

Does Continuous Peripheral Nerve Block Provide Superior Pain Control to Opioids? A Meta-Analysis

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Although most randomized clinical trials conclude that the addition of continuous peripheral nerve blockade (CPNB) decreases postoperative pain and opioid-related side effects when compared with opioids, studies have included relatively small numbers of patients and the majority failed to show statistical significance during all time periods for reduced pain or side effects. We identified studies primarily by searching Ovid Medline (1966–May 21, 2004) for terms related to postoperative analgesia with CPNB and opioids. Each article from the final search was reviewed and data were extracted from tables, text, or extrapolated from figures as needed. Nineteen articles, enrolling 603 patients, met all inclusion criteria. Inclusion criteria were a clearly defined anesthetic technique (combined general/regional anesthesia, general anesthesia alone, peripheral nerve block), randomized trial, adult patient population (≥ 18 yr old), CPNB (or analgesia) used postoperatively (intrapleural catheters were deemed

not to be classified as a peripheral nerve catheter), and opioids administered for postoperative analgesia in groups not receiving peripheral nerve block. Perineural analgesia provided better postoperative analgesia compared with opioids ($P < 0.001$). This effect was seen for all time periods measured for both mean visual analog scale and maximum visual analog scale at 24 h ($P < 0.001$), 48 h ($P < 0.001$), and 72 h (mean visual analog scale only) ($P < 0.001$) postoperatively. Perineural catheters provided superior analgesia to opioids for all catheter locations and time periods ($P < 0.05$). Nausea/vomiting, sedation, and pruritus all occurred more commonly with opioid analgesia ($P < 0.001$). A reduction in opioid use was noted with perineural analgesia ($P < 0.001$). CPNB analgesia, regardless of catheter location, provided superior postoperative analgesia and fewer opioid-related side effects when compared with opioid analgesia.

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Single injection peripheral nerve blocks are effective for postoperative pain after both upper and lower extremity surgery but are limited by the duration of action of local anesthetics. Continuous peripheral nerve blockade (CPNB) provides the potential benefits of single injection techniques (e.g., decreased pain, respiratory depression, and nausea/vomiting) well into the postoperative period (1,2). Furthermore, the introduction of mechanical and

electronic pumps for the continuous infusion of local anesthetic has allowed patients to receive the benefits of continuous catheters after leaving the hospital (4–7).

Numerous clinical trials have been published examining the efficacy of CPNB for the treatment of postoperative pain after both upper and lower extremity surgery compared with systemic opioids. Although most randomized clinical trials conclude that CPNB decreases postoperative pain and opioid-related side effects when compared with opioids, studies have included a relatively small number of patients and the majority failed to show statistical significance during all time periods for reduced pain or side effects. The objectives of this meta-analysis were to evaluate data from randomized clinical trials (RCTs) to determine 1) efficacy of perineural catheters for reducing postoperative pain, 2)

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Table 1. Categories of Data Analyzed from Each Study

Methodology
Blinding: yes, no
Region of surgery: thoracic, pelvic, abdominal, lower extremity, upper extremity
Peripheral Nerve Catheter Data
Catheter Location: axillary brachial plexus, interscalene brachial plexus, infraclavicular brachial plexus, other brachial plexus, sciatic, femoral, popliteal, paravertebral
Opioid Data
Type: Intravenous, intramuscular, oral, other
Supplemental Analgesic Data
Type: NSAIDs, COX-2, propacetamol, other, combination
VAS Pain Scores (Converted to 0–10 Scale)
Type: mean VAS, maximum VAS
Dosage Use and Technique
Dose: average daily consumption of intravenous and oral opioid given
Major Complications
Death
Stroke
Cardiovascular complications: hypotension, myocardial infarction, myocardial ischemia, arrhythmia
Pulmonary complications: respiratory depression, incidence of desaturation events, pneumonia, other
Renal complications, deep venous thrombosis, pulmonary embolism, transfusion reaction, wound infection, sepsis, other
Minor Complications
Nausea or vomiting
Confusion or delirium
Sedation
Pruritus
Constipation
Urinary retention
Headache
Backache
Motor block/weakness
Patient satisfaction

NSAIDs = nonsteroidal antiinflammatory drugs; COX-2 = cyclooxygenase-2 inhibitor; VAS = visual analog scale.

side effects (nausea/vomiting, sedation, pruritus, motor/sensory block), 3) opioid use, 4) and patient satisfaction compared with opioid analgesia.

Methods

A search of Ovid Medline to identify RCTs comparing CPNB with opioids for the management of postoperative pain from 1966 to the third week of May 2004 with the terms “Pain, postoperative” (13,752 articles) combined with “nerve block” (7399 articles) yielded 788 articles. Limiting this to RCTs, human and all adults (≥ 19 yr) yielded 236 articles. We reviewed each of the abstracts of these articles to determine if there was a description of the use of continuous peripheral nerve catheters for postoperative pain in one of the randomized groups and opioids (either oral or parenteral) in the other randomized group. This search identified 37 articles for further review of the full article to determine if inclusion criteria were met. A review of the author’s files and references from the original search yielded an additional 7 articles for review. Inclusion criteria were a clearly defined anesthetic technique (combined general/regional anesthesia, general anesthesia [GA] alone, peripheral nerve

block), randomized trial, adult patient population (≥ 18 yr old), CPNB (or analgesia) used postoperatively (intrapleural catheters were deemed not to be classified as a peripheral nerve catheter), and opioids administered for postoperative analgesia in groups not receiving peripheral nerve block. Exclusion criteria were no measurement of pain score that could be converted to visual analog scale (VAS) or no comparison of opioid to CPNB. Each article was reviewed by two separate authors with a third author used to resolve any disputes on the inclusion of any articles.

