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The Neurolytic Celiac Plexus Block Efficacy in Patients with Severe, Chronic Upper-abdominal Cancer Pain

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Objectives: To study of the efficacy of the neurolytic celiac plexus block (NCPB) in patients with severe, chronic upper-abdominal cancer pain in reducing pain score, morphine consumption, side effects of morphine, and improving performance score. **Methods:** Fifty-six patients with abdominal cancer who suffered chronic, severe pain were enrolled in this study. All patients received a morphine dose of <100 mg/day. Patients were divided into 2 groups: group I included patients who received NCPB, group II included patients who used morphine continuously. The patients' pain score, performance status, morphine consumption and morphine-related side effects were recorded at regular two-week intervals with a final follow-up at eight weeks. **Results:** After the NCPB administration, the pain score, morphine consumption and morphine-related side effects decreased in group I more than in group II ($p < 0.0001$). The physical performance improved in group I more than group II ($p < 0.001$). In group II, pain scores were consistently elevated and patients continued to receive high doses of opioids with inadequate pain control ($p < 0.001$). In group I, morphine-related side effects (nausea, anorexia, and constipation) had lower grades than in group II ($p < 0.001$). **Conclusion:** NCPB is one of the choices for palliation of severe, chronic upper-abdominal cancer pain.

Keywords: Celiac Plexus, Chemical Neurolysis, Pain, Opioid, Side Effects

Introduction

Since 1990, cancer has been the second-leading cause of population mortality in Mongolia. In 2014, the cancer-related mortality rate was 24.3% of the total mortality and was 15.5 per 10,000 in males and 11.7 per 10,000 in females. The five leading types of cancer in males in Mongolia are liver, stomach, lung, esophagus, and pancreatic and, in females are liver, stomach, cervix, esophagus and breast [1].

Conventional drugs do not provide adequate analgesia and a variety of adverse effects are usually seen with opioids [2]. NCPB is a technique that can reduce the upper abdominal cancer pain and further escalation of opioid consumption [3]. Neurolytic sympathetic block should be considered early in the diseases [2].

Pain related to gastric cancer, esophageal cancer, colorectal cancer, liver metastasis, gallbladder cancer, and cholangiocarcinoma have been treated effectively with a neurolytic celiac plexus block (NCPB) [4]. Patients who have chronic abdominal pain due to malignant conditions, which are unresponsive to large doses of opioid analgesics, can be treated with this procedure. A celiac plexus block has been shown to reduce opioid requirements and to limit opioid dose-related side effects [5].

The location of the celiac plexus often varies with regard to bone landmarks and can be located anywhere from the T12–L1 disk space to the middle of the L2 vertebral body [6]. The posterior retrocrural approach is the traditional technique used for a celiac plexus block. Neurolysis alleviates pain by disrupting pain signals along the neural pathway. Many studies have evaluated the efficacy of these techniques for pain from upper abdominal cancer [7], but no study has been conducted in Mongolia.

Therefore, the main goal of our study was to evaluate the efficacy of neurolytic celiac plexus blocks in patients with upper-abdominal cancer pain. Under the main goal there were four specific outcomes studied regarding the efficacy of neurolytic celiac plexus blocks (1) in reducing pain score, (2) in reducing morphine consumption, (3) in improving performance score, and (4) in reducing the side effects of morphine. This is the first study about interventional procedures in the practice of palliative care in Mongolia.

Materials and Methods

This study was conducted with 56 patients, who were referred by the Achtan Clinical Hospital of Ulaanbaatar, Mongolia during 2012-2015. All patients had upper abdominal pain, which radiated to their backs. The diagnosis of tumor or metastasis was based on primary ultrasonography examination and computed tomography and was confirmed after biopsy. Patients were evaluated regarding pain characteristics (localization, intensity, duration, quality and radiation) and randomly assigned to one of two experimental groups with 28 patients each. All patient's pain intensity scores were 6-8 (on a scale of 10) and used oral morphine at a total dose of <100 mg/day before the study period. In these patients, the pain management by morphine was insufficient.

