ORIGINAL ARTICLE

Intercostal nerve blockade for cancer pain: effectiveness and selection of patients

CME

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Objectives To review treatment results of intercostal nerve blockade at our centre and those reported in the literature, and to determine which patients benefit most from this procedure.

Design Retrospective study.

Setting Regional palliative care centre in a regional hospital in Hong Kong.

Patients Oncology patients who had intercostal nerve blockade at Tuen Mun Hospital from 1995 to 2005 were divided into three groups: (1) those who appeared not to tolerate opioids; (2) those deemed to have inadequate pain control, despite high doses of analgesics; and (3) those referred to avoid early use of high-dose opioids and tolerance.

Main outcome measures The effectiveness and complications of intercostal nerve blockade, and the extent of benefit derived from intercostal nerve blockade in different patient groups.

Results This study found that 80% of the 25 patients noted optimal local pain control and 56% experienced reduction in analgesic use after intercostal nerve blockade. About 32% did not notice recurrence of the targeted pain till the end of their lives. None of the patients developed pneumothorax. Most benefit from intercostal nerve blocks were derived by group 2 patients, 90% of whom obtained optimal local pain control (P=0.23) and enjoyed a significant reduction in analgesics use (P=0.019), and in 40% their target pain was controlled till the end of life. Only about one third of group 3 patients had subsequent reduction in use of analgesics, mainly because they had co-existing pain other than at the target selected for treatment. Half (50%) of group 1 patients achieved optimal pain control.

Conclusion Our treatment results from intercostal nerve blockade are comparable to those reported in the literature. The procedure is safe if closely monitored. Good selection of cases is important for optimising the therapeutic gain. The largest benefit is obtained in patients who have inadequate pain control after high-dose morphine.

Key words
Anesthesia, local; Intercostal nerves; Nerve block; Pain clinics; Palliative care

Hong Kong Med J 2007;13:266-70

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Introduction

Pain is a frequently encountered symptom that affects the quality of life of patients with advanced cancer.[1] According to the World Health Organization guideline, in most situations, pain can be dealt with through analgesics.[2] Nevertheless, a small proportion of patients do not achieve adequate pain control, which can be due to the development of tolerance (particularly in association with neuropathic pain), or analgesic-related adverse effects. In which case, other interventional means of pain management should be considered.[3] Such techniques include local anaesthetic neural blockade, neurolytic blockade (using chemical such as phenol, or physical means such as radiofrequency neurolysis, cryoneurolysis, or surgical ablation), and neuraxial administration of pharmacological agents (such as epidural administration of morphine). The targets for neurolytic block include the peripheral nerves or ganglia (eg intercostal nerves, paravertebral nerve roots, the brachial plexus and nerve roots), the sympathetic nervous system (eg the coeliac and superior hypogastric plexuses, the impar and stellate ganglia), or the central spinal pathway (eg via cordotomy).[3-5]

Neurolytic intercostal nerve blockade (ICB) is frequently used for the management of intractable cancer pain, as motor blockade is not a major concern. It may be considered for patients with: (a) inadequate pain control after optimal use of systemic analgesics, (b) intolerance to opioid side-effects, and (c) a reason to pre-empt the development of opioid tolerance.[4] Although this procedure is quite popular, reports of its effectiveness for cancer patients with respect to success rate for pain control, duration of response, and the recurrence rate, are surprisingly limited.[5] According to the available literature, almost all patients experience immediate pain relief after neural blockade, but usually the response is not long-lasting (mean duration of 3 weeks).[6] In addition, in up to 30% of patients neuritis or deafferentation neuralgia is liable to develop after weeks or months.[4] It has therefore been proposed that such procedures should be limited to patients with a short life expectancy only.[4]

Since 1995, our hospital has set up a pain management clinic—staffed by one consultant anaesthetist and one clinical oncologist, and is dedicated to the treatment of cancer patients with inadequate pain control. Interventional pain therapies are considered for appropriate cases. The most common procedures include: ICB, coeliac ganglion blocks, and epidural morphine infusion. In this paper, we describe the results with ICBs performed at our centre, and review those reported in the literature.