The analyzed items are reported in Table 1. Methodology and results were recorded for each study. Incidence rates for complications were recorded for each study as reported, using the larger number for nausea and vomiting if both were recorded. Although opioids were used in both treatment groups, a classification of opioid or CPNB was made to more easily indicate the two separate groups for the purpose of data analysis.

All recorded data were separated into individual subgroups as described in Table 1. Each VAS pain score was converted based on a 0 to 10 scale (all data measured using a 0–100 VAS scale were converted to a 0 to 10 scale). The standard error of each mean, if not

given, was computed using the given standard deviation and sample size. If a median and interquartile range were reported, these were converted to a mean and standard deviation based on the assumption of a lognormal distribution of the original measure.

Overall, pooled means for each of the measures were computed by taking a sample size-weighted average of the reported (or estimated) means from each study as follows:

$$\bar{X}_{overall} = \frac{\sum_{i=1}^N (n_i \times \bar{X}_i)}{\sum_{i=1}^N n_i},$$

where i indexes a specific study, \bar{X}_i is the study-specific mean, and n_i the study specific sample size. The standard error (SE) of each overall mean was computed by the following formula:

$$se(\bar{X}_{overall}) = \sqrt{\frac{\sum_{i=1}^N (n_i^2 \times se^2(\bar{X}_i))}{\left(\sum_{i=1}^N n_i\right)^2}},$$

where $se(\bar{X}_i)$ is the study specific standard error of the mean. Articles that included data for multiple time points were included in the analysis. For VAS pain scores measured on postoperative days 1 through 3, time values of 24 h, 48 h, and 72 h were respectively assigned to account for differences in data observation among included studies. Opioid consumption other than IV morphine (e.g., oral, IM, or non-morphine IV opioid) was converted to IV morphine equivalents.

Data were extrapolated from graphs as needed using averaged manual measurements by two of the authors. VAS data were weighted by sample size, with the number reported for each article being the number of subjects in each treatment group. The VAS scores for each time period and complication rates were compared between treatment groups. Peripheral nerve catheter analgesia may not provide equivalent analgesia for all catheter locations; therefore, we subdivided the data by catheter location and compared perineural catheters to opioid analgesia. All peripheral catheter local anesthetic infusions were considered equivalent, including those with and without additives (e.g., clonidine). Similarly, all opioids were considered equivalent. Both rest and maximal pain were included in the analysis and were further subdivided based on catheter location.

Complications and side effects reported in the studies were recorded and analyzed, although not every article reported all possible complications. A complication rate of 0% was not assumed if studies failed to report a particular complication.

The level of significance for all tests was set at an α level of 0.05 and variances were not assumed to be equal. A Kolmogorov test showed that the data were normally distributed. One-way analysis of variance tests, weighted by sample size, were used to compare VAS pain scores. A χ^2 analysis was used to analyze complication data between treatment groups. The resulting odds ratio was used to compute number needed to treat (NNT) for complication data. All statistical analyses performed used SPSS 11.5.1. (SPSS Inc., Chicago, IL).

Cost data for local anesthetic infusion pumps were pooled from that reported by Ilfeld et al. (8) for C-Bloc (I-Flow Corporation) \$250, AutoMed 3200 (AceMedical/Algos) \$200, and Accufuser Plus (McKinley Medical) \$260 disposable pumps. The cost for peripheral nerve catheter sets (Arrow International) quoted from a company representative was \$60. Daily costs of morphine and bupivacaine are negligible and accurate data could not be located in the literature to compare with our institutional costs. Cost data for prevention of nausea and vomiting were pooled from recent publications examining a variety of antiemetic strategies (dexamethasone, dolasetron, droperidol, and ondansetron) in Europe and North America (9-12). The average incremental cost for one additional nausea-free and vomiting-free patient was \$40.49 (United States dollars). Cost data for the treatment of pruritus were not found in the literature, although the costs of naloxone and diphenhydramine (two of the commonly used drugs for the treatment of pruritus) are minimal. Cost data for sedation are not available. The actual cost associated with catheter placement was not found in the literature.

At the completion of the data collection and analyses, additional analyses were done to assess the validity of the conclusions that were drawn. An analysis of the file drawer problem was performed to calculate how many subjects that displayed no difference between treatment groups would be needed to invalidate our results.

A funnel plot was also created to indicate any publication bias or other biases in our meta-analysis (English language, citation, and multiple publications) (13). The natural logarithm of relative VAS scores versus precision of the studies was used to create the funnel plot. Relative VAS was calculated by dividing the mean VAS score at 24 h for patients who received a peripheral nerve catheter by the mean VAS score at 24 h for patients who received an opioid for each trial. A relative VAS of <1 signified better analgesia with peripheral nerve catheter techniques. The precision of studies was calculated by using the inverse of the standard deviation of the mean difference between the same VAS scores.