For the purposes of the study, patients were divided into two groups and pain scores, performance status, morphine consumption, and morphine-related side effects (appetite, nausea and constipation) of each patient were recorded at regular two-week intervals for a total of eight weeks. Group I included the patients who received NCPB, while group II included the patients who continuously used morphine. The exclusion criteria were patients having coagulopathy, alcohol abuse, heart disease, delirium, bowel obstruction, or a communication barrier.

1. Data collection

The intensity of pain was evaluated by the Wong-Baker FACES® Pain Rating Scale [8], in which patients rate their pain according to the following: face 0 does not hurt at all, face 2 hurts just a little bit, face 4 hurts a little bit more, face 6 hurts even more, face 8 hurts a whole lot, and face 10 hurts as much as can be imagined, although one does not have to be crying to have this worst pain. This scale uses face pictures and a numeric scale to describe the pain intensity.

The physical performance status was measured by the Karnofsky Performance Score according to the following: 100 (A) - normal, no complaints, no evidence of disease; 90 (A) - able to carry on normal activity, minor signs or symptoms; 80 (A) - normal activity with effort, some signs or symptoms of disease; 70 (B) - cares for self, unable to carry on normal activity or to do active work; 60 (B) - requires occasional assistance but is able to care for most of his/her needs; 50 (B) - requires considerable assistance and frequent medical care; 40 (C) - disabled, requires special care and assistance; 30 (C) - severely disabled, hospitalization is necessary, active supportive treatment is necessary; 20 (C) - very sick, hospitalization is necessary, active supportive treatment is necessary; 10 (C) - moribund, fatal processes progressing rapidly; 0 - dead.

The side effects of morphine, such as anorexia, nausea, vomiting and constipation were recorded. Each side effect was graded from 1 to 4 (1 = no side effects, 2 = moderate, 3 = severe

but tolerable, 4 = severe and intolerable) [4]. The grade was subjectively determined by the patients.

2. Neurolytic celiac plexus block (technique)

NCPBs were performed bilaterally by a percutaneous posterior approach with X-ray guidance. The patient was placed in the prone position with a pillow placed under the abdomen. The inferior margins of the 12 ribs were identified and traced to the 12th vertebral body. The needles were initially oriented 45 degrees toward the midline and about 15 degrees cephalad to ensure contact with L1 vertebral body. On the fluoroscopic anteroposterior view, contrast was confined to the midline and concentrated near the L1 vertebral body. Contrast should have appeared lateral and behind the aorta. After confirming the placement of the blocking needle, the celiac plexus block was completed by injection of 15 mL of 0.5% bupivacaine contrast medium (Ultravist 300) and 10 mL of 96% alcohol. Injection was done bilaterally. All patients had a venous access to allow intravenous infusion of Lactated Ringer's solution. Blood pressure, heart rate and oxygen saturation of the patients were continuously monitored by a modulated monitor apparatus. After the block, 1.5-2.0 L of Lactated Ringer's solution was infused intravenously for an 8 to 24-hour period.

Table 1. Patient characteristics in two experimental groups

	Group I (n = 28)	Group II (n = 28)	p-value
	n	n	
Age	58.96 ±10.38[a]	53.61 ±11.4[a]	0.81
Sex			
Male	16	12	0.42
Female	12	16	
Primary tumor			
Pancreatic	12	10	
Hepatic	11	12	0.89
Gastric	5	6	

[a]Values are mean ± SD

3. Ethical statement

The Research and Ethical Committee of the Mongolian National University of Medical Sciences approved the study methodology and the patients' informed consent. All patients signed the consent form. The procedure was made according to the 'Pain Management Guide' protocol which was approved by the Mongolian Ministry of Health in 2012.

4. Statistical analysis

All statistical analyses were performed using SPSS 21.0. Intergroup comparisons in demographic characteristics of patients were analyzed by using the unpaired t-test or the Fisher's exact test. A repeated ANOVA test was used to compare pain score, morphine consumption, Karnofsky performance score and side-effect grade variables during the observation period between and within two groups at two-week intervals. Mann-Whitney tests were used to find which means were significantly different than others. The level of significance was $p < 0.05$.

Results

Of 70 patients assessed for eligibility, 56 patients with upper abdominal cancer were randomly assigned to two experimental groups with 28 patients in each group. Fourteen patients were excluded from the study because six patients did not meet the inclusion criteria and eight patients refused to participate in the study.

