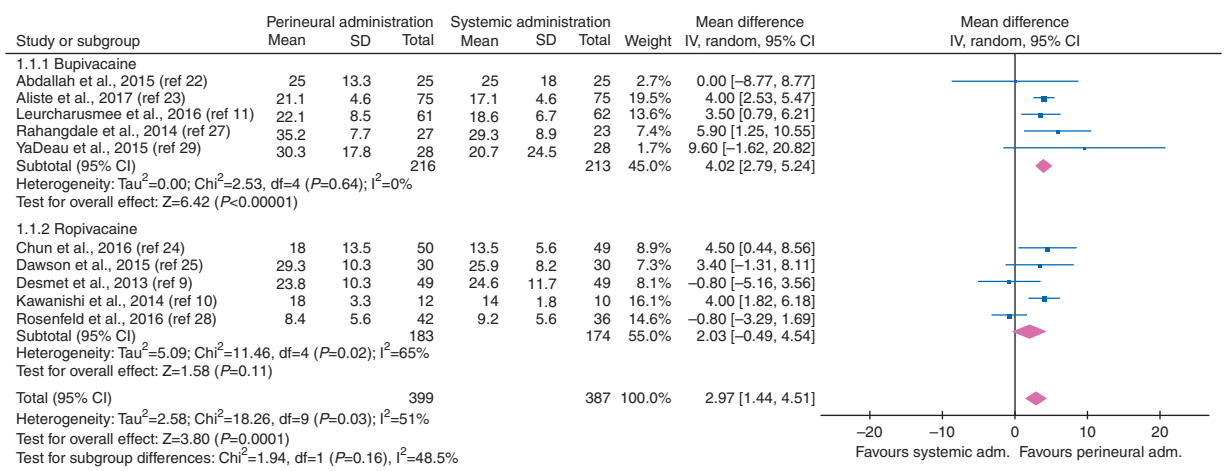

Fig 3 Duration of analgesia according to type of local anaesthetic (bupivacaine *vs* ropivacaine).

Table 2 Acute pain-related outcomes and opioid-related side effects. CI, confidence interval; *n*, number of events; *N*, total number of participants

