

REVIEW

Evidence of peripheral nerve blocks for cancer-related pain: a systematic review

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ABSTRACT

The European Association for Palliative Care has initiated a comprehensive program to achieve an over-all review of the evidence of multiple cancer pain management strategies in order to extend the current guideline for treatment of cancer pain. The present systematic review analyzed the existing evidence of analgesic efficacy for peripheral nerve blocks in adult patients with cancer. A search strategy was elaborated with words related to cancer, pain, peripheral nerve and block. The search was performed in PubMed, EMBASE, and Cochrane for the period until February 2014. The number of abstracts retrieved was 155. No controlled studies were identified. Sixteen papers presented a total of 79 cases. The blocks applied were paravertebral blocks (10 cases), blocks in the head region (2 cases), plexus blocks (13 cases), intercostal blocks (43 cases) and others (11 cases). In general, most cases reported good pain relief and no side effects. The use of peripheral blocks is based upon anecdotal evidence. However, this review only demonstrates the lack of studies, which does not equal a lack of effectiveness.

(*Minerva Anestesiologica* 2015;81:789-93)

Key words: Nerve block - Pain - Neoplasms - Palliative care.

The majority of patients with chronic cancer pain obtain satisfactory pain relief from treatment according to current recommendations such as those by published the World Health Organization and the European Association for Palliative Care (EAPC).^{1, 2} These recommendations consist of the use of non-opioid analgesics, opioids and coanalgesics^{1, 2} and spinal opioids.² However, some patients do not achieve adequate pain relief with systemic administered analgesics.³ These patients may obtain pain relief from other pain therapies such as intrathecal or epidural local anesthetics and/or opioids, radiotherapy

or surgical interventions.^{4, 5} Another intuitively logical approach is to block peripheral nerves with local anesthetics and thereby block the signaling of pain stimuli from the tumor to the central nervous systems.⁴ However, peripheral blocks are in clinical practice infrequently used to relieve cancer pain. The lack of use may be caused by limited evidence. Therefore, we analyzed the published evidence regarding analgesic efficacy of peripheral nerve blocks for cancer pain. This work is a part of an EAPC initiative to achieve an over-all review of the evidence of multiple cancer pain management strategies in order to extend the former guideline, which only comprised opioid use.¹

*On behalf of the European Palliative Care Research Collaborative (EPCRC).

Methods

Search strategy

The search strategy was based on the PICO framework and comprised MeSH terms and text words (Figure 1). The searches were performed in the databases PubMed, Embase and Cochrane Central Register of Controlled Trials and retrieved all information available up to 3 February 2014. Limits were set up to restrict the search to humans and English language. The searches were run individually in each database and the retrieved abstracts were transferred to EndNote. Duplicated abstracts were excluded. A final list of the relevant abstracts was generated and each abstract was checked and selected according to the inclusion and exclusion criteria.

Abstracts that matched the inclusion criteria and those with no clear information to be considered for exclusion were selected for full reading. The inclusion criteria are: 1) studies which

have been conducted to investigate the effects of peripheral nerve blocks; 2) adult patients with chronic pain due to cancer; 3) data on the relevant outcomes, pain intensity; 4) written in English language. The exclusion criteria were: 1) double publications; 2) postoperative pain management or other irrelevant therapies; 3) studies with mixed populations not providing separate results for cancer patients; 4) trials without assessment of pain; 5) experimental studies.

The papers were grouped according to the type of intervention.

Results

The number of abstracts screened was 155; 114 papers were unrelated, ten papers were double-publications, 15 papers were reviews, and 16 papers presented case stories or case series. No papers presented a randomised controlled trial (RCT). The sixteen papers reporting cases pre-

Strategy	
Patients	cancer or neoplasm or tumor or tumour or oncol* or carcinoma* or malignan*
	AND
Patients	pain
	AND
Intervention	peripheral nerve OR nerve, peripheral OR nerves, peripheral
	AND
Intervention	block, nerve OR blocks, nerve OR nerve blocks OR nerve blockade OR blockade, nerve OR blockades, nerve OR nerve blockades OR chemical neurolysis OR chemical neurolyses OR neurolyses, chemical OR neurolysis, chemical OR chemodenervation OR chemodenervations OR deafferentation
	NOT
Title/Abstract	procedural pain OR postoperative pain OR perioperative pain OR non-malignan* pain OR noncancer pain OR non-cancer pain OR nonmalignan* OR vertebroplast* OR celiac plexus OR plexus, celiac OR celiac plexus OR plexus, celiac or plexus coeliacus OR coeliacus, plexus OR solar plexus OR plexus, solar OR hypogastric plexus OR plexus, hypogastric OR pelvic plexus OR plexus, pelvic OR child* OR pediatric* OR paediatric*

Figure 1.—Search strategy.

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sented a total of 79 cases (Table I). The blocks applied were paravertebral blocks (N.=10), blocks in the head region (N.=2), plexus blocks (N.=13), intercostal blocks (N.=43) and others (N.=11). The local anesthetics used were bupivacaine (N.=37), ropivacaine (N.=3), levobupivacaine (N.=1) and butamben (N.=25). Thirty-five patients received neurolytic blocks, often after a trial period with local anesthetics, with either phenol (N.=33) or alcohol (N.=2). In general, most cases reported good pain relief and no

side effects. The durations of efficacy were usually in the range of several weeks, often until death.