Patient characteristics of the experimental groups are presented in Table 1. Neither group had significant differences regarding sex ($p = 0.42$), age ($p = 0.81$), or cancer diagnosis ($p = 0.89$).

Table 2. Intensity of the pain in group I and group II during eight weeks of observation

Week number	Group I	Group II	p-value
	Mean ±SD	Mean ±SD	
Before NCPB	5.95 ±1.19	5.69 ±0.75	0.17
1	1.75 ±0.91	3.85 ±1.40	0.0001
2	1.95 ±0.60	3.23 ±1.09	0.0001
4	1.90 ±0.30	3.15 ±0.55	0.0001
6	2.10 ±0.72	3.29 ±0.60	0.0001
8	2.55 ±0.88	4.10 ±1.00	0.0001

Mean Wong-Baker pain scores for both groups are shown in Table 2. The Wong-Baker pain score in groups I and II had no significant difference before NCPB ($p = 0.17$). The pain scores were strongly reduced in group I throughout the period of observation after the NCPB, particularly, during the 1st to 4th weeks when the pain scores were decreased from 5.95 ±1.19 to 1.90 ±0.30 ($p<0.0001$). Pain scores for the 4th and 8th weeks were 2.10 ±0.72 and 2.55 ±0.88, respectively, which was a slight increase from previous weeks, but scores were much lower

than group II (p <0.0001). Although group II increased their morphine consumption from week one to week eight, their pain score was almost stable ranging from 3.15 ±0.55 to 4.10 ±1.00 after an initial drop from 5.69 ±0.75. The pain score in group II was higher than in group I over eight weeks (p <0.0001).

Table 3. Comparison of morphine consumption (mg) in both groups

Weeks	Group I	Group II	p-value
	Mean ±SD	Mean ±SD	
Before NCPB	78.0 ±11.5	76.1 ±13.3	0.20
1	17.0 ±18.9	100.8 ±18.5	0.0001
2	16.6 ±11.0	131.5 ±35.8	0.0001
4	15.0 ±10.5	148.5 ±30.5	0.0001
6	18.5 ±8.8	176.2 ±29.9	0.0001
8	18.0 ±9.2	210.0 ±55.0	0.0001

Table 3 shows morphine consumption of both groups. On the day before the NCPB, the groups did not have a significant difference in morphine consumption (p = 0.20). After NCPB, the daily doses of the morphine consumption was greatly reduced in group I from 78.0±11.5 mg to 18.0±9.2 mg at week eight. In the end of the study morphine consumption was stable and significantly lower in group I than in group II (p<0.001). On the other hand, the morphine consumption increased by more than double for adequate pain relief in group II by week eight.

Table 4. Karnofsky Performance Score in both groups during eight weeks of observation

Weeks	Group I	Group II	p-value
	Mean ±SD	Mean ±SD	
Before NCPB	41.0 ±8.0	41.5 ±8.0	0.59
1	65.0 ±6.9	50.0 ±8.2	0.0001
2	60.5 ±5.1	50.8 ±6.4	0.0001
4	54.5 ±7.6	41.5 ±6.9	0.0001
6	50.0 ±8.6	37.6 ±7.3	0.0001
8	43.0 ±5.7	31.5 ±5.5	0.0001

Karnofsky Performance Score is summarized in Table 4 for both groups. Both groups had no significant difference regarding the physical performance status on the day before the NCPB (p = 0.50). After NCPB the physical performance score significantly improved from 41.0 ±8.0 to 65.0 ±6.9 in week one for group I. Improvement was observed between two and six weeks in group I (p <0.001). The physical performance score decreased until the eighth week in group I, but in this week, group I had a higher score than group II (p <0.001). Transient improvement of the physical performance score was observed in group II in the first two weeks, but was lower than in group I (p <0.001).

