Section: Anaesthesiology

Original Research Article

THE ROLE OF PREGABALIN VERSUS TRAMADOL IN MANAGEMENT OF ACUTE POST OPERATIVE PAIN IN MASTECTOMY PATIENT & REDUCTION IN POST MASTECTOMY PAIN SYNDROME

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Abstract

Background: Worldwide, breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of cancer death among women. The objective is to determine a better analgesic among the two namely tramadol and pregabalin in management of acute pain in mastectomy patient and reduction in post mastectomy pain syndrome. **Materials and Methods:** The present study was conducted at Baby Memorial Hospital, Calicut Kerala on patients undergoing mastectomy. The study design was randomized, double blind, prospective study conducted from August 2010 to July 2012. This study was conducted in the Department of Anaesthesiology, Baby Memorial Hospital, Calicut. Patients posted for Mastectomy at Baby Memorial Hospital, Calicut were selected for the study. A total of 60 patients undergoing Mastectomy at Baby Memorial Hospital, Calicut were enrolled in the study. Based on the hospital statistics, 80% of average of surgeries during past three years, a total of 60 patients were enrolled in the study. **Result:** In this study most of the women were aged more than 60 years that is, 35% in group A and 75% in group C. However, in group C, most (40%) of the women were aged between 46 to 60 years. These differences were statistically not significant (p=0.034). The mean age in group A was 53.05 ± 13.22 years, in group B it was 53.20 ± 12.34 years and in group C the mean age was 52.60 ±14.99 years. 15% patient in group A and 10% in group required rescue analgesia. However this difference was statistically not significant (p=0.633). Among the patients with group A PMPS was reported by 50% patients compared to 5% in group B and this difference was statistically significant (p<0.001). **Conclusion:** Administration of pre operative Pregabalin 150 mg provides better analgesia in management of acute pain in mastectomy patient.

INTRODUCTION

Worldwide, breast cancer is the most frequently diagnosed life- threatening cancer in women and the leading cause of cancer death among women. Breast cancer is the first cause of death in women in the United States, Canada, and Europe.[1] It has been observed that both the incidence and the gross mortality rate have been increasing significantly over the last few decades. Over the past 25 years, breast cancer incidence rates have risen globally, with the highest rates in Westernized countries. Reasons for this trend include change in reproductive patterns, increased screening, dietary changes and decreased activity.[2] In most cases, breast cancer is treated surgically, according to the clinical staging at the time of the diagnosis.[3]

The incidence of PMPS is high, ranging from 20 to 50%.[4,5] The presence of pain affects activities of daily life in general. There are reports on pain interfering with driving, taking care of the children, leisure time, and sex, resulting in poor quality of life.[5] Since the neuropathic component predominates,[6] the use of drugs proven to be effective in the treatment of neuropathic pain can relive the symptoms of patients with post-mastectomy pain syndrome.[7-10]

However, there are only few studies which examine the impact of analgesic regimens on PMPS,[7-10] and many unanswered questions remain about the optimal doses, timing and coordination of therapy with ongoing adjuvant treatment for breast cancer. Considering the high incidence of chronic postoperative pain secondary to the treatment of breast cancer, along with the small number of studies

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on the subject, it is necessary to better understand it. Adopting the preventing measures such as anesthetic techniques that attenuate postoperative pain, performing surgical procedures with minimal nerve damage and strict postoperative follow- up to identify the development of PMPS, can establish therapeutic guidelines to minimize pain and the limitations it causes.

Hence, this study performed to determine a better analgesic among the two namely tramadol and pregabalin in management of acute pain in mastectomy patient and reduction in post mastectomy pain syndrome.

MATERIALS AND METHODS

The present study was conducted at Baby Memorial Hospital, Calicut Kerala on patients undergoing mastectomy. The study design was randomized, double blind, prospective study conducted from August 2010 to July 2012. This study was conducted in the Department of Anaesthesiology, Baby Memorial Hospital, Calicut. Patients posted for Mastectomy at Baby Memorial Hospital, Calicut were selected for the study.

A total of 60 patients undergoing Mastectomy at Baby Memorial Hospital, Calicut were enrolled in the study. Based on the hospital statistics, 80% of average of surgeries during past three years, a total of 60 patients were enrolled in the study.

Patients in this study were randomly categorized into these groups

- Group A (n=20) – Patients receiving Tab Tramadol 100 mg.
- Group B (n=20) – Patients receiving Cap Pregabalin 150 mg.
- Group C (n=20) – Patients receiving multi drug regime with no premedication.

Inclusion Criteria

Carcinoma breast patients posted for mastectomy under General Anaesthesia. Age between 20 to 70 years. ASA 1 & 2.

Exclusion Criteria

Patients with history of Allergy to Tramadol/Pregabalin, Asthma and an episode less than two years, Patients with renal and hepatic Failure.