Table 2. Characteristics of Included Studies

Surgical site	
Lower extremity	12 [360] (60%)
Upper extremity	7 [243] (40%)
Location of catheter	
Femoral/lumbar plexus	10 [310] (51%)
Interscalene	6 [213] (35%)
Other	0
Infraclavicular	1 [30] (5%)
Popliteal	2 [50] (8%)
Gender	
Male	[235] (39%)
Female	[258] (43%)
Undefined	[110] (18%)
Location	
Europe	11 (58%)
USA	5 (27%)
Canada	2 (11%)
Asia	1 (5%)

Numbers in brackets represent total number of subjects in trials; numbers outside brackets represent number of trials. A total of 19 studies met inclusion criteria. Three trials totaling 110 patients did not document the breakdown of male/female patients, but did state that no significant differences occurred between the two sexes. Because of rounding, the sum of values expressed in % may not equal 100%.

Results

A total of 19 articles, enrolling 603 patients, were ultimately included in the meta-analysis (Appendix). The characteristics of included studies, which also contain additional data (demographics and study location) recorded but not necessarily quantified for analysis, are shown in Table 2. Included articles came primarily from hospitals in Europe (58%) and North America (38%). More studies involved lower extremity surgery (60%) than upper extremity (40%) with femoral nerve/lumbar plexus the most common catheter location for analgesia (51%) followed by interscalene (35%). Randomized clinical trials comparing perineural catheters with opioids were very limited for other locations (13%). Individual study results were summarized according to upper extremity (Table 3) and lower extremity (Table 4).

Studies in the analysis included 11 with data obtained by intention-to-treat (all enrolled patients were included in the data analysis with no treatment failures), whereas only adequately functioning catheters were included in the remaining 8 studies. A total of 13 patients were withdrawn from the catheter group after randomization and 7 excluded from the opioid group in these 8 studies. Ten additional patients were withdrawn before randomization. Overall, there were 10 catheter placement failures, 11 catheter dislodgements, and 2 patients in the catheter groups excluded for other reasons, whereas 5 patients in the opioid group were withdrawn because of nausea and 2 for failure to complete surveys.

When all studies and observations were combined, perineural analgesia provided better postoperative analgesia compared with opioids ($P < 0.001$). This effect was seen for all time periods measured for both mean VAS (Fig. 1) and maximum VAS (Fig. 2) at 24 h ($P < 0.001$), 48 h ($P < 0.001$), and 72 h (mean VAS only) ($P < 0.001$) postoperatively. When analyzed by catheter location, perineural analgesia provided superior analgesia to opioids ($P < 0.05$) for all locations and time periods (Table 5). The funnel plot demonstrated a relative VAS of less than one for all trials, indicating better analgesia with the CPNB technique. Analysis of the file drawer problem indicates 148 subjects who displayed no difference between treatment groups would be needed to invalidate our results. This indicates that this meta-analysis is not very resistant to the file drawer problem, which is likely attributed to the small overall number of studies with small numbers of study subjects in each.

There were no major complications reported in any of the 19 studies. Twelve of the 19 studies (63%) reported at least one minor complication, with sedation occurring most frequently overall. Motor block was the adverse effect most attributable to peripheral nerve block ($P < 0.001$) whereas nausea/vomiting, sedation, and pruritus all occurred more commonly with opioid analgesia ($P < 0.001$) (Table 6). The NNT was calculated for nausea/vomiting, sedation, and pruritus with 4, 4, and 6 patients receiving perineural analgesia expected to result in one less patient with nausea/vomiting, sedation, and pruritus, respectively, compared with opioid analgesia (Table 6).

Four trials measured patient satisfaction on a VAS and demonstrated a higher composite mean VAS satisfaction for catheters 9.6 ($n = 93$) (95% confidence interval [CI], 9.5–9.7) compared with opioids 7.1 ($n = 90$) (95% CI, 6.9–7.2). Total opioid consumption for both groups for the duration of catheter use was calculated for 12 of 19 studies. Seven studies either failed to document total opioid consumption for both groups or did not provide the data in a manner that could be converted for direct comparison. Total opioid consumption over 48 h was significantly less ($P < 0.001$) with the use of perineural analgesia (20.8 mg morphine, $n = 165$ patients [95% CI 18.5–23.1]) compared with opioid analgesia (54.1 mg morphine, $n = 174$ patients [95% CI, 50.8–57.4]). A limited cost analysis demonstrated an average cost of the catheter kit and disposable infusion pumps to total \$296.67 (US dollars). Based on a NNT of 4, the use of CPNB analgesia would result in an average savings of \$10.12 (US dollars) per patient for the treatment of nausea/vomiting.

Discussion

CPNB has been proposed to offer similar benefits to single injection techniques extending well into the

Table 3. Included Prospective Randomized Controlled Trials Comparing Upper Extremity Continuous Peripheral Nerve Block to Opioid Analgesia