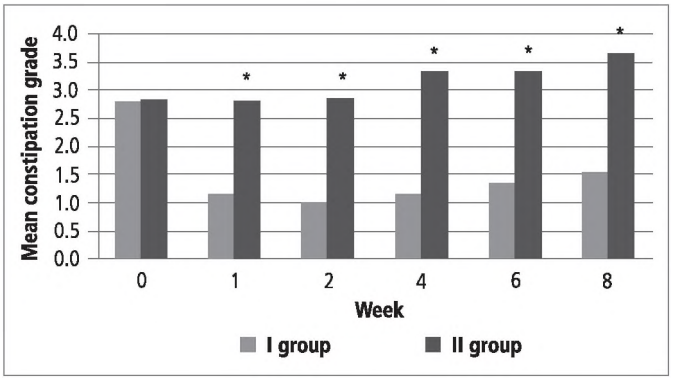

Figure 1. Grade of the constipation in both groups (*p-value <0.05).

The constipation grade is shown in Figure 1 for the two groups. It had no difference between groups on the day before NCPB (p = 0.64). After NCPB, the constipation grade was strongly decreased in group I, more than in group II (p <0.0001). Constipation grade had a tendency to be higher in group II than group I for all eight weeks (p <0.0001).

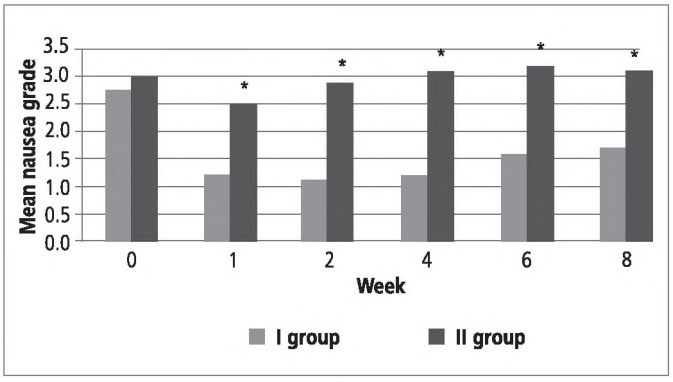

Figure 2. Nausea grade in both groups (*p-value <0.05).

The grade of nausea is shown in Figure 2. It had no difference in both groups on the day before NCPB (p <0.41). After NCPB the grade of the nausea was strongly decreased in group I for one to two weeks and it was lower than in group II (p <0.0001). On the other hand, in group II the grade of the nausea was higher for eight weeks than in group I (p <0.0001).

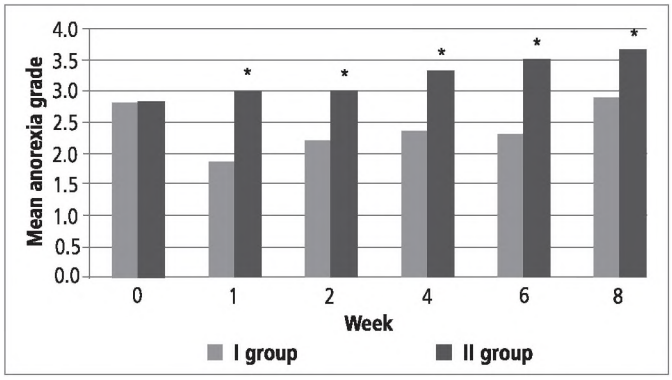

Figure 3. Grade of anorexia in the both groups (*p-value <0.05).

The grade of anorexia is shown in Figure 3. There was no difference between the groups on the day before NCPB ($p = 0.15$). After NCPB, the grade of anorexia was more decreased in group I than in group II ($p < 0.0001$). In contrast, in group II, the grade of anorexia was higher than in group I for eight weeks ($p < 0.0001$).

Discussion

This study compared the effectiveness of NCPB and morphine treatment in decreasing pain score, morphine consumption, morphine-related side effects and improving physical performance of patients with severe, chronic upper-abdominal cancer pain. The results of our study confirmed other studies and showed for the first time in Mongolia that NCPB significantly reduced the intensity of the pain, opioid consumption and the drug-induced side effects such as anorexia, constipation and nausea, compared to the group treated with morphine. The consumption of opioid analgesics was significantly increased in group II and this group had a significantly increased incidence of side effects due to the high dosage of morphine. There was difficulty in reducing the intensity of pain in group II despite the increase in opioid dosage. In our study, the intensity of pain was significantly lower in group I throughout the eight weeks of observation after NCPB.

