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Effect of Pre-Emptive and Intraoperative Intravenous Paracetamol on Post Operative Analgesia in Laparoscopic Sterilisation

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Abstract: ***Background:*** *To compare the effects of pre-emptive and intraoperative intravenous paracetamol on post operative analgesia in laparoscopic sterilisation.* ***Methods:*** *62 patients who underwent laparoscopic sterilisation were divided into two groups. One group received pre-emptive intravenous paracetamol and another group received intraoperative intravenous paracetamol.* ***Results:*** *There is no significant difference in analgesia between both the groups.* ***Conclusion:*** *Intravenous paracetamol can be administered preoperatively or intraoperatively during laparoscopic sterilisation for analgesia.*

Keywords: pain; Pre-emptive analgesia; VAS score; analgesia; paracetamol.

1. Introduction

Pain is an extensive public health problem globally. Earlier analgesia was only restricted to peri operative periods, but now it is well understood that if pain is not properly controlled it may lead to delayed recovery and chronic pain syndrome. Pre-emptive analgesia is very important as it controls pain before it starts or blocks initiation of pain pathway [1,2]. This study attempts to evaluate intravenous paracetamol administration as an effective pre-emptive analgesia in laparoscopic sterilisation.

Though laparoscopic surgeries are associated with less severe and less prolonged discomfort when compared to their counterpart open procedure, they still cause considerable postoperative pain. Post-operative pain in laparoscopic surgeries is mainly due to the operative port site and intraperitoneal CO_2 gas. Appropriate management of postoperative pain reduces the hospital stay as well as related complications [3].

Pre-emptive analgesia is initiated before surgery which acts by preventing the establishment of central sensitization due to the incisional and inflammatory injuries during surgery and in the early post-operative period. It reduces the incidence of immediate post-operative pain and also can block development of chronic pain by reducing the altered central sensory processing [4,5].

Paracetamol, an acetanilide derivative, is a well proven analgesic which is safe and well tolerated. It acts by inhibiting prostaglandins and activation of descending serotonergic inhibitory pathways but clinical effects are mostly owing to its central action. Intravenous administration yields rapid and predictable therapeutic plasma concentrations [6,7].

Pre-emptive paracetamol administration is not a routinely used mode of analgesia. If found beneficial in this study, pre-emptive paracetamol administration may prolong post-operative analgesia, decrease intraoperative opioid requirements, intubation and extubation stress response. Also paracetamol is more economical compared to other current analgesic modes with less side effects.

2. Materials and methods

Aims and Objectives
To assess the effect of pre-emptive intravenous paracetamol on postoperative pain scores and analgesic requirements in patients undergoing laparoscopic sterilisation compared with a group of patients receiving intraoperative intravenous paracetamol.

Design:
Prospective observational study

Sample size:
Total sample size was 62.

Consecutive sampling method was followed. Each patient who underwent laparoscopic sterilisation during the study period and satisfying inclusion criteria was selected for the study.

Methodology:
An institution based prospective observational study was conducted among 62 women who underwent laparoscopic sterilisation in the study period from August 2019 to November 2021.

Selection criteria:
- Patients who are willing to give consent for the study.

- Patients of age 20-45.
- Patients belonging to ASA 1 or 2.
- All patients who underwent elective laparoscopic sterilisation and received intravenous paracetamol as per the practice in our institution.

Exclusion criteria:

- Patients with known allergy to paracetamol.
- Patients with contraindication to paracetamol or to NSAIDs (liver disease).
- Patients those on treatment by steroids, NSAIDs, or opioids.
- Patients who developed any complications in the intraoperative or immediate postoperative period.