Study	Type of Surgery	Catheter location	N	Infusion in catheter	Opioid used	Both groups received single shot blocks?	Was placebo catheter used?	Summary
Borgeat et al. 1998	Major shoulder surgery	Interscalene	30 C 30 O	0.2% ropivacaine*	Nicomorphine IV PCA (O) No opioid for catheter group	Y	N	SS higher patient satisfaction, decrease in nausea, pruritus, and mean VAS pain with CPNB
Borgeat et al. 1997	Major shoulder surgery	Interscalene	20 C 20 O	0.15% bupivacaine*	Nicomorphine IV PCA (O) No opioid for catheter group	Y	N	SS decrease in vomiting and pruritus and SS decrease mean VAS pain at 12 and 18 h only with CPNB
Borgeat et al. 2000	Major shoulder surgery	Interscalene	18 C 15 O	0.2% ropivacaine*	Nicomorphine IV PCA (O) No opioid for catheter group	Y	N	SS higher patient satisfaction, decreased nausea/vomiting and median VAS pain at 12 and 24 h with CPNB. No SS change in diaphragm excursion
Klein et al. 2000	Open rotator cuff repair	Interscalene	22 C 18 O	0.2% ropivacaine†	Morphine IV PCA (O) (C)	Y	Y	SS decreased mean VAS pain 12-24 h, reduction in morphine consumption with CPNB
Ilfeld et al. 2003	Outpatient shoulder surgery	Interscalene	10 C 10 O	0.2% ropivacaine*	Oxycodone PO (O) (C)	Y	Y	SS decrease in nausea, sedation, pruritus, opioid consumption and average and max. VAS pain with CPNB (24 and 48 h)
Lehtipalo et al. 1999	Acromioplasty	Interscalene	10 C 10 O‡	0.25% bupivacaine†	Morphine IV PCA (O) Morphine IV (C)	N	N	SS decrease in mean VAS pain at 12 and 24 h with CPNB. No difference in side effects or opioid consumption
Ilfeld et al. 2002	Outpatient upper extremity surgery at or below elbow	Infraclavicular	15 C 15 O	0.2% ropivacaine*	Oxycodone PO (O) (C)	Y	Y	SS decrease in nausea, sedation, difficulty sleeping (24 h) and SS decrease average and max. VAS pain and opioid consumption (24 and 48 h) with CPNB

C = catheter group; O = opioid group; PCA = patient-controlled analgesia; SS = statistically significant; VAS = visual analog scale score; CPNB = continuous peripheral nerve block.

* Continuous infusion with bolus available; †Continuous infusion with no bolus; ‡Third group with IM/IV morphine not included in analysis.

postoperative period in both the ambulatory and inpatient settings. We performed a meta-analysis of RCTs and found that, when compared with opioid (parenteral and oral), perineural analgesia with local anesthetic provided significantly better analgesia for postoperative pain. Improvements in analgesia were noted through postoperative day 3. When analyzed according to catheter location, (e.g., interscalene, femoral, popliteal) and type of pain assessment (rest versus maximal pain), CPNB provided superior postoperative analgesia compared with opioids. Perineural analgesia also resulted in fewer minor complications,

including nausea/vomiting, pruritus, and sedation, and improved patient satisfaction.

Single injection peripheral nerve blocks have been demonstrated to provide superior pain control and decreased side effects compared with the use of opioids (14,15). These techniques are limited by the relatively short (12-24 hours) duration of analgesia provided by a single injection nerve block. Although epidural patient-controlled analgesia (PCA) and IV PCA provide adequate analgesia for inpatients with postoperative pain, these techniques are unsuitable for postoperative pain management after

Table 4. Included Prospective Randomized Controlled Trials Comparing Lower Extremity Continuous Peripheral Nerve Block to Opioid Analgesia

Study	Type of surgery	Catheter location	N	Infusion in catheter	Opioid used	Both groups received single shot blocks?	Placebo catheter used?	Summary
Hirst et al. 1996	Total knee arthroplasty	Femoral 3-in-1	11 C 11 O 11 O*	0.125% bupivacaine‡	Morphine IV PCA (O) (C)	Y	Y	SS reduction in nausea with CPNB. No SS decrease in VAS pain or opioid consumption
Ganapathy et al. 1999	Total knee arthroplasty	Femoral 3-in-1	22 C 20 O 20 C†	0.2% bupivacaine‡	Morphine IV PCA (O) (C)	N	Y	No SS decrease in VAS pain or opioid consumption
Serpell et al. 1991	Total knee replacement	Femoral 3-in-1	13 C 16 O	0.5% bupivacaine§	Morphine IV PCA. Morphine IM PRN (O) (C)	N	N	SS decrease in morphine use with catheter. No SS decrease in VAS pain, nausea, or vomiting
Griffith et al. 1996	Femoropopliteal bypass	Femoral	10 C 10 O	0.5% bupivacaine‡	Morphine IV PCA Dihydrocodeine PO >48 h (O) (C)	N	N	SS decrease in VAS pain and opioid requirements at 24, 48 and 72 h within CPNB
Cuignet et al. 2004	Skin graft on burn patients	Femoral	10 C 10 O	0.2% ropivacaine‡	Morphine IV PCA (O) (C)	N	N	SS decrease in opioid requirements and VAS pain at donor site (24 and 48 h) with CPNB. No SS difference in nausea/vomiting or pruritus
Edwards et al. 1992	Total knee replacement	Femoral 3-in-1	19 C 18 O	0.125% bupivacaine‡	Papaveretum IM (O) (C)	N	N	SS decrease in VAS pain at 24 h and opioid requirements with CPNB
Singelyn et al. 1998	Total knee arthroplasty	Femoral 3-in-1	15 C 15 O	0.125% bupivacaine 0.1 µg/ml sufentanil 1 µg/mL clonidine‡	Morphine IV PCA (O) IM Piritramide (C)	N	N	SS decrease in VAS pain rest (24 and 48 h) and max (24 h) and improvement in knee flexion (up to 6 wk) with CPNB. No SS difference in nausea
Chudinov et al. 1999	Hip fractures	Psoas compartment 3-in-1	20 C 20 O	0.25% bupivacaine§	Meperidine IM	N	N	SS decrease in VAS pain (24, 32, and 64 h) and higher satisfaction with CPNB
Capdevila et al. 1999	Major knee surgery	Femoral	20 C 19 O	1% Lidocaine 2 µg/ml clonidine 0.03 mg/ml morphine‡	Morphine IV PCA (O) Morphine SC (C)	N	N	SS decrease VAS pain (24 and 48 h), improved knee flexion (day 5 and discharge) with CPNB
Spansberg et al. 1996	Femoral neck fracture	Femoral 3-in-1	10 C 13 O	0.25% bupivacaine‡	Morphine IV/IM (O) (C)	N	N	No SS difference VAS pain or side effects
Ilfeld et al. 2002	Ambulatory orthopedic surgery below knee in sciatic distribution	Sciatic popliteal fossa	15 C 15 O	0.2% ropivacaine	Oxycodone PO (O) (C)	Y	Y	SS decreased max. and average VAS pain (24, 48 h), decreased awakenings, opioid ingestion, sedation, nausea, pruritus, insomnia (24 and 48 h) with CPNB
White et al. 2003	Ambulatory orthopedic surgery below knee	Sciatic politeal fossa	10 C 10 O	0.25% bupivacaine‡	Morphine IV PCA IV PRN and hydrocodone PO (O) (C)	Y	Y	SS decreased VAS pain (24, 48, 72 h), opioid requirements and improved satisfaction with CPNB. Fewer admission with CPNB

