RANDOMIZED COMPARISON OF EFFICACY, DURATION OF ACTION, ADVERSE REACTIONS AND COST EFFECTIVENESS OF PENTAZOCINE AND TRAMADOL ON RELIEF OF POST OPERATIVE PAIN

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ABSTRACT

Background: Many options are available for the treatment of postoperative pain. By considering patients' preferences and making an individualized assessment of the risks and benefits of each treatment modality, the clinician can optimize the postoperative analgesic regimen for each patient. **Material method:** Female patients of age between 30 to 60 years undergoing elective abdominal and vaginal hysterectomies were included in this study. Hysterectomies performed under spinal anesthesia. Group I constituted patients who received Tramadol 50 mg intravenously; Group II constituted patients who received Pentazocine 30 mg intravenously for post-operative analgesia. The study drugs were administered postoperatively to the patients after the effect of spinal anesthesia wears off and patient complained pain. Before administering the study drug an assessment Visual analogue score of was done, and after giving the study drug, pain was assessed subjectively at 0 minutes and at every 30 minutes for 6 hrs. Each patient's pain was recorded on a scale 0-10 by their response to a visual analogue pain scale. Onset of analgesic action, time at which maximum pain relief occurs, duration of minimal pain, total duration of analgesic action and any acute side effects were noted, the average cost-effective ratio was studied. **Results:** The range of onset of analgesia in both the groups was 10 to 20 minutes, when comparing the mean value of onset of analgesia of the two groups, the mean value of the tramadol group was 14.92 ± 3.89 minutes and that of pentazocine was 14.66 ± 3.23 minutes. The range of duration of analgesia in the two groups was same, which was 5 to 6 hours. The mean duration of postoperative analgesia in the tramadol group was 5.77 ± 0.33 hours, whereas in the pentazocine group it was 5.67 ± 0.39 hours. In tramadol group 45 patients (90%) had only mild pain and 5 patients (10%) had moderate pain. Whereas in pentazocine group 40 (80%) patients had mild pain and 10 patients (20%) had moderate pain. The duration of minimal pain in both groups was 1.5 hours (from 2 to 3.5 hours). The common side effects were nausea, vomiting, headache, drowsiness, respiratory depression. **Conclusion:** We conclude that intravenous tramadol 50 mg and intravenous pentazocine 30 mg produced adequate post operative analgesia and intravenous tramadol 50 mg was safe and more cost effective.

Keywords: Pentazocine; Tramadol; Relief of post operative pain; Efficacy; Duration of action; Adverse reactions.

INTRODUCTION

Uncontrolled postoperative pain may produce a range of detrimental acute and chronic effects. The attenuation of perioperative pathophysiology that occurs during surgery through reduction of nociceptive input to the CNS and optimization of perioperative analgesia may decrease complications and facilitate recovery during the immediate postoperative period and after discharge from the hospital.[1]

The perioperative period is associated with a variety of pathophysiologic responses that may be initiated or maintained by nociceptive input. Although these responses may have had a benefited teleologic purpose, the same response to the iatrogenic nature of modern day surgery may be harmful.[2] Uncontrolled perioperative pain may be potentiated some of these perioperative pathophysiologies and increase patient morbidity and mortality.[3,4]

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Many detrimental pathophysiologic effects occur in the perioperative period and are associated with activation of nociceptors and stress response.[5] Uncontrolled pain may result in activation of the sympathetic nervous system, which can cause a variety of potentially harmful physiologic responses that may adversely influence the extent of morbidity and mortality.[6,7]

Nociceptor activation may also result in several detrimental inhibitor spinal reflexes. Control of the pathophysiologic process associated with acute postoperative pain may attenuate the stress response, sympathetic outflow, and inhibitory spinal reflexes and contribute to improvement in morbidity, mortality and patient reported outcomes (e.g. Health related quality of life, patient satisfaction).[8]

Many options are available for the treatment of postoperative pain, including systemic (i.e. opioid and nonopioid) analgesics and regional (i.e. neuraxial and peripheral) analgesic techniques. By considering patients' preferences and making an individualized assessment of the risks and benefits of each treatment modality, the clinician can optimize the postoperative analgesic regimen for each patient.[9]

Pentazocine, a synthetic partial agonist- antagonist com-

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pound, is one of the most widely available analgesics. It has the theoretical advantage of being safe when administered by trained paramedical personnel, and has been thought to be less addictive and possibly to cause less euphoria than other narcotics. However , its relatively slow onset of action, low potency and poor efficacy, short duration of action and its side effects which include nausea, vomiting and dizziness have prompted the search for new powerful analgesics [10].