Statistical Analysis:

Data was collected using a predesigned semi structured proforma. Patients were given intravenous paracetamol either pre-emptive or intraoperatively according to the preference of the attending consultant. Pain was assessed using VAS scores at 15, 30, 45, 60, 120 and 360 minutes post-operative. All collected data was entered into Microsoft Office Excel 2019 and analysis was done using SPSS version 20. Entire study group was included for the analysis of general characteristics like age, VAS scores, post-operative shivering, need of rescue analgesics, and stress response during extubation. The VAS scores were then reanalysed after dividing into groups according to the time of administration of paracetamol and were compared against each other for any statistically significant differences. VAS score being a categorical variable, median was chosen as the measure of central tendency and Mann Whitney U test was used as test of significance. Chi-square tests were done for any differences in the need of rescue analgesics and stress response during extubation between the two groups. One way ANOVA was performed for any association between age and the VAS scores at different postoperative intervals. For all tests, p value <0.05 was considered a statistically significant difference.

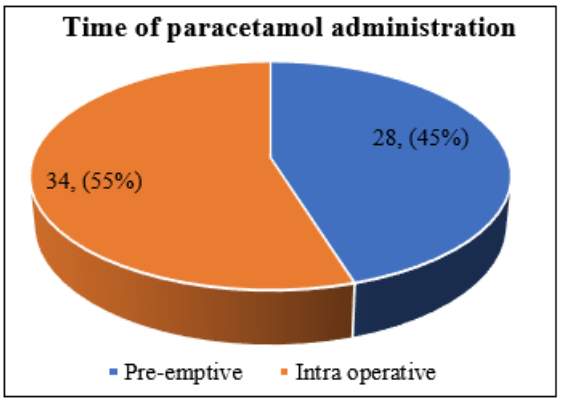
3. Results

The study included 62 subjects who underwent laparoscopic sterilisation at our hospital during the period 2019 - 2021. The study group included subjects in the age range 22-39 years with a mean age of 27.71 +/- 3.452 years. The average duration of surgery lasted around 48.55 minutes.

Among the study participants, 34 patients (54.8%) received 1 gm intravenous paracetamol intraoperatively and 28 patients (45.2%) received it pre-emptively 30 minutes prior to the incision.

Table 1: Grouping of patients according to time of administration of paracetamol

Time of paracetamol administration	No. of patients	Percentage
Pre-emptive	28	45.2%
Intra operative	34	54.8%



The age distribution of patients among the two study groups were assessed for any statistical difference to ensure that they were comparable (t test: p value 0.77)

Table 2: Group wise age distribution of patients

Time of paracetamol administration	No. of patients	Mean Age	Std. Deviation	Std. Error Mean
Intra operative	34	27.82	3.424	.587
Pre-emptive	28	27.57	3.543	.669

(t test: t value 0.284, p value 0.77)

One way ANOVA was performed for any association between age and the VAS scores at different post-operative time intervals. Generally higher pain scores were noticed in younger individuals even though statistically significant relation could be demonstrated only in VAS scores at 30 and 60 minutes post-operatively (p value 0.048 and 0.038 respectively).

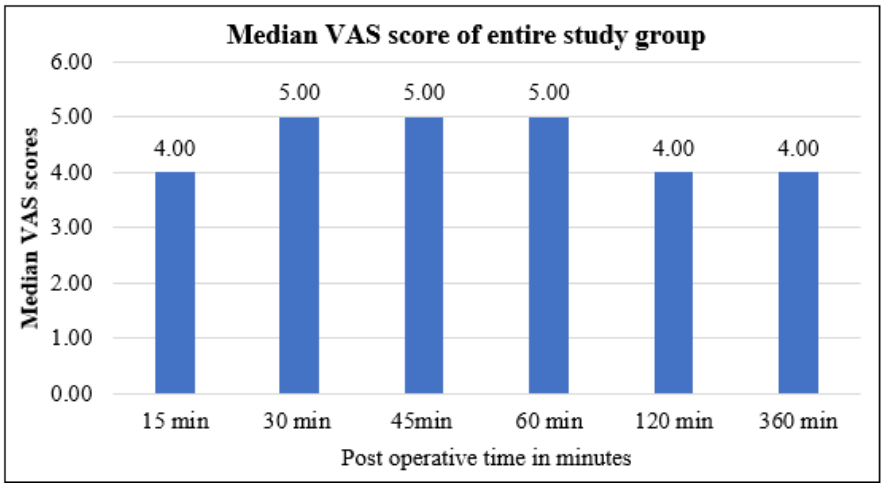
Table 3: Association between age and post-operative pain scores

