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Comparing the Effect of Stellate Ganglion Block and Gabapentin on the Post Mastectomy Pain Syndrome.

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Abstract:

Background: The reported incidence of post mastectomy pain syndrome following surgery for breast cancer varies considerably with reports from as low as 4-6% to as high as 100%. This pain can be severe enough to interfere with sleep and performance of daily activities. Post mastectomy pain syndrome is a neuropathic pain condition that can follow surgical treatment for breast cancer. The purpose of this study is to evaluate the effect of stellate ganglion block with gabapentin on post mastectomy pain.
Materials and Methods: Sixty patients referred from department of oncology and surgery to pain clinic were allocated to two groups. In group A stellate ganglion block was performed with 8ml bupivacaine 0.25%. In group B, patients were treated with gabapentin 900mg per day in three divided doses. Drug dose was increased if necessary until eight weeks. Pain score and quality of life were determined. Data were collected before treatment, 48 hours and every 15 days after treatment until three months.
Results: Pain scores at 48 hours after treating were higher in group B than group A and lower at one week, one month and three months after treatment which were statically significant. ($P<0.001$, 0.024, 0.047 and <0.001 respectively)
Conclusions: In our study gabapentin was used as an ideal treatment technique for chronic pain following breast surgery.

Key Words: post mastectomy, pain, stellate ganglion, gabapentin.

Introduction:

Neuropathic pain, a persistent chronic pain resulting from damage to the central or peripheral pain signaling pathway, has become as an interesting research activity, largely because it represents a disorder with high unmet medical need. It is not a single entity but rather includes a range of heterogenous conditions that differ in etiology, location and initiating cause [1].

Post mastectomy pain syndrome (PMPS) is a neuropathic pain condition that can follow surgical treatment for breast cancer, including radical mastectomy, modified radical mastectomy, and segmental mastectomy (Lumpectomy) [2,3].This syndrome consists of persistent pain in the anterior chest, axilla, medial and posterior parts of the arm following breast surgery. The reported incidence of PMPS following surgery for breast cancer varies considerably with reports from as low as 4-6% [4] to as high as 100% [5]. This pain can be sufficiently severe enough to interfere with sleep and performance of daily activities [6,7]. In addition, if poorly treated, patients may develop an immobilized arm, which can lead to severe lymph edema, frozen shoulder and complex regional pain syndrome [8,9].

PMPS can develop from surgical damage to the intercostobrachial nerve, the lateral cutaneous branch of the second intercostal nerve that is often resected at mastectomy [10]. Because it is believed that this nerve is injured in 80-100% of mastectomy patients who undergo an axillary dissection [11], stellate ganglion block can be a therapeutic way for PMPS. The high prevalence surgical procedures are in the upper trunk, such as mastectomy, thoracotomy and sternotomy [12]. Symptoms include an electric shock-like pain sensation overlying a continuous aching and burning pain associated with chronic dysesthesia [13]. Pain typically begins in the immediate postoperative period but may be delayed six or more months after surgery. The pain characteristically persists beyond the normal healing period. As a result, the ability to perform activities of daily living and occupational activities may be impaired [14].

The clinical efficacy of anticonvulsants is clearly established in chronic neuropathic pain. Gabapentin is effective in relieving indexes of allodynia and hyperalgesia, so it could be considered for treatment of neuropathic pain [15]. The analgesic effect of addition of gabapentin to opioids in the

management of neuropathic cancer pain indicated that gabapentin is effective in improving analgesia in patients with neuropathic cancer pain. In adults 600-1800mg per day in three divided doses is used through oral route. The adverse events reported are usually mild to moderate in intensity and are in the form of dizziness, somnolence, peripheral edema, asthenia and diarrhea. The adverse events that most frequently lead to discontinuation in gabapentin therapy are dizziness and somnolence [16].

So, in this study we compared the effect of stellate ganglion block and gabapentin on the post mastectomy pain syndrome.

Materials and Methods:

After obtaining informed consent from patients and approval in the ethics committee of hospital, sixty patients referred from department of oncology and surgery to pain clinic for the treatment of post mastectomy pain syndrome (PMPS) were enrolled in this trial. This study was performed from April 2003 to July 2006 in Tabriz Imam Khomeini hospital. Patients were randomly allocated to two groups (block randomization). Inclusion criteria were patients with history of simple mastectomy, lumpectomy, or modified radical mastectomy for breast cancer without any metastasis. Participants had a wide range of neuropathic pain syndromes with at least two of the following symptoms: allodynia, burning pain, shooting pain, hyperalgesia. Exclusion criteria were history of radiation, chemotherapy, receiving any concomitant analgesics or other drugs acting on central nervous system, neurological disorders, diabetes mellitus, metastasis and other painful disabling condition such as arthritis.