* Third group in trial receiving placebo block also included in analysis; † third group receiving catheter with 0.1% bupivacaine not included in the analysis; ‡ continuous infusion used with no bolus; § bupivacaine administered in intermittent bolus by physician as needed but did not have continuous infusion; || continuous infusion used with bolus available.

N = number of patients in each group; C = catheter group; O = opioid group; IV = intravenous; SS = statistically significant; VAS = visual analog scale; CPNB = continuous peripheral nerve block; PCA = patient-controlled analgesia; IM = intramuscular; SC = subcutaneous.

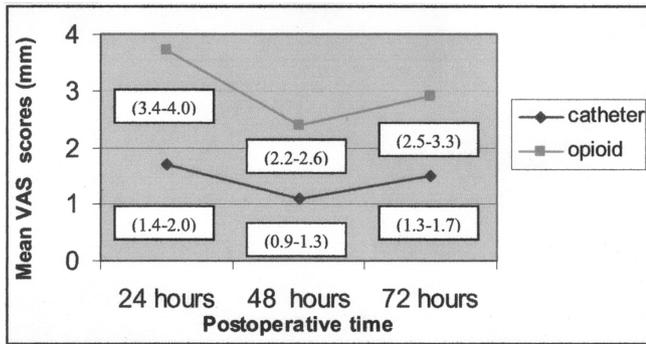


Figure 1. Mean visual analog scale (VAS) pain scores for each treatment group are shown at 24, 48, and 72 h postoperatively. $P < 0.001$ for all days after surgery. Number of patient observations $n = 278, 217,$ and 30 respectively at 24, 48, and 72 h for continuous catheters (e.g., the number of patients with recorded mean VAS pain scores receiving perineural catheters at 24 h from the combined studies was 278). Number of patient observations $n = 286, 227,$ and 30 respectively at 24, 48, and 72 h for opioids. Numbers in parenthesis represent 95% confidence intervals.

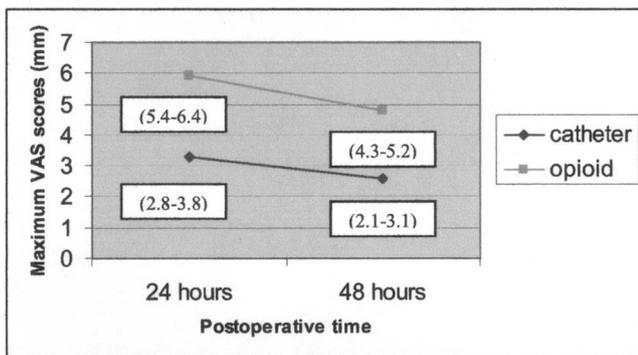


Figure 2. Maximum visual analog scale (VAS) pain scores for each treatment group are shown at 24 and 48 h postoperatively. ($P < 0.001$) Number of patient observations $n = 86$ at 24 and 48 h for continuous catheters (e.g., the number of patients with recorded maximum VAS pain scores receiving perineural catheters at 24 h from the combined studies was 86). Number of patient observations $n = 97$ at 24 and 48 h for opioids. Numbers in parenthesis represent 95% confidence intervals.

outpatient surgical procedures. More than 40% of patients undergoing ambulatory orthopedic procedures experience moderate to severe pain postoperatively (16). There are several reasons that perineural catheters may provide better postoperative analgesia compared with parenteral opioids, including the fact that local anesthetics may attenuate or block painful input into the central nervous system.