Ethical Clearance was obtained for the study from Institutional Ethical Committee of Baby Memorial Hospital, Calicut. Patients fulfilling the selection criteria were briefed about the nature of the study and a written informed consent was obtained from the selected patients.

Pre-anesthetic Evaluation

A thorough pre-anaesthetic evaluation was performed by taking history and clinical examination. In all the patients weight, basal heart rate, respiratory rate, blood pressure and clinical signs if any were recorded. Investigations like complete blood count, urine for Albumin, Sugar and Microscopy were done. Investigations like Electrocardiogram and Chest x-ray were taken. Patients were allocated into Group A / Group B or Group C by general randomization on the day before surgery. At night sedation was given to all patients that is, oral Nitrazepam 5 mg, pre-emptive analgesia treatment either compound A or B according to the allotment of group respectively by a nurse who was blinded to the study drug. On the day of surgery, at 6.00 am all patients received pre-emptive analgesia treatment either with compound A or B, Tab Metaclopramide 10 mg and Tab Ranitidine 150mg with a sip of water. Patients were taken to premedication room and intravenous cannula was inserted, and infusion of normal saline was started and 1 gm of intravenous Paracetamol given. Half an hour before surgery patients were premedicated with intravenous injection Midazolam 1 mg and injection Ondansetron 4 mg. In the operating room, routine monitors, emergency airway equipments, anaesthesia machine were checked, drugs were loaded and intubating material were checked and kept ready.

Statistical Analysis

The data obtained was coded and entered into Microsoft Excel spreadsheet. Categorical data was expressed as rates, ratios and percentages and the comparison was done by chi-square test. Continuous data was expressed as mean ± standard deviation (SD) and the comparison was done using ANOVA test. A 'p' value of less than 0.05 was considered as statistically significant.

RESULTS

As per [Table 1] In this study most of the women were aged more than 60 years that is, 35% in group A and 75% in group C. However, in group C, most (40%) of the women were aged between 46 to 60 years. These differences were statistically not significant (p=0.034). The mean age in group A was 53.05 ± 13.22 years, in group B it was 53.20 ± 12.34 years and in group C the mean age was 52.60 ±14.99 years. The mean weight in group A, B and C were 59.40 ± 7.71 Kg, 63.05 ± 6.88 Kg and 64.90 ± 10.47 Kg respectively. All the three groups namely, A, B and C were comparable in terms of age and weight (p>0.050).

In the present study the mean surgical time in group A was 121.25 ±32.24 minutes, in group B it was 112.80 ± 25.30 minutes and in group C the mean surgical time was 116.00 ± 37.12. However this difference between the surgical time between group A, B and C was statistically not significant (p=0.720). In the present study duration majority of the patients (75% in group B and 70% in group C had duration of surgery between 60 to 120 minutes. In group A, most of the women required surgical time about 121 to 180 minutes (p=0.063). [Table 2]

In the present study through the hospital stay that is post operative day three to day seven the mean pain scores significantly remained low in patients with group B (4.20 ± 1.51 on day three and 2.05 ± 0.51 on day seven) compared to group A (4.15 ± 1.53 on day

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three and 2.10 ± 1.02 on day seven) and group C (5.35 ± 0.99 on day three and 3.35 ± 1.04 on day seven) ($p<0.05$). In this study, the mean pain score at one month follow up in group A were 0.53 ± 0.80 and in group B the mean scores were 0.33 ± 0.49. In patients with group C the mean pain scores were 0.60 ± 0.50. Overall, the mean pain score in group B were significantly low when compared to group A and C but this difference was statistically not significant ($p=0.280$). [Table 3]

As per [Table 4] in the present study 15% patient in group A and 10% in group required rescue analgesia. However this difference was statistically not significant ($p=0.633$).

In the present study 50% of patients in group A had constipation compared to 35% patients in group B with sedation. However this difference in the side effects between group A and B was statistically not significant ($p=0.337$). [Table 6]

As per [Table 6] in the present study among the patients with group A PMPS was reported by 50% patients compared to 5% in group B and this difference was statistically significant ($p<0.001$).

Table 1: Age distribution

Age group (Years)	Group A (n=20)		Group B (n=20)		Group C (n=20)	
	No	%	No	%	No	%
20 to 30	1	5.00	0	0.00	0	0.00
31 to 45	5	25.00	7	35.00	0	0.00
45 to 60	7	35.00	8	40.00	5	25.00
> 60	7	35.00	5	25.00	15	75.00
Total	20	100.00	20	100.00	20	100.00
x2=13.60			Df=6			p=0.034

Table 2: Duration of surgery

Duration	Group A (n=20)		Group B (n=20)		Group C (n=20)		"f" value	"p" value
	Mean	SD	Mean	SD	Mean	SD		
Minutes	121.25	35.24	112.80	25.30	116.00	37.12	0.335	0.72