Outcomes	References	Group						Mean difference [95% CI] or relative risk [95% CI]	I^2 (%)	P-value	Quality of evidence (GRADE)
		Perineural dexamethasone			Systemic dexamethasone						
		Mean or *n*	SD	N	Mean or *n*	SD	N				
Cumulative morphine i.v. consumption equivalent (mg)											
Postoperative day 1	Abdallah *et al.* (2015)[22]	4	10	25	4	8	25	−1 [−2, 1]	37	0.29	Moderate
	Dawson *et al.* (2016)[25]	3	4	30	3	3	30				
	Rahangdale *et al.* (2014)[27]	7	7	27	11	7	23				
	Rosenfeld *et al.* (2016)[28]	12	9	42	17	16	37				
Postoperative day 2	Rahangdale *et al.* (2014)[27]	10	7	27	8	9	23	2 [−2, 7]	–	0.29	Very low
Pain scores at rest (analog scale, 0–10)											
Early postoperative period	Abdallah *et al.* (2015)[22]	0.0	0.1	25	0.0	0.1	25	−0.3 [−0.9, 0.2]	51	0.26	Low
	Chun *et al.* (2016)[24]	2.0	2.2	50	3.0	3.0	49				
	Rosenfeld *et al.* (2016)[28]	1.5	1.7	42	2.4	3.0	36				
	YaDeau *et al.* (2016)[29]	1.0	2.7	27	0.9	2.2	27				
Postoperative day 1	Abdallah *et al.* (2015)[22]	2.1	1.8	25	3.1	1.4	25	−0.5 [−1.0, 0.02]	60	0.06	Low
	Chun *et al.* (2016)[24]	1.5	1.5	50	2.0	2.2	49				
	Fredrickson *et al.* (2013)[26] (sciatic nerve block)	0.0	1.5	33	0.0	0.7	33				
	Fredrickson *et al.* (2013)[26] (ankle block)	0.0	1.5	28	0.0	0.7	32				
	Rahangdale *et al.* (2014)[27]	0.0	1.5	27	2.5	3.7	24				
	Rosenfeld *et al.* (2016)[28]	3.6	2.7	35	3.2	2.4	35				
	YaDeau *et al.* (2016)[29]	0.8	1.6	28	1.8	2.5	27				
Postoperative day 2	Chun *et al.* (2016)[24]	1.0	1.5	50	1.0	1.5	49	0.2 [−0.3, 0.6]	0	0.50	Low
	Rahangdale *et al.* (2014)[27]	4.0	3.0	27	3.0	3.0	24				
	Rosenfeld *et al.* (2016)[28]	3.8	2.2	42	3.7	2.7	36				
	YaDeau *et al.* (2016)[29]	3.3	2.6	25	2.7	2.7	26				
Pain scores on movement (analog scale, 0–10)											
Early postoperative period	YaDeau *et al.* (2016)[29]	0.7	2.1	24	0.9	2.2	27	−0.2 [−1.4, 1.0]	–	0.74	Very low
Postoperative day 1	Rahangdale *et al.* (2014)[27]	0.0	3.0	27	3.5	5.2	24	−1.9 [−4.7, 1.0]	78	0.19	Very low
	YaDeau *et al.* (2016)[29]	1.3	2.1	28	1.9	2.6	27				
Postoperative day 2	Rahangdale *et al.* (2014)[27]	5.0	3.7	27	5.0	3.0	24	0.3 [−0.9, 1.6]	0	0.59	Very low
	YaDeau *et al.* (2016)[29]	4.3	2.8	25	3.7	3.1	26				
Postoperative nausea and vomiting											
	Abdallah *et al.* (2015)[22]	1		25	1		25	0.88 [0.37, 2.12]	0	0.78	Low
	Dawson *et al.* (2016)[25]	0		30	0		30				
	Kawanishi *et al.* (2014)[10]	0		12	1		10				
	Rosenfeld *et al.* (2016)[28]	1		42	0		37				
	YaDeau *et al.* (2016)[29]	5		26	6		27				
Patient satisfaction (at 24 h)											
	Abdallah *et al.* (2015)[22]	9.0	2.7	25	9.0	2.4	25	0 [−0.4, 0.3]	0	0.96	Low
	Rahangdale *et al.* (2014)[27]	10.0	0.0	27	10.0	0.0	23				
	Rosenfeld *et al.* (2016)[28]	7.8	2.7	34	7.9	2.6	28				
	YaDeau *et al.* (2016)[29]	10.0	0.7	28	10.0	0.7	27				

Table 3 Side-effects. CI, confidence interval; *n*, number of events; *N*, total number of participants

Outcome	Reference	Group				Relative risk [95% CI]	I^2 (%)	P-value	Quality of evidence (GRADE)
		Perineural dexamethasone		Systemic dexamethasone					
		n	*N*	*n*	*N*				
Neurological complication									
	Abdallah *et al.* (2015)[22]	0	25	0	25	1.22 [0.65, 2.29]	0	0.53	Moderate
	Chun *et al.* (2016)[24]	1	50	2	49				
	Fredrickson *et al.* (2013)[26] (sciatic nerve block)	9	33	6	33				
	Fredrickson *et al.* (2013)[26] (ankle block)	5	28	4	32				
	Leurcharusmee *et al.* (2016)[11]	0	61	0	62				
	Rahangdale *et al.* (2014)[27]	2	27	2	24				
	YaDeau *et al.* (2016)[29]	1	28	1	27				
Rate of infection									
	Desmet *et al.* (2013)[9]	0	49	0	49	0.29 [0.01, 7.02]	–	0.45	Low
	Leurcharusmee *et al.* (2016)[11]	0	61	0	62				
	Rosenfeld *et al.* (2016)[28]	0	42	1	37				