The overall incidence of side effects was similar to that noted in reviews of opioid analgesia and single injection peripheral nerve blocks. An expected incidence of 15% for pruritus (17) and 50% for nausea/vomiting (18) are similar to results obtained for our opioid group. The use of CPNB resulted in less side effects (nausea/vomiting, sedation, and pruritus) than opioid analgesia. CPNB do not generally obviate the

need for opioids entirely. The description of opioid use varied significantly in the RCTs, making it difficult to analyze data on reduced opioid consumption; however, a statistically significant decrease in opioid requirements was noted overall with the use of CPNB. The use of opioids in this group may contribute to the sedation, pruritus, and possibly nausea/vomiting that were noted in patients with CPNB analgesia. The group receiving CPNB reported more frequent motor block, although the incidence (31.4%) was less than would be expected for single injection blocks, likely as a result of decreased concentration and smaller volumes of local anesthetic associated with continuous infusions.

Individual RCTs suggest additional benefits including improved patient satisfaction (6,19), better sleep patterns (6,7), improved rehabilitation (1,20), and shorter hospital stays (1,19). Improved patient satisfaction in our study was statistically significant; however, data came from only 4 studies. Further studies to confirm these benefits, in addition to the advantage of decreased pain and decreased opioid-related side effects, may be incorporated into a cost-benefit analysis.

There are several limitations to this study, including those that relate to the general use of a meta-analysis and others which pertain specifically to the issue examined (opioid versus perineural catheter analgesia). The clinical significance of our findings with regard to decreases in mean and maximal VAS may not correlate with the finding of a statistically significant decrease in pain with the use of perineural catheters. Although an approximate 50% reduction in VAS scores was noted at all time periods, a decrease of 2 cm (on a 0–10 cm scale) may not be clinically meaningful (e.g., a 50% reduction from a VAS of 0.5 to 0.25 is likely to be clinically insignificant whereas a decrease in VAS from 10 to 5 is likely to have a large clinical impact). Reductions in VAS scores of the magnitude observed in our study are consistent with values that have been suggested to be a clinically relevant reduction in pain scores (21,22).

Although the data were weighted by trial size, they were not weighted by the quality of the RCTs used nor were they assessed in a blinded fashion. The effects of assessing quality of the RCTs or assessment in a blinded fashion of the estimate of intervention efficacy reported in a meta-analysis are unclear (23). This may play a significant role in the analysis, as several of the trials were of poor quality. Only 11 of the 19 studies were double-blind with catheters placed in both groups. One study did not involve continuous infusion or patient-controlled intermittent bolus of local anesthetic but rather a physician-controlled bolus every 6 hours (24). This study was among those that failed to show a benefit for the use of perineural catheters, and exclusion of

Table 5. Visual Analog Scale Pain Scores by Catheter Location

Location	Mean VAS Scores			Maximum VAS Scores	
	24 h	48 h	72 h	24 h	48 h
Infraclavicular	<i>P</i> < .001	<i>P</i> < .001	–	<i>P</i> < .001	<i>P</i> < .001
Catheter	1.0 (0.3–1.7)	0.6 (0.0–1.3)	–	2.5 (1.7–3.3)	1.5 (0.7–2.3)
Opioid	4.3 (3.1–5.5)	4.0 (2.9–5.1)	–	6.1 (4.8–7.4)	5.1 (3.9–6.3)
Number of studies	1	1	–	1	1
Interscalene	<i>P</i> < .001	<i>P</i> < .001	–	<i>P</i> < .001	<i>P</i> = 0.05
Catheter	1.4 (1.1–1.7)	0.5 (0.3–0.7)	–	3.8 (1.9–5.7)	3.9 (2.0–5.8)
Opioid	3.6 (2.0–4.2)	2.3 (1.9–2.7)	–	8.0 (6.7–9.3)	6.5 (4.5–8.5)
Number of studies	6	6	–	1	1
Femoral/Lumbar					
Plexus	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> < .001
Catheter	2.1 (1.5–2.7)	1.6 (1.2–2.0)	1.5 (1.3–1.7)	3.8 (3.2–4.4)	2.7 (2.3–3.1)
Opioid	4.0 (3.7–4.3)	3.2 (2.9–3.5)	2.7 (2.1–3.3)	5.4 (4.8–6.0)	4.6 (4.1–5.1)
Number of studies	8	8	–	3	3
Sciatic	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> < .001	<i>P</i> < .01
Catheter	0.9 (0.6–1.2)	0.9 (0.6–1.2)	1.6 (1.4–1.8)	1.9 (0.2–3.6)	2.6 (0.9–4.3)
Opioid	4.6 (4.0–5.2)	3.5 (2.9–4.1)	3.2 (2.8–3.6)	7.2 (6.4–8.0)	5.6 (4.4–6.8)
Number of studies	2	2	1	1	1

Mean and maximum visual analog scale (VAS) shown for each treatment group broken down by catheter location site. Number in parenthesis represents 95% confidence intervals.

Table 6. Side Effects

Side effects	Catheter	Opioid	<i>P</i> value	Odds ratio	NNT
Nausea/vomiting	38/182 (20.9%)	95/195 (48.7%)	<0.001	0.28	4
Sedation	12/45 (26.7%)	23/44 (52.3%)	<0.012	0.33	4
Pruritus	11/113 (9.7%)	29/109 (26.6%)	<0.001	0.30	6
Sensory/motor block	22/70 (31.4%)	9/60 (15.0%)	<0.023	0.39	

In results, numerator represents total number of patients noted to have side effect. Denominator represents total number of patients in group from studies that listed complications in the given category. Results weighted by subject number; e.g. 38/182 indicates that studies documenting nausea and vomiting as a side effect had 182 patients randomized to the catheter group and reported 38 of those patients having either nausea or vomiting. Number in parenthesis represents percentage of patients reported to have side effects. NNT = number needed to treat. NNT was not calculated for motor block since it is not a treatable event.

the results would only strengthen the overall conclusion that analgesia is improved with perineural catheters.