In group A stellate ganglion block was performed with 8ml bupivacaine 0.25% under guided fluoroscopy in anterior approach (Para tracheal) with patients in supine position. According to Malmqvist EL study we injected drug toward C7 instead of injection toward C6, and high concentration instead of low that seemed to be more advantageous. (whereas volume seemed to be less important) [17]. During block patients received sedation and safety precaution like contrast dye injection to rule out inadvertent intravascular or intrathecal injection while performing block. We confirmed the block with registering the following changes in effector organ activity:

1- observed signs (e.g, Horner's syndrome: miosis, ptosis, enophtalmus and redding of sclera), 2- objective measurements of changes in skin temperature, skin blood flow (laser doppler flowmetry) and digital pletismography. Stellate ganglion block was performed every 5 day (maximum 5 blocks). Patients who received stellate ganglion block were examined with appropriate sensory nerve block from possible diffusion of local anesthetic solution which pain relief can be subsequent to sensory and not sympathetic blockade.

In group B patients received gabapentin 900mg per day in three divided doses and drug dose was increased if necessary until a maximum of eight weeks (maximum dose of 1800mg per day). When any complication occurred gabapentin was discontinued. Demographic data were recorded. Location, onset, quality and degree of pain were assessed by asking patients to rate their pain at the time of responding to the questionnaire. (numerical rating scale,0:without pain-10:the most severe pain). The quality of life which measured satisfaction of life and difficulties of activity such as daily horce and quality of sleep were measured by numerical rating scale (0-10).

All data were collected before treatment,48 hours and every 15 days after treatment until three months. All data were analyzed using the SPSS 13 statistical software package. We used the sample t test for independent variables and repeated measure t- test for pain scores. $P<0.05$ was considered statistically significant.

Results:

Patients' age and weight in two groups didn't have statistical difference. ($P>0.05$). Type of surgery, onset and site of pain are shown in table 1. Success rate in stellate ganglion block was 83% and in 5 patients block was failed (they were non-responders but remained in the study and analysis to show the true treatment response). In group A block was performed three times in twenty patients, four times in seven patients, and five times in three patients. Five patients with anterior chest wall pain noted incomplete pain relief from block and needed adjunctive therapy. In group B 70% of patients were medicated for four weeks, 20% for six weeks and

10% for eight weeks. There were no significant differences in pain score between two groups before intervention (table 2). There were significant differences in pain scores after treating between two groups. The mean of multiple measured pain scores after block showed that pain scores at 48 hours after treating were higher in group B than group A but lower at one week, one month and three months after treatment ($P < 0.001$, 0.024, 0.047 and <0.001 respectively) (table 2). Mean life quality (satisfaction) score after intervention indicated that life satisfaction in group A was significantly higher than group B (table 3). Sleep quality scores indicated that patients in group B slept better than group A. ($P=0.03$) (Table 3). Daily horce scores indicated that patients in group A had good general daily activity than group B. ($P<0.001$) (table 3)

In this study the onset of pain in 71.6% was immediately after operation and in the others it was later. Common sites of pain were axilla, upper arm, anterior chest wall and shoulder, in order. Pain worsened with general activity in 60% of patients and 40% had continues pain. 54% of patients had sleep disturbances after intervention which was more in group A than group B.

Table 1: Type of surgery, site and onset of pain.

		Group A		Group B		Total	
		n	%	n	%	n	%
Type of surgery	Lumpectomy	8	26.66	7	23.33	15	25
	Mastectomy	4	13.33	3	10	7	11.6
	Axillary ND*	18	60	20	66.66	38	60.33
Site of pain	Axilla	22	73.3	21	70	43	71.66
	Medial upper arm	21	70	19	63.3	40	66.66
	Chest wall	7	23.3	6	20	13	21.66
Onset of pain (post operative)	immediate	20	66.66	23	76.66	43	71.66
	One month	6	20	4	13.33	10	16.66
	Three months	4	13.33	3	10	7	11.66

* node dissection

Table 2: Pain score, before and after therapy in two groups.