Tramadol hydrochloride is a new synthetic centrally acting opioid analgesic with activity similar to that of morphine. However unlike other potent analgesics, tramadol does not induce respiratory depression or cardiovascular effects when administered in therapeutic dosage, furthermore, its dependence potential is low.[11]

Aim: To study the efficacy, duration of action, adverse reactions and cost-effectiveness of Pentazocine and Tramadol on comparative basis for relief of post operative pain.

MATERIAL AND METHODS

Study design: An observational study

Ethical approval: The study was approved by Institutional Ethics Committee of a medical college

Place of research: The study was conducted at the Gynecology Department of a 700 bedded tertiary care teaching hospital in V. M. Govt. Medical College, Solapur

Inclusion criteria: Female patients of age between 30 to 60 years undergoing elective abdominal and vaginal hysterectomies. Hysterectomies performed under spinal anesthesia.

Exclusion criteria: Female patients of age group between 30 to 60 years undergoing emergency hysterectomies. Hysterectomies performed under general and epidural anesthesia. Patients with cardiovascular and respiratory diseases

Grouping: Randomization technique was used for grouping of patients. Group I constituted patients who received Tramadol 50 mg intravenously; Group II constituted patients who received Pentazocine 30 mg intravenously for post-operative analgesia.

Sample size: Total 100 patients were included in the study.

Methodology: The study drugs were administered postoperatively to the patients after the effect of spinal anesthesia wears off and patient complained pain.

Before administering the study drug an assessment Visual analogue score of was done, and after giving the study drug, pain was assessed subjectively at 0 minutes and at every 30 minutes for 6 hrs.

Each patient's pain was recorded on a scale 0-10 by their response to a visual analogue pain scale. The pain score was obtained by measuring the distance in centimeters between the mark made by each patient and the left hand margin of this ten centimeter long visual analogue pain scale.

Parameters were studied: Onset of analgesic action, Time at which maximum pain relief occurs, duration of minimal pain, total duration of analgesic action and any acute side effects were noted.

Duration of analgesia was calculated as the time gap between the administration of the study drug and subsequent dose on demand by the patient or return of pain with the same intensity as that of pre-injection level.

Cost effective study: The average cost-effective ratio = health care costs (in money)/clinical outcome (not in money).

All the patients were observed for the following side effects throughout the study period – nausea and vomiting, pruritus, respiratory depression, hypotension, bradycardia, drowsiness, anxiety and headache etc.

Statistical analysis: Statistical analysis was carried out by 'Z- test' for difference between two means and 'Z-test' for difference between two proportions. P value <0.05 was considered significant.

RESULTS

The age of the patients selected was between 30 to 60 years. The patient distribution based on age is shown in the table 1.

Table 1. Age distribution of patients

Age (years)	Tramadol (%)	Pentazocine (%)
30-40	15 (30)	14 28%
41-50	15(30)%	15(30)
51-60	20(40)	21(42)
100	50	50

Table 2. The surgical procedure they underwent

Surgical procedure	Tramadol	Pentazocine	Total
AH	21	20	41
VH	29	30	59
Total	50	50	100

Table 3. Time of onset of analgesia

Groups	Onset of analgesia (min)		Z test	P value
	Range	Mean±SD		
Tramadol	10-20	14.92±3.89	0.36	>0.05
Pentazocine	10-20	14.66±3.23		

Table 4. Total duration of analgesia

Groups	Duration of analgesia (hrs)		Z test	P value
	Range	Mean±SD		
Tramadol	5-6	5.77±0.33	1.38	>0.05
Pentazocine	5-6	5.67±0.39		

The range of onset of analgesia in both the groups was 10 to 20 minutes, when comparing the mean value of onset of analgesia of the two groups, the mean value of

the tramadol group was 14.92 ± 3.89 minutes and that of pentazocine was 14.66 ± 3.23minutes. The difference between the onset of analgesia in the two groups was statistically nonsignificant.