Table 3: Mean pain scores during post operative hospital stay

Post op days	Group A (n=20)		Group B (n=20)		Group C (n=20)		f-value	p-value
	Mean	SD	Mean	SD	Mean	SD		
3	4.15	1.53	4.20	1.51	5.35	0.99	4.942	0.010

Table 4: Requirement of rescue analgesia

Rescue analgesia	Group A (n=20)		Group B (n=20)	
	No	%	No	%
Required	3	15.00	2	10.00
Not required	17	85.00	18	90.00
Total	20	100.00	20	100.00
x2=0.229	Df=1			p=0.633

Table 5: Comparison of Side effects

Side effects	Group A (n=20)		Group B (n=20)	
	No	%	No	%
Yes	10	50.00	7	35.00
No	10	50.00	13	65.00
Total	20	100.00	20	100.00
x2=0.921		Df=1		p=0.337

Table 6: Post mastectomy pain syndrome

PMPS	Group A (n=20)		Group B (n=20)		
	No	%	No	%	
Yes	10	50.00	1	5.00	
No	10	50.00	19	95.00	
Total	20	100.00	20	100.00	
x2=10.200		Df=1			p<0.001

DISCUSSION

This randomized, double blind, prospective study was conducted at Baby Memorial Hospital, Calicut, Kerala on 60 patients undergoing mastectomy from August 2010 to July 2012. Based on computer generated randomization patients were randomized into three groups namely Group A (Patients receiving Tab Tramadol 100 mg) Group B (Patients receiving Tab Pregabalin 150 mg) and Group C (Patients receiving multi drug regime with no premedication). In this study most of the most common age group was more than 60 years in group A and group C (35% and 75% respectively) and in group C, 40% of the women were aged between 46 to 60 years suggesting equal distribution women's age in all the three groups

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(p=0.034). The mean age in group A was 53.05±13.22 years. In group B the mean age was 53.20±12.34 years and in group C the mean age was 52.60 ±14.99 years (p=0.990). These findings suggest that, the mean age in all three groups was comparable.

A cancer incidence and survival in Asian Indian-American patient study reported comparable finding with age range of breast cancer patients from 25 to 79 years and the median age at diagnosis as 52 years.[11] Another study on 50 breast carcinoma patients reported in 2011 from South India observed a median age of 47.5 years at diagnosis (range, 30 to 65 years).[12] A study from Pakistan on 120 breast cancer patients reported a mean age of 47 years at diagnosis (range, 22 to 75 years).[13]

The strongest risk factor for breast cancer is age. The older the woman, the higher her risk. Most women are over the age of 60 years when they are diagnosed although there is evidence that Indian women are more likely to develop breast cancer at earlier ages than their Western counterparts and that breast cancer peaks from ages 45-50 years in India. Recent data comparing Indians and Caucasians in the US show that 29.9% of Indians/Pakistanis living in the US had pre-menopausal breast cancer compared to 18.9% of Caucasians.[14]

Pregabalin is indicated for the treatment of NP. The mechanism of action for pregabalin, insofar as it is currently understood, appears to be the same as that for gabapentin. It binds with high affinity to a2d subunits of voltage-activated calcium channels, blocks Ca2+ influx into nerve terminals, and decreases transmitter release. Thus, the mechanism of action of pregabalin appears to be identical to that of gabapentin. Currently available information supports the view that the pharmacologic profiles for these drugs are indistinguishable: both exert their effects via inhibition of calcium currents mediated by high-voltage-activated channels that include the a2d-1 subunit. This leads to reduced neurotransmitter release and attenuation of postsynaptic excitability.[15]

So far few studies have assessed the effect of pregabalin in the setting of mastectomy. A randomized, double-blinded, placebo-controlled trial was conducted by Kim SY et al,[16] to investigate the efficacy and safety of pregabalin for reducing post-operative pain in patients after mastectomy. The study included 84 women scheduled for elective mastectomy who were randomly assigned to groups that received either pregabalin (75 mg) or placebo, 1 h before surgery and 12 h after the initial dose. Assessments of pain [verbal numerical rating scale (VNRS), at rest and with arm abduction] and side effects were performed at 1, 6, 24 and 48 h post-operatively. After discharge from the hospital, pain was assessed by telephone interview at post-operative 1 week and 1 month. VNRS scores for pain at rest were lower in the pregabalin group (n=42) than the placebo group (n=42) at 1, 24 and 48 h post-operatively (P<0.05). Though findings of the present study were similar with a stud by Kim SY et al it could not be compared as due to the difference in dose, method of administration and method of post operative pain assessment.

CONCLUSION

The present study showed significantly lower mean pain score during the post operative day 2, post operative hospital stay and one month follow up in patients who received Tab Pregabalin 150 mg. Also, few patient required analgesia and had fewer side effects. The incidence of PMPS was significantly low. Hence it may be concluded that administration of pre operative Pregabalin 150 mg provide better analgesia in management of acute pain in mastectomy patient.

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