ANOVA (age and post-operative VAS scores)		
Post-operative VAS scores	F	Significance (p value)
VAS 15min	.963	.500
VAS 30min	1.946	.048
VAS 45min	.493	.918
VAS 60min	2.035	.038
VAS 120min	.291	.991
VAS 360min	1.710	.089

The VAS pain scores of the study groups were assessed at 15, 30, 45, 60, 120 and 360 minutes post operatively. Median was chosen as the measure of central tendency, VAS score being an ordinal variable.

Table 4: Median post-operative VAS scores of the entire study group

Post-operative time	15 min	30 min	45 min	60 min	120 min	360 min
Median VAS score	4.00	5.00	5.00	5.00	4.00	4.00
Inter quartile range	3-5	4-6	4-5	4-5	4-5	4-5



The respective VAS scores at the post-operative time periods were also assessed after dividing into groups according to the time of paracetamol administration

Table 5: Median VAS scores in patients grouped according to time of paracetamol administration

		15 min	30 min	45 min	60 min	120 min	360 min
Intra-operative paracetamol administration	Median VAS score	4	5	5	5	4	4
	Inter quartile range	4-5	4-6	4-5	4-5.25	4-5	4-5
Pre-emptive paracetamol administration	Median VAS score	4	5	5	4	4	4
	Inter quartile range	3-5	4-6	4-5	4-5	4-5	4-5

Table 6: Frequency distribution of VAS pain scores at 15 minutes post-operatively among the two groups.

	No: of patients	
VAS score (15 min)	Intraoperative paracetamol	Pre-emptive paracetamol
3	7	10
4	18	9
5	9	7
6	0	2
7	0	0
Total	34	28

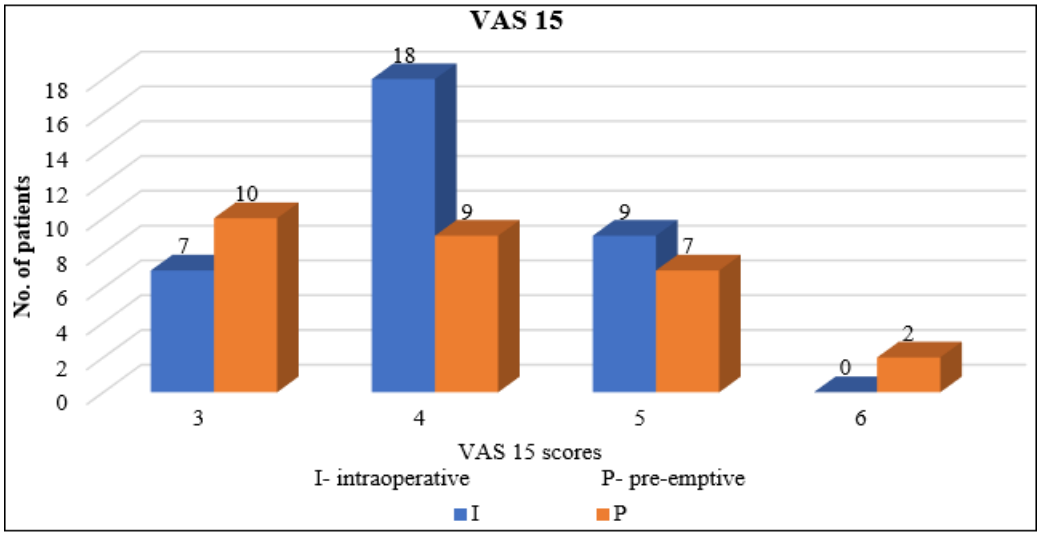


Table 7: Frequency distribution of VAS pain scores at 30 minutes postoperatively among the two groups.