Table 5. Quality of analgesia

VAS score	Tramadol	Pentazocine	Z test	P value
	No. of pt's (%)	No. of pt's (%)		
0 (no pain)	0	0	-	-
1-3 (mild pain)	45 (90)	40 (80)	1.4	>0.05
4-6 (moderate pain)	5(10)	10(20)	1.4	>0.05
7-9 (severe pain)	0	0	-	-
10 (worst pain imaginable)	0	0	-	-

Table 6: Visual analogue score changes

Time	Tramadol	Pentazocine	Z test	P value
	Mean±SD	Mean±SD		
Before the drug	7.76±0.25	7.79±0.25	-0.612	>0.05
0 min	7.76±0.25	7.79±0.25	-0.612	>0.05
30 min	4.51±0.81	4.79±1.02	-1.520	>0.05
60 min	2.59±1.04	2.99±1.41	-1.614	>0.05
1.5 hr	1.81±0.94	2.15±1.32	-1.491	>0.05
2 hr	1.3±0.9	1.54±1.16	-1.155	>0.05
2.5 hr	1.3±0.9	1.54±1.16	-1.155	>0.05
3 hr	1.3±0.9	1.54±1.16	-1.155	>0.05
3.5 hr	1.3±0.9	1.54±1.16	-1.155	>0.05
4 hr	1.9±1.21	2.48±1.54	-2.094	>0.05
4.5 hr	3.48±1.01	3.8±1.18	-1.462	>0.05
5 hr	5.42±0.83	5.71±1.01	-1.568	>0.05
5.5 hr	6.6±0.80	6.85±0.84	-1.523	>0.05
6 hr	7.73±0.25	7.83±0.27	-1.921	>0.05

The range of duration of analgesia in the two groups was same, which was 5 to 6 hours. The mean duration of postoperative analgesia in the tramadol group was 5.77 ± 0.33 hours, whereas in the pentazocine group it was 5.67 ± 0.39 hours. The difference between the duration of analgesia in the two groups was statistically nonsignificant.

In tramadol group 45 patients (90%) had only mild pain and 5 patients (10%) had moderate pain. Whereas in pentazocine group 40 (80%) patients had mild pain and 10 patients (20%) had moderate pain. The duration of minimal pain (maximal pain relief) in both groups was 1.5 hours (from 2 to 3.5 hours).The difference between the pain relief in the two groups was statistically nonsignificant. Thus, thus this study showed that tramadol and pentazocine were equianalgesics for postoperative pain relief.

In tramadol group, the mean visual analogue score before its administration was 7.76 ± 0.25. The mean visual analogue score recorded at 0 minutes was 7.76 ± 0.25, then it was decreased upto 1.3 ± 0.90 at 2 hours and it was remained constant upto 3.5 hours. The minimal pain remained constant for 1.5 hours. Then it was increased slowly upto 7.73 ± 0.25 at 6 hours. In pentazocine group, the mean visual analogue score before it's administration was 7.79 ± 0.24. The mean visual analogue score at 0 minutes was 7.79 ± 0.24, then it was decreased upto1.54 ± 1.16 at 2 hours and it was remained constant upto 3.5 hours. The minimal pain remained constant for 1.5 hours. Then it was increased slowly upto 7.83 ± 0.27 at 6 hours. The changes between the mean visual analogue score in the two groups were statistically significant at 4 hours and nonsignificant at other time intervals.

Table 7. Side effects

Side effects	Tramadol	Pentazocine	Z test	P value
Nausea	3 (6%)	7 (14%)	1.77	>0.05
Vomiting	0 (0%)	2 (4%)	1.42	>0.05
Drowsiness	0 (0%)	5 (10%)	2.29	<0.05
Headache	0 (0%)	0 (0%)	-	-
Respiratory depression	0 (0%)	0 (0%)	-	-
TOTAL	3(6%)	14(28%)		

Cost-effectiveness: As per the DMER rate contract rates, cost of tramadol 50 mg/ampoule was 1.84 rupees and the cost of pentazocine 30mg/ampoule was 3.51rupees. We had measured clinical outcome as patients having minimal or no pain and measured cost as only the direct cost of the drugs. Tramadol was effective in 45 out of 50 (90%) patients in relieving the postoperative pain. Pentazocine was effective in 40 out of 50 (80%) patients in relieving postoperative pain.