We limited our meta-analysis to English language articles. This may introduce publication bias if only positive findings are published primarily in English language journals (25). The effect of excluding non-English language trials on the results of a meta-analysis is equivocal; however, some data suggest that omission of trials published in non-English journals may have little effect on the summary treatment effects and may result in a more conservative estimate of treatment effect (26). Our funnel plot showed little publication bias or other biases because almost all data points were plotted around a relative VAS of <1.0.

In examining the included studies for methodology, there was no consistency in analgesic regimen for either the opioid or peripheral nerve catheter group. The opioid group included a variety of opioids, routes of administration (oral, parenteral), and frequency of

administration, whereas the catheter group included different local anesthetics (bupivacaine and ropivacaine), concentrations (ranging from 0.125% to 0.5%), infusion rates, boluses, and catheter locations. Both groups also commonly had supplemental analgesics administered, including various nonsteroidal anti-inflammatory drugs. This variability in protocol could affect the results of the study, although a trend towards a benefit with perineural analgesia appears to occur regardless of the analgesic regimen. Further studies to determine the ideal local anesthetic, concentration, infusion rate, bolus dose, and additives for each catheter site and surgical location are still needed to determine the optimal use of CPNB.

In summary, we performed a meta-analysis of RCTs to determine the analgesic efficacy of postoperative perineural catheter analgesia compared with opioid. Peripheral nerve catheter analgesia provided a statistically and clinically significant improvement in postoperative pain control compared with opioids and a decrease in opioid-related side effects. This effect was

seen at all time periods studied after surgery, for mean and maximal pain, and with all catheter locations.

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Appendix: Articles Meeting Inclusion Criteria

1. Borgeat A, Perschak H, Bird P, et al. Patient-controlled interscalene analgesia with ropivacaine 0.2% versus patient-controlled IV analgesia after major shoulder surgery: effects on diaphragmatic and respiratory function. *Anesthesiology* 2000;92:102-8.
2. White PF, Issioui T, Skrivanek GD, et al. The use of a continuous popliteal sciatic nerve block after surgery involving the foot and ankle: does it improve the quality of recovery? *Anesth Analg* 2003;97:1303-9.
3. Griffith JP, Whiteley S, Gough MJ. Prospective randomized study of a new method of providing postoperative pain relief following femoropopliteal bypass. *Br J Surg* 1996;83:1735-8.
4. Capdevila X, Barthelet Y, Biboulet P, et al. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. *Anesthesiology* 1999;91:8-15.
5. Cuignet O, Pirson J, Boughrouph J, Duville D. The efficacy of continuous fascia iliaca compartment block for pain management in burn patients undergoing skin grafting procedures. *Anesth Analg* 2004;98:1077-81.
6. Chudinov A, Berkenstadt H, Salai M, et al. Continuous psoas compartment block for anesthesia and perioperative analgesia in patients with hip fractures. *Reg Anesth Pain Med* 1999;24:563-8.
7. Borgeat A, Schappi B, Biasca N, Gerber C. Patient-controlled analgesia after major shoulder surgery: patient-controlled interscalene analgesia versus patient-controlled analgesia. *Anesthesiology* 1997;87:1343-7.
8. Ilfeld BM, Morey TE, Enneking FK. Continuous infraclavicular brachial plexus block for postoperative pain control at home: a randomized, double-blind, placebo-controlled study. *Anesthesiology* 2002;96:1297-304.
9. Ilfeld BM, Morey TE, Wang RD, Enneking FK. Continuous popliteal sciatic nerve block for postoperative pain control at home: a randomized, double-blind, placebo-controlled study. *Anesthesiology* 2002;97:959-65.
10. Ilfeld BM, Morey TE, Wright TW, et al. Continuous interscalene brachial plexus block for postoperative pain control at home: a randomized, double-blind, placebo-controlled study. *Anesth Analg* 2003;96:1089-95.

11. Ganapathy S, Wasserman RA, Watson JT, et al. Modified continuous femoral three-in-one block for postoperative pain after total knee arthroplasty. *Anesth Analg* 1999;89:1197-202.

12. Spansberg NL, Anker-Moller E, Dahl JB, et al. The value of continuous blockade of the lumbar plexus as an adjunct to acetylsalicylic acid for pain relief after surgery for femoral neck fractures. *Eur J Anaesthesiol* 1996;13:410-2.

13. Lehtipalo S, Koskinen LO, Johansson G, et al. Continuous interscalene brachial plexus block for postoperative analgesia following shoulder surgery. *Acta Anaesthesiol Scand* 1999;43:258-64.

14. Borgeat A, Tewes E, Biasca N, Gerber C. Patient-controlled interscalene analgesia with ropivacaine after major shoulder surgery: PCIA vs. PCA. *Br J Anaesth* 1998;81:603-5.

15. Edwards ND, Wright EM. Continuous low-dose 3-in-1 nerve blockade for postoperative pain relief after total knee replacement. *Anesth Analg* 1992;75:265-7.