Discussion

This systematic review failed to identify any RCT investigating the efficacy of peripheral nerve blocks for cancer pain. Therefore, obviously, no formal analyses were performed and no evidence based conclusion can be made. However, several papers reported the successful use

TABLE I.—*Clinical series.*

Authors, year	Intervention	Number of cases	Cancer	Outcome	Complications
Paravertebral blocks					
Antila and Kirvela ⁶	Neurolytic paravertebral block with phenol	7	Thoracic cancer pain	Limited efficacy	None reported
Esch <i>et al.</i> ⁷	Continuous cervical paravertebral block with ropivacaine	2	Pancoast tumor and lung cancer with shoulder metastasis	Pain relief for 40 days and 44 days	Catheter displacement
Pelaez <i>et al.</i> ⁸	Cervical paravertebral block with levobupivacaine	1	Pancoast tumor	Pain relief for 7-8 weeks	None reported
Blocks in the head regions					
Bedder and Lindsay ⁹	Glossopharyngeal nerve block with alcohol	1	Carcinoma of the tongue	Pain relief for six weeks	None reported
Kohase <i>et al.</i> ¹⁰	Mandibular nerve block with bupivacaine and neurolysis with alcohol	1	Carcinoma of the tongue	Pain relief for 2 months	None reported
Plexus blocks					
Buchanan <i>et al.</i> ¹¹	Continuous interscalene block with ropivacaine	1	Renal cancer with shoulder metastasis	Pain relief for 4 months	Catheter displacement
Neill ¹²	Brachial plexus block with bupivacaine and neurolysis with phenol	1	Metastasis to the humerus	Pain relief. Duration not reported	None reported
Okell and Brooks ¹³	Interscalene plexus block with bupivacaine	1	Breast cancer	Pain relief for 10 weeks	None reported
Vranken <i>et al.</i> ¹⁴	Continuous plexus block with bupivacaine	6	Pancoast tumor	Pain relief for 4-31 weeks	None reported
Sato <i>et al.</i> ¹⁵	Continuous interscalene block with bupivacaine	1	Pancoast tumor	Pain relief for 2 weeks	None reported
Vranken <i>et al.</i> ¹⁶	Continuous brachial plexus block with bupivacaine	2	Tumor infiltration of brachial plexus and metastasis to the humerus	Pain relief for 2 and 6 weeks	None reported
Other blocks					
Kaki and Lewis ¹⁷	Inguinal paravascular block with bupivacaine and neurolysis with phenol.	1	Lung cancer with metastasis to the acetabulum	Pain relief three days with bupivacaine and 4 days with neurolysis before discharge.	None reported
Khor and Ditton ¹⁸	Continuous femoral nerve blockade with bupivacaine	1	Renal cancer with metastasis to the hip	Pain relief for 7 weeks	None reported
Vranken <i>et al.</i> ¹⁹	Continuous sacral root blockade with bupivacaine	1	Ovarian cancer with nerve root compression	Pain relief for 5 weeks	None reported
Wong <i>et al.</i> ²⁰	Intercostal block with bupivacaine followed by neurolysis with phenol	25	Various cancers with rib metastasis	20 patients local pain control for 5-158 days	None reported
Shulman <i>et al.</i> ²¹	Various nerve (18 intercostal nerve) blocks with butamben	25	Various cancers	68% of patients pain relief. Median pain relief 12.8 weeks	4 patients toxic effect during injections

of peripheral nerve block in selected cases with cancer pain (Table I). The most frequently applied blocks were paravertebral blocks, brachial plexus blocks and intercostal nerve blocks.

The lack of controlled studies may have several causes. First, patients with pain not responsive to other treatment modalities are few and it is therefore difficult to recruit the number of patients needed for a controlled study. Second, as illustrated in the identified cases such treatment has to be highly individualized. This limits the feasibility of applying a standardized treatment protocol to an intervention group in a controlled study. Third, the medical management of such patients is often done in a clinical environment with several barriers that preclude the inclusion of patients in a clinical study.²²

This review highlights that the use of peripheral blocks for cancer pain is based upon anecdotal evidence. The low number of reports argues that there is a selection bias for which cases that is reported. A selection bias may be caused by several factors. First, treatment successes and cases with advanced technical procedures are more likely to be reported. Second, clinicians may often believe a peripheral block is a routine procedure, which not merit a case report. Third, busy clinicians will often not prioritize the effort involved in publishing.

Despite the limited formal evidence, the reported cases illustrate that peripheral nerve blocks can give pain relief to patients with intractable or very difficult treatable cancer pain. For localized pain peripheral nerve block could also lower the needed dose of conventional analgesics and, thereby, reduce the intensity of drug induced adverse effects. This raises the question; perhaps the use of peripheral nerve block is underused? This position is supported by that for surgical procedures innovation in anesthetic techniques, including the use of ultrasound to identify nerves, have expanded the use of peripheral nerve blocks.²³ To introduce the new expertise developed in orthopedic anesthesia to cancer pain therapy could be beneficial. However, the introduction of peripheral blocks in routine cancer pain should be done guided by results from controlled trials assessing efficacy, adverse effects and duration of analgesia.

Conclusions

The use of peripheral blocks for cancer pain is based upon anecdotal evidence. However, the case reports demonstrate the potential for peripheral block to give pain relief to selected cancer pain patients.

Key messages

- Peripheral blocks for cancer pain can be administered to several nerves of which intercostal, paravertebral and plexus brachialis blocks are most frequent reported.
- Peripheral blocks can give good pain relief for cancer pain
- Peripheral blocks can be administered continuously for at least several weeks
- There are no randomised trials investigating the use of peripheral blocks for cancer pain. Current knowledge is based upon case stories or case series.

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Acknowledgments.—This systematic review is a contribution to the European Association for Palliative Care (EAPC) guidelines for cancer pain management, a project of EAPC Research Network led by Augusto Caraceni and Alessandra Pigni.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Received on September 18, 2014. - Accepted for publication on November 5, 2014. - Epub ahead of print on November 11, 2014.

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