施行肋間神經阻滯以舒緩癌痛：鎮痛效果和接受手術的病者挑選

目的 檢討文獻紀錄和本院施行肋間神經阻滯的治療效果，以及確定哪一類病人能從中得益最大。

設計 回顧研究。

安排 香港一所分區醫院的地區性舒緩治療中心。

患者 1995至2005年在屯門醫院接受肋間神經阻滯術的腫瘤病人。研究把患者分為三組：第一組是無法忍受阿片類藥物；第二組已用大劑量鎮痛劑，但仍不足以控制疼痛；第三組則避免過早使用大劑量阿片類藥物，從而避免產生耐受性。

主要結果測量 肋間神經阻滯的療效和併發症，以及不同組別的病人從肋間神經阻滯得益的程度。

結果 研究結果顯示，接受肋間神經阻滯術後，25名病人中，有八成達致最好的局部鎮痛效果，56%的鎮痛劑用量減少，約32%的病人藉肋間神經阻滯控制的疼痛直至生命終結並無復發。沒有病人出現氣胸。第二組病人從肋間神經阻滯術得益最大，當中九成病人達致最好的局部鎮痛效果（P=0.23），鎮痛劑用量顯著減少（P=0.019），四成病人藉肋間神經阻滯控制的疼痛直至生命終結不見復發。第三組病者中，有三分之一持續減少鎮痛劑用量，主要是因為這組病人中有部分除了要舒緩的疼痛外還有其他痛症。第一組病者中，則有一半人達致最好的鎮痛效果。

結論 本院施行肋間神經阻滯的治療效果與文獻紀錄的相若。在嚴密監控下，這種手術是安全的。要這種手術發揮最好的療效，仔細選擇接受手術的病人十分重要。研究發現，給使用大劑量嗎啡後而抗痛效果不夠理想的病人施行肋間神經阻滯的效果是最好的。

Methods

From 1995 to 2005, the Pain Management Team of the Tuen Mun Hospital evaluated 37 patients who had suboptimally controlled cancer pain with a view to considering interventional pain therapy. In all, 26 of the patients received ICB. The hospital record of one of them could not be traced. Thus, the remaining 25 constituted the patients for the purpose of this audit. Both the hospital in-patient notes and the out-patient follow-up notes were traced for review.

The ICBs were performed in the operating theatre of the Department of Clinical Oncology, under fluoroscopic guidance. The intercostal nerve was approached proximal to the angle of the rib. It could be very close to the neck for the upper ribs as the scapula makes a more lateral approach impossible. A small quantity of contrast medium was injected to confirm appropriate location. A diagnostic block with 0.5% bupivicaine was performed at the level where the rib secondary was present. If adequate pain relief could be obtained, a neurolytic block was performed at that level in a later session. One level above and below would also be blocked if the analgesia was unsatisfactory after single level blockade. If analgesia then became satisfactory, all three levels would receive neurolytic blockade. Neurolytic blockade using 10% phenol dissolved in contrast medium was performed subsequently, allowing gaps of several days between sessions.

Complications recorded after each of the procedures were charted. The effectiveness of pain control was determined as: (a) the percentage of patients with decrease in pain at the target site (a subjective decrease of more than 50% after the entire procedures was defined as a response); (b) any subsequent decrease in the use of analgesics (in terms of dosage or medication type); (c) the response duration (days between last blockade and recurrence of pain over the target site); and (d) the proportion of patients who continued to have good local pain control till the end of their lives.

In this study, we also tried to determine which type of patients gained the greatest benefit from ICB, based on effectiveness, complications, and whether the aim of selecting that patient was or was not fulfilled. The patients were divided into three groups according to the initial indication: group 1—those experiencing intolerable opioid side-effects; group

TABLE 1. Characteristics of the 25 audited patients treated by intercostal nerve blockade

Characteristic	All patients, n=25	Group 1, n=4	Group 2, n=10	Group 3, n=11	P value
Sex (M:F)	16:9	2:2	7:3	7:4	0.78
Median age (range) [years]	55 (24-75)	49 (36-65)	60 (24-70)	49 (38-62)	0.18
No. having prior palliative chemotherapy	8	2 (50%)	3 (30%)	3 (27%)	0.69
No. having prior local palliative radiotherapy to target painful site	20	2 (50%)	10 (100%)	8 (73%)	0.078
No. of prior analgesic users					
Morphine	17	0	10 (100%)	7 (64%)	0.001
Methadone	7	1 (25%)	3 (30%)	3 (27%)	0.98
Dologesic	6	2 (50%)	0	4 (36%)	0.062
Non-steroidal anti-inflammatory drug	12	2 (50%)	6 (60%)	4 (36%)	0.55
Amitriptyline	12	3 (75%)	3 (30%)	6 (55%)	0.26
Anticonvulsant	6	1 (25%)	1 (10%)	4 (36%)	0.37
Gabapentin	2	0	2 (20%)	0	0.19
Ketamine	1	0	1 (10%)	0	0.45
Co-existing pain beyond the target site	14	2 (50%)	5 (50%)	7 (64%)	0.79
Severe symptoms other than pain	8	1 (25%)	5 (50%)	2 (18%)	0.28

2—those with inadequate pain control despite high analgesic doses (≥180 mg/day of morphine or an equivalent dosage of an alternative); and group 3—those referred for early interventional pain therapy to avoid early use of opioids or dose escalation, that could lead to the development of tolerance.