Similar results were observed in other cases of upper-abdominal cancer pain [9-12]. A meta–analysis conducted by Eisenberg et al. showed that a bilateral posterior approach with 15-50 mL of 50%-100% alcohol was the most common technique [11]. Good to excellent pain relief was reported in 878 out of 989 patients (89%) during the first two weeks after NCPB and long-term follow up beyond three months revealed persistent benefit [11]. Partial to complete pain relief continued in approximately 90% of patients alive at three months post-NCPB and in 70%-90% until death even if beyond three months post-NCPB [11]. Patients with pancreatic cancer responded similarly to those with other intra-abdominal malignancies [11].

Common adverse effects compiled in the meta-analysis were transient, including local pain (96%), diarrhea (44%), and hypotension (38%) and complications occurred in 2% of patients [11]. This analysis suggests that: (1) NCPB has long-lasting benefit for 70-90% of patients with pancreatic and other intra-abdominal cancers, regardless of the technique used, (2) adverse effects are common but transient and mild, and (3) severe adverse effects are uncommon [11]. Rykowski and Hilgier also reported similar duration of the analgesia induced by NCPB intervention [13]. In our study, transient complications were reported in 1.6%, or six, patients occurring post-NCPB including hypotension ($n = 5$), diarrhea ($n = 4$) and shoulder pain ($n = 2$). After two days of observation and treatment those complications were resolved. No major complications (paresis, urine and bowel incontinence, thrombosis, pleurisy) were recorded in our study.

Mercadante et al. concluded that the NCPB reduced the opioid consumption needed to control pancreatic cancer pain with an effect that was evident for four weeks and persisted partially until death [14]. Lillemoe et al. compared chemical splanchnicectomy with placebo injection of saline for 1193 patients [15]. The pain score was significantly lower in the group undergoing chemical splanchnicectomy at two, four and six-month follow-ups ($p < 0.05$) [15]. Kawamata et al. found significantly lower pain score in the first four weeks after the NCPB procedure than in participants given analgesics [4]. Wong et al. concluded that in the first week after NCPB, pain intensity decreased by 53% from the baseline ($p = 0.05$) and quality of life improved in NCPB patients [16]. Zhang et al. found that participants who received the NCPB had significantly lower pain scores than those given pharmacological therapy [17]. In most cases, NCPB shows only a transient effect and persistent pain relief is maintained in only about 10% of 90 total patients over 24 weeks [18]. Therefore, this therapeutic option seems to be more effective and reasonable in patients with malignant disease and short anticipated lifespan [19]. NCPB prolongs survival compared with celiac ganglion neurolysis [20].

Ultrasound-guided celiac plexus neurolysis technique is a safe, effective procedure in decreasing pain severity in

patients suffering from upper-abdominal cancer with no major complications and high success rates [21]. Invasive pain treatment methods have resulted in significant reductions of pain and fatigue [22]. Based on the result of our study, we will continue to study ultrasound-guided and CT guided methods for NCPB in this field.

The widespread applicability of NCPB is limited. First, most palliative care cancer patients with severe pain were treated by increased dose of morphine. According the World Health Organization, 70-90% of patients with cancer pain can be palliated by pharmacological treatment, including opioids [23]. Procedure pain management is a limited pain management just for the remaining 10-30% of cancer patients with intractable pain [23]. Second, NCPB is a more limited procedure because it is only used for palliation of severe intractable upper abdominal pain and cannot be used for pain in other locations. Third, this procedure can be performed only by an experienced anesthesiologist together with radiologist. Fourth, we performed the NCPB using fluoroscopy. In the future, we recommend that doctors' anesthesiologist work together with radiologists who are more experienced on ultrasound- and CT-guided methods, and with palliative care doctors, who deliver their patients for procedure pain management and have experience in management of morphine-related side effects.

In conclusion, NCPB is recommended to reduce chronic, severe upper-abdominal cancer pain since it allows for decreased morphine consumption and morphine-related side effects and it improves the performance of patients in their last days and months of life, which means that NCPB improves quality of life terminally ill patients.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgements

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