trial sequential analysis indicated that firm evidence was reached and that perineural was superior to systemic dexamethasone when combined with bupivacaine (Supplementary Fig. S1). With ropivacaine, the finding of equivalence between both routes of administration remains underpowered, and a total of 1124 patients would be needed before suggesting a definitive conclusion (Supplementary Fig. S2). The quality of evidence for our primary outcome was moderate according to the GRADE system. With regard to the funnel plots for our primary outcome (Supplementary Fig. S3), the Duval and Tweedie's trim and fill test revealed the point estimates for the combined studies to be 0.40 (95% CI: 0.15, 0.67), suggesting an absence of publication bias.

There were no significant differences in the other secondary pain outcomes (Table 2) or side-effects (Table 3). Blood glucose concentrations were not increased when dexamethasone was injected systematically compared with the perineural route, but this outcome was reported by only two trials (mean difference −0.8 mmol litre^{-1}; 95% CI: −1.8, 0.3 mmol litre^{-1}; I^2=89%; *P*=0.17; quality of evidence: very low).[9 24]

Discussion

This systematic review and meta-analysis compared the analgesic efficacy and side-effects of perineural *vs* systemic administration of dexamethasone as an adjunct to local anaesthetic for peripheral nerve block in adult patients. Based on 11 randomized controlled trials, including a total of 914 patients, we showed that perineural dexamethasone slightly prolongs duration of analgesia without an impact on other pain-related outcomes and without side-effects. The subgroup analysis demonstrated that the increased duration of analgesia was statistically significant with bupivacaine but not with ropivacaine. A trial sequential analysis revealed that firm evidence was reached for the bupivacaine analysis but that a total of 1124 patients should be accumulated in order to avoid a type II error with ropivacaine. Of note, when ropivacaine, but not bupivacaine, is combined with dexamethasone during *in vitro* studies, crystallization may occur because of the elevated dexamethasone pH and the incompatibility of ropivacaine with alkaline solutions.[30] Perineural injection of this combination should therefore be cautioned, given the marginal clinical advantage over the systemic route and the 'off-label' nature of this route of administration. Systemic dexamethasone administration at moderate doses is therefore a recommended option that provides effective postoperative analgesia, associated with peripheral nerve block,[31] or not.[8]

There are notable limitations to this meta-analysis. First, despite a low risk of bias in the majority of included trials, and with the exception of moderate evidence for the primary outcome, the quality of evidence was low to very low. In addition, variation in the anaesthetic strategies used (i.v. sedation *vs* general anaesthesia *vs* spinal anaesthesia) or in the mixtures of local anaesthetics injected (long-acting *vs* combination of long- and short-acting local anaesthetics, with or without epinephrine) may undermine the generalizability of our conclusions. Consequently, the existing literature would benefit from additional trials using a consistent methodology to provide better definition of the clinical benefit of perineural dexamethasone compared with systemic administration. In particular, study methodologies examining peripheral nerve block without additional general or neuraxial anaesthesia would strengthen conclusions with regard to pain scores and opioid consumption.

Moreover, we were unable to draw any conclusions regarding the use of dexamethasone when combined with short- or intermediate-acting local anaesthetics, because no trials have investigated these mixtures.

In conclusion, there is moderate evidence that perineural dexamethasone combined with bupivacaine but not with ropivacaine slightly prolongs the duration of analgesia when compared with systemic dexamethasone, without an impact on the other secondary pain-related outcomes. The administration of dexamethasone in this setting should be balanced properly with recognition of the off-label indication of perineural administration and with consideration for the possibility of crystallization when combined with ropivacaine.

Authors' contributions

Study design, literature search, statistical analysis, and manuscript preparation: E.A.
Assessment of articles: A.J.-G., K.R.K., E.A.
Data extraction: A.J.-G.
Primary manuscript preparation: M.B.
Manuscript editing: K.R.K.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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Declaration of interest

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