Data were analysed using the Statistical Package for the Social Sciences (Windows version 9.0; SPSS Inc, Chicago [IL], US). Categorical data were compared by Chi squared tests. Survival rates were compared using the log rank test.

Results

All the patients had rib metastases, with or without pathological fracture; most had some element of both neuropathic and somatic pain. Twelve and thirteen patients respectively suffered from right-sided and left-sided chest wall pain. The characteristics of all 25 patients in each of the three predefined groups are summarised in Table 1. The source of these patients' primary malignancy and their corresponding histologies are summarised in Table 2.

TABLE 2. Source of primary malignancy site and corresponding histologies

Primary malignancy site (with histology underneath)	No. of patients
Lung	13
Adenocarcinoma	6
Squamous cell carcinoma	2
Non–small cell carcinoma	4
Unknown	1
Cervix	
Squamous cell carcinoma	3
Nasopharynx	
Undifferentiated carcinoma	1
Breast	
Invasive ductal carcinoma	1
Thyroid	
Anaplastic carcinoma	1
Buttock	
Malignant haemangiopericytoma	1
Thymus	
Squamous cell carcinoma	1
Oesophagus	
Squamous cell carcinoma	1
Ampulla of Vater	
Adenocarcinoma	1
Unknown	
Adenocarcinoma	2

Overall response rate of optimal local pain control

Only one patient did not notice immediate pain relief after diagnostic nerve block. In the remaining 24 (96%) who achieved immediate pain relief after the initial diagnostic block with 0.5% bupivicaine, subsequent neurolytic blocks were carried out with 10% phenol; once in 11 (46%) of them, twice in 4 (17%), thrice in 2 (8%), and not at all in 7 (29%). Among these 24 patients, 20 were classified as having optimal pain control at the target site on completion of the procedure. Thus, the calculated overall optimal local-pain-control response

TABLE 3. Treatment results in three groups of patients*

Treatment results	Group 1, n=4	Group 2, n=10	Group 3, n=11	P value
Median time gap between onset of target pain and first ICB† (range) [weeks]	24 (2-57)	19 (5-104)	16 (3-52)	-
Optimal local pain control	2 (50%)	9 (90%)	9 (82%)	0.23
Reduction in use of analgesics	1 (25%)	9 (90%)	4 (36%)	0.019
Recurrence of pain at target site	1 (50%)	5 (55%)	6 (66%)	0.59
Median time of onset of recurrence of local pain control (range) [days]	120 (120-120)	12 (5-35)	40 (10-90)	0.17
With local pain controlled till the end of their lives	1 (25%)	4 (40%)	3 (27%)	0.49
Median survival after ICB (range) [days]	300 (158-1065)	66 (8-210)	70 (5-385)	0.063

* Results are shown in No. (%), unless otherwise stated
† ICB denotes intercostal nerve blockade

rate for the whole group was 80%.

Successful reduction in the rate of analgesia use

Only 14 of these 20 responders experienced subsequent reduction in the use of analgesics, giving an overall rate of 56%. Presence of pain other than at the target site was the only reason why analgesic reduction did not ensue in six of the cases.

Duration of response and subsequent life expectancies

Of the 20 patients who had optimal local pain control, 12 (60%) developed subsequent pain recurrence at the same target site. The median duration of local pain control was 25 days (range, 5-158 days). Altogether eight (32%) patients did not experience target pain up to the end of their lives, their median survival time after ICB was relatively short (40 days; range, 5-158 days); three having median survival times of less than 10 days. After ICB, the median overall survival time for the whole group was 90 days (range, 5-1065 days).

Complications

No pneumothorax, wound complication, pain with neuropathic features, or other significant complication was recorded in the hospital records. The treatment results of the patients in the three predefined patient groups are summarised in Table 3.

Group 1: patients who could not tolerate morphine

These four patients could not tolerate even a very small dose of morphine (P=0.01) [Table 1]. Opioid rotation was considered for three of them (one switched to methadone, the other two to dologesic), but their pain control remained suboptimal. Only two achieved optimal local pain control after ICB. Another patient had co-existing pain other than at the target site. Analgesics were successfully reduced in only 25% of these patients. In this group, non-opioids (anti-depressants and anticonvulsants) had not been used 'optimally' before ICB.