DISCUSSION

In the present study the onset and duration of analgesia were studied by recording the visual analogue score. This study was continued up to the 6 hours after administration of the study drug. During the study period any acute side effects observed were recorded.

Carilo et al (1992) compared tramadol 100 mg versus tramadol 50 mg for post operative pain relief following major orthopedic surgery. They concluded that onset of action of 50 mg tramadol was 18 minutes and that of 100 mg was 11 minutes.[12]

In the present study mean onset of analgesia with intravenous tramadol 50 mg was 14.92 ±3.89 and the mean onset of analgesia with intravenous pentazocine 30 mg was 14.66±3.23. Piepenbroack S et. al (1983) compared intravenous buprenorphine 0.3mg and intravenous pentazocine 30mg for postoperative pain relief and con-

cluded that mean duration of action of pentazocine was 2.35±0.24 hours (median 2 hours; range 0.5-5 hours) and the duration of action.[13]

In the present study the mean duration of action of tramadol was 5.77±0.33 hours and the mean duration of action of pentazocine was 5.67±0.39 hours.

Mondal et. Al (1996) compared intravenous tramadol 50 mg with intravenous pentazocine 30 mg for postoperative pain relief in 75 elective abdominal surgeries. Pain scores and overall patient satisfaction were similar in both the groups so the author concluded that tramadol 50mg intravenous and intravenous pentazocine 30mg were equianalgesics for postoperative analgesia. The authors observed that 4% patients had vomiting and 4% complained of dryness of mouth in tramadol group and in pentazocine group 70% patients complained of nausea and 32% patients had vomiting.[14]

Tulsiani KL et al (1997) compared intravenous tramadol hydrochloride (1mg/kg) and intravenous pentazocine lactate (0.5mg/kg) for post operative pain relief in 100 patients aged between 20-60 years after major surgical procedures and concluded that intravenous tramadol 50mg was superior than intravenous pentazocine 30mg for postoperative analgesia. The authors observed that, in the immediate postoperative period (within 6 hours), in the pentazocine group 20 (40%) patients had tachycardia, 10 (20%) patients had rise in blood pressure, 5 (10%) patients had nausea, vomiting and drowsiness, while 8 (16%) patients had respiratory depression, that is decrease in respiratory rate and 10 (20%) patients had fall in the oxygen saturation. [11]

In this present study pain scores and overall quality of analgesia were similar in both the groups. Thus the present study found that tramadol 50 mg IV and pentazocine 30 mg IV were equianalgesics for postoperative pain relief.

Faisal Shamin compared the efficacy and side effects related to tramadol with pethidine in patient controlled intravenous analgesia (PCSA) after total abdominal hysterectomies. The analgesia achieved in tramadol group was comparable to pethidine. The incidence of nausea and vomiting was similar in both groups tramadol causes significantly less sedation than pethidine ($P<0.05$).[11]

In the present study, in tramadol group the only side effect reported was nausea in 3 (6%) patients. In pentazocine group 7 (14%) patients had nausea, 2 (4%) patients had vomiting, 5 (10%) patients had drowsiness.

The cost of tramadol 50mg/ampule as per DMER rate contract was 1.84 rupees and it was effective in 45 out of 50 patients for relief of post operative pain. The cost of pentazocine 30mg/ampoule as per DMER rate contract was 3.51 rupees and it was effective in 40 out of 50 patients for relief of post operative pain. The average cost effectiveness ratio of tramadol was 2.04 rupees per dose per patient for complete or near complete relief of post operative pain and the average cost effectiveness ratio of pentazocine was 4.3875 rupees per dose per patient for complete or near complete relief of postoperative pain. Thus by comparing the average cost effectiveness ratio of tramadol and pentazocine the present study found that tramadol was more cost effective than pentazocine for post operative pain relief.

CONCLUSION

Both intravenous tramadol 50 mg and intravenous pentazocine 30 mg produced equivalent analgesia. However intravenous tramadol has added advantages like it have lower incidence of side effects and more cost effective. Therefore we conclude that intravenous tramadol 50 mg and intravenous pentazocine 30 mg produced adequate post operative analgesia and intravenous tramadol 50 mg was safe and more cost effective.

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Conflict of interest: Nil

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