16. Hirst GC, Lang SA, Dust WN, et al. Femoral nerve block. Single injection versus continuous infusion for total knee arthroplasty. *Reg Anesth* 1996;21:292-7.

17. Serpell MG, Millar FA, Thomson MF. Comparison of lumbar plexus block versus conventional opioid analgesia after total knee replacement. *Anesthesia* 1991;46:275-7.

18. Singelyn FJ, Deyaert M, Joris D, et al. Effects of IV patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. *Anesth Analg* 1998;87:88-92.

19. Klein SM, Grant SA, Greengrass RA, et al. Interscalene brachial plexus block with a continuous catheter insertion system and a disposable infusion pump. *Anesth Analg* 2000;91:1473-8.

References

1. Singelyn FJ, Deyaert M, Joris D, et al. Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. *Anesth Analg* 1998;87:88-92.
2. Capdevila X, Barthelet Y, Biboulet P, et al. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. *Anesthesiology* 1999; 91:8-15.
3. Deleted in proof.
4. Chelly JE, Delaunay L, Williams B, Borghi B. Outpatient lower extremity infusions. *Best Pract Res Clin Anaesthesiol* 2002;16: 311-20.
5. Grant SA, Nielsen KC, Greengrass RA, et al. Continuous peripheral nerve block for ambulatory surgery. *Reg Anesth Pain Med* 2001;26:209-14.

6. Ilfeld BM, Morey TE, Wang RD, Enneking FK. Continuous popliteal sciatic nerve block for postoperative pain control at home: a randomized, double-blinded, placebo-controlled study. *Anesthesiology* 2002;97:959–65.
7. Ilfeld BM, Morey TE, Wright TW, et al. Continuous interscalene brachial plexus block for postoperative pain control at home: a randomized, double-blinded, placebo-controlled study. *Anesth Analg* 2003;96:1089–95.
8. Ilfeld BM, Morey TE, Enneking FK. New portable infusion pumps: real advantages or just more of the same in a different package? *Reg Anesth Pain Med* 2004;29:371–6.
9. Zarate E, Watcha MF, White PF, et al. A comparison of the costs and efficacy of ondansetron versus dolasetron for antiemetic prophylaxis. *Anesth Analg* 2000;90:1352–8.
10. Frighetto L, Loewen PS, Dolman J, Marra CA. Cost-effectiveness of prophylactic dolasetron or droperidol vs rescue therapy in the prevention of PONV in ambulatory gynecologic surgery. *Can J Anaesth* 1999;46:536–43.
11. Hill RP, Lubarsky DA, Phillips-Bute B, et al. Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. *Anesthesiology* 2000;92:958–67.
12. Pueyo FJ, Lopez-Olaondo L, Sanchez-Ledesma MJ, et al. Cost-effectiveness of three combinations of antiemetics in the prevention of postoperative nausea and vomiting. *Br J Anaesth* 2003;91:589–92.
13. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
14. Biboulet P, Morau D, Aubas P, et al. Postoperative analgesia after total-hip arthroplasty: Comparison of intravenous patient-controlled analgesia with morphine and single injection of femoral nerve or psoas compartment block: a prospective, randomized, double-blind study. *Reg Anesth Pain Med* 2004;29:102–9.
15. Hadzic A, Arliss J, Kerimoglu B, et al. A comparison of infraclavicular nerve block versus general anesthesia for hand and wrist day-case surgeries. *Anesthesiology* 2004;101:127–32.
16. Rawal N, Hylander J, Nydahl PA, et al. Survey of postoperative analgesia following ambulatory surgery. *Acta Anaesthesiol Scand* 1997;41:1017–22.
17. Kjellberg F, Tramer MR. Pharmacological control of opioid-induced pruritus: a quantitative systematic review of randomized trials. *Eur J Anaesthesiol* 2001;18:346–57.
18. Tramer MR, Walder B. Efficacy and adverse effects of prophylactic antiemetics during patient-controlled analgesia therapy: a quantitative systematic review. *Anesth Analg* 1999;88:1354–61.
19. White PF, Issioui T, Skrivaneck GD, et al. The use of a continuous popliteal sciatic nerve block after surgery involving the foot and ankle: does it improve the quality of recovery? *Anesth Analg* 2003;97:1303–9.
20. Chelly JE, Greger J, Gebhard R, et al. Continuous femoral blocks improve recovery and outcome of patients undergoing total knee arthroplasty. *J Arthroplasty* 2001;16:436–45.
21. Farrar JT, Portenoy RK, Berlin JA, et al. Defining the clinically important difference in pain outcome measures. *Pain* 2000;88:287–94.
22. Farrar JT, Berlin JA, Strom BL. Clinically important changes in acute pain outcome measures: a validation study. *J Pain Symptom Manage* 2003;25:406–11.
23. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996;17:1–12.
24. Serpell MG, Millar FA, Thomson MF. Comparison of lumbar plexus block versus conventional opioid analgesia after total knee replacement. *Anaesthesia* 1991;46:275–7.
25. Moher D, Pham B, Lawson ML, Klassen TP. The inclusion of reports of randomised trials published in languages other than English in systematic reviews. *Health Technol Assess* 2003;7:1–90.
26. Juni P, Holenstein F, Sterne J, et al. Direction and impact of language bias in meta-analyses of controlled trials: empirical study. *Int J Epidemiol* 2002;31:115–23.