Group 2: patients with inadequate pain control on high-dose analgesics

All 10 patients were receiving prior high doses of oral morphine, as well as proportionally greater use of non-opioids (gabapentin, ketamine). The results of ICB were the most encouraging in this group; 90% enjoyed optimal local pain control (P=0.23) and a reduction in analgesic use (P=0.019). Five had recurrence of pain at the local site after a median interval of 12 days. The median overall survival of this group was 66 days, 40% of whom had their target pain controlled till the end of life.

Group 3: early use of intercostal nerve blockade to minimise the chance of developing morphine tolerance

Around 60% of these patients had been taking low-dose morphine. Intercostal nerve blockade was initiated early in anticipation of tolerance. In all, 82% obtained optimal local pain control, though analgesic dosages were successfully reduced in only 36%. Most had co-existing pain at sites other than the target. Six of them developed recurrence of pain at the original site, after a median interval of 40 days, and 27% of them had their target pain controlled till the end of life. The recurrence rate of target pain was greater than that in group 2, possibly related to longer overall median survival (70 days; range, 5-385 days).

Discussion

Interventional pain therapy offers a specialised anaesthetic technique for managing cancer pain.[3] However, the indications and timing for these procedures remain controversial. Bruera and Kim[7] argued that such intervention procedures are 'complex and expensive', and their utility is not currently supported by large randomised controlled trials. Other authors criticised these comments, arguing that neurolytic blocks could provide prolonged pain relief and avoid many of the usual opioid-related adverse effects.[8,9] A review by Kim[3] concluded that such procedures 'can play a major role in palliation of intractable pain conditions' and that appropriate selection of patients is critical for

successful outcomes. The duration of analgesic effect from neurolytic blockade directed at peripheral nerves is not long-lasting and up to 30% of patients may experience neuritic pain.[4] Doyle[6] reported a mean duration of total pain relief to be 3 weeks only. Green et al[10] performed intercostal cryoneurolysis in patients with non-malignant intercostal neuralgia, 25% of whom reported significant and sustained pain relief of up to 6 months. Pneumothorax is one of the possible complications, but is very rare.[5]

In this audit, 80% of patients noted optimal local pain control. A total of 32% of patients enjoyed target site pain relief at the end of their lives; the mean duration of local pain control was 25 days. Both figures are consistent with those reported in the literature.[6,10] However, the true rate of pain recurrence at the target site also depends on the life expectancy of the studied group. The median overall survival after ICB of our entire patient cohort was 90 days. Among the eight patients who did not experience recurrence of target site pain, three survived less than 10 days. In order to minimise the number of patients developing late recurrences of pain associated with longer follow-up, it has been argued that only those with short life expectancy should be selected.[4] None of our 25 patients developed pneumothorax, confirming that the procedure is relatively safe.

According to our study, group 2 patients (ie those with inadequate pain control despite high-dose morphine) gained most benefit from ICB; significantly 90% obtained optimal local pain control and enjoyed reduced analgesic usage. Moreover, 40% of them had their target pain controlled till the end of their lives. Notably, prior to ICB these patients had been tried on high doses of morphine and many other analgesics. The median survival time of this group of patients after ICB was also relatively short (66 days), which may account for the low recurrence rate. Intervention pain therapy should be considered for these types of patients.

Intercostal nerve blockade did not serve the initial purpose well (ie reduce development of opioid tolerance) for group 3 patients. Only about one third of them subsequently reduced their use of analgesics; most had co-existing pain other than at the target site. It is therefore recommended that when ICB is applied for patients early in the course of pain therapy, close monitoring of analgesics use after ICB is still crucial for those with co-existing pain at sites other than chest wall.

Other non-invasive treatment options should be considered for patients who cannot tolerate usual treatment with morphine due to side-effects (group 1). These include: adjustment of dose, dosing schedule and route of administration, opioid rotation, addition of adjuvant analgesia, psychosocial interventions, and other means of palliation (eg radiotherapy or chemotherapy). According to our experience, the effectiveness of ICB for this group of patients was not very satisfactory; only 50% achieved optimal pain control. In addition, the overall median survival (300 days) was the longest among our three groups. A high recurrence rate after ICB was therefore to be expected. One of the four patients had switched to methadone and another two to dologesic, but their pain control was still suboptimal. Usage of other agents (such as gabapentin, anti-depressants, and anticonvulsants) in this group of patients was evidently low.

Conclusion

This study showed that our treatment results following ICB are comparable with those reported in the literature, and that the procedure is safe if appropriately performed. The greatest benefit accrued to patients who have inadequate pain control after high-dose morphine. As ICB is an invasive procedure, recurrence of pain may occur due to neuritis or deafferentation neuralgia. Appropriate selection of cases is important for achieving optimal results. If ICB is considered for patients during the early phases of pain therapy, continuous monitoring of analgesic use is still crucial, especially for those with co-existing pain at sites other than the chest wall.

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