Pain score	Group A	Group B	P value
Before treatment	7.46±1.07*	7.40±0.85	0.712
After 48 hours	3.86±2.27	6.48±1.00	<0.001
After one week	3.06±1.70	2.33±0.54	0.024
After one month	2.13±1.50	1.36±1.18	0.047
After three months	1.73±1.59	0.53±0.50	<0.001

*: mean±SD

Table 3: Life satisfaction, general activity and sleep quality scores before and after therapy in two groups.

		Group A	Group B	P value
Life satisfaction	before	2.66±0.92*	2.26±0.82	0.103
	after	7.03±1.15	5.40±1.40	<0.001
General activity	before	2.56±0.89	2.50±0.90	0.670
	after	7.96±0.99	3.50±1.19	<0.001
Sleep quality	before	3.10±0.88	2.80±0.93	0.080
	after	5.50±1.40	6.60±1.01	0.030

*: mean±SD

Discussion:

Different therapies are suggested for PMPS which include:

1- medical treatment (antidepressants[18], NSAIDS [19], antiepileptics [20], opioids [21], NMDA receptor antagonists [22-23], lidocain[24], magnesium [25], adenosine [26], ….)

2- peripheral nerve stimulation and spinal cord stimulation [27]

3- nerve blocks [28-30]

4- surgery [31]

5- prevention [32].

But none of them are associated with complete improvement.

The clinical efficacy of anticonvulsants is clearly established after years of use in patients with chronic neuropathic pain. Not all anticonvulsant drugs have the same mode of action, which explains why their relief of different symptoms of neuropathic pain (allodynia, hyperalgesia, burning pain) is varied. Gabapentin is the first-choice drug for relieving allodynia and hyperalgesia, but it is usually less effective for decreasing paresthesia and dysesthesia. Henkel K showed that combination of gabapentin and amitriptyline reduced the neuropathic pain markedly whereas opioids failed to provide sufficient analgesia [33].

The neuropathic pain cannot be satisfactorily treated with non-steroidal anti-inflammatory drugs. Dependent on the underlying mechanism, the pain is treated with either antidepressants (for more or less continuous pain) or antiepileptics (for paroxysmal pain).19 Fukusaki concluded that nerve blocks are useful for earlier relief of severe pain associated with cervical radiculopathy.[30] Gonzalez et al showed that preventive analgesia by direct transoperational block on nerves turned out to be an effective alternation with low level of systemic morbidity, which must be considered to prevent moderate to severe post operative pain in radical mastectomy [32]. Fas-

soulaki compared mexiletin(600 mg/day) with gabapentin (1200 mg/day) and reported that gabapentin seemed to be the ideal analgesic for managing acute and chronic pain following breast cancer surgery, since it possesses antihyperalgesic and antiallodynic effects in the setting of peripheral tissue injury [34]. In multi central study for treatment of phototherapeutic neuralgia, side effects reported for gabapentin were somnolence, dizziness, confusion and ataxia. However these patients were treated for eight weeks, and the dose was titrated up to 3600 mg /day unless intolerable adverse effects were developed [35].

According to previous studies showing that brachial nerve branches are injured in 80-100% of patients who undergo an axillary dissection [11], stellate ganglion block seems to be an appropriate method for treatment of PMPS. Like the study of Malmqvist EL [17], we injected a high concentration of drug toward C7 but same as the other studies it didn't have very good results but better than previous results, which is mostly due to incomplete block. As Malmqvist EL et al concluded that complete criteria of stellate ganglion block were seen in less than 50% of patients.

In comparison of two groups, pain was less in group A than group B in the first post operative day($P<0.001$) but after that, it was significantly less in group B than group A. This shows more rapid onset of analgesic effect in group A which is lost during periods of time (Fukusaki M et al showed the same results in their study) [30]. So, the patient will experience periods of pain. Regarding different etiologic factors of this syndrome, we concluded that this method is not sufficient for analgesia, lonely and it can be used in addition to other therapies to provide rapid onset of analgesia after surgery. Since gabapentin has sedative effects, patients in group B had better quality of sleep. But quality of life and general activities were less in group B because of its sedative effect and complications.

So, gabapentin is efficacious in neuropathic pain, well tolerated within minimal side effects(lower doses) that may occur during titration phase and are transient only, as well as it can potentient the analgesic effects of other conventionally available drugs. In addition it has been also shown to improve the quality of sleep in patients.

In view of all these advantages and some disadvantages, gabapentin can be used as one of the important drugs in treatment of neuropathic pain.

In conclusion, stellate ganglion block reduces pain score for short duration and is superior in controlling of pain scores but usually the pain is chronic, so low dose gabapentin can be used as an adjunct analgesic in these cases.

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