	No: of patients	
VAS score (30min)	Intraoperative paracetamol	Pre-emptive paracetamol
3	1	2
4	9	7
5	14	11
6	8	5
7	2	3
Total	34	28

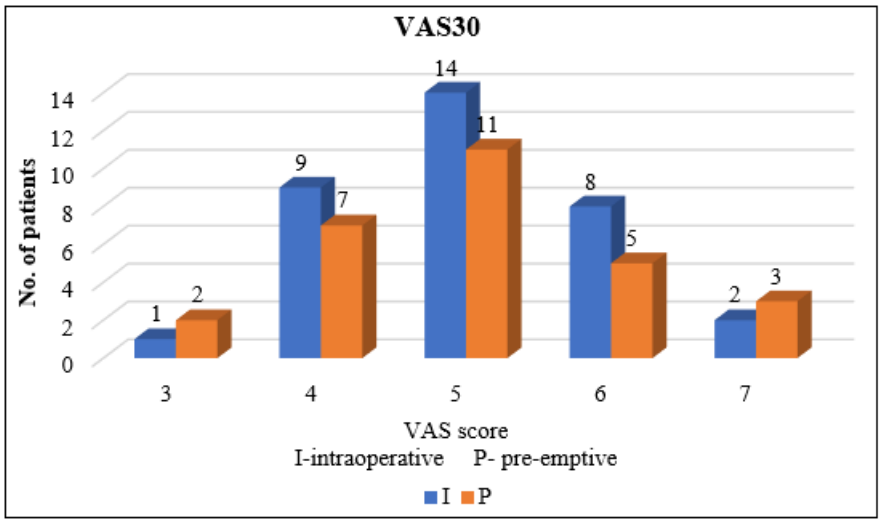


Table 8: Frequency distribution of VAS pain scores at 45 minutes postoperatively among the two groups.

	No: of patients	
VAS score (45min)	Intraoperative paracetamol	Pre-emptive paracetamol
3	0	0
4	9	12
5	20	12
6	5	4
7	0	0
Total	34	28

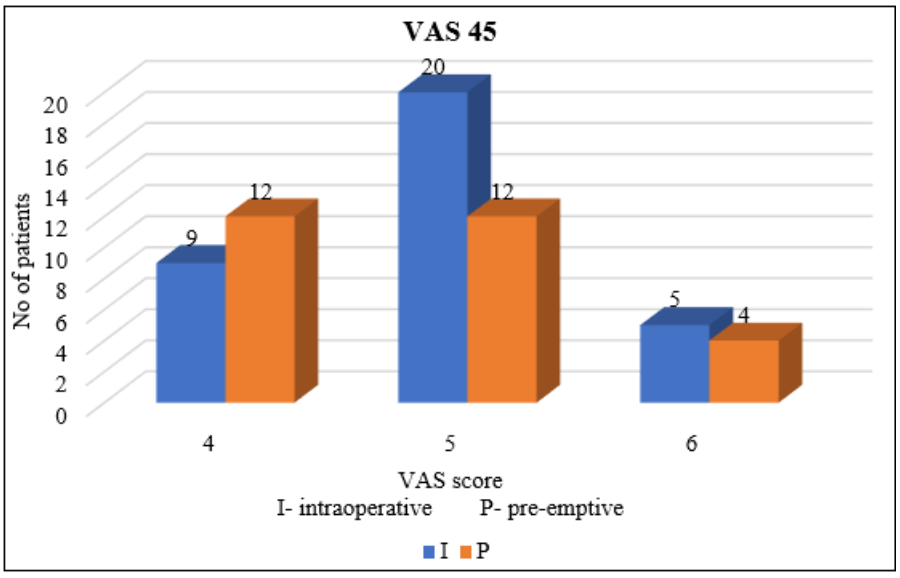


Table 9: Frequency distribution of VAS pain scores at 60 minutes postoperatively among the two groups.

	No: of patients	
VAS score (60min)	Intraoperative paracetamol	Pre-emptive paracetamol
3	0	0
4	13	15
5	13	8
6	3	2
7	5	3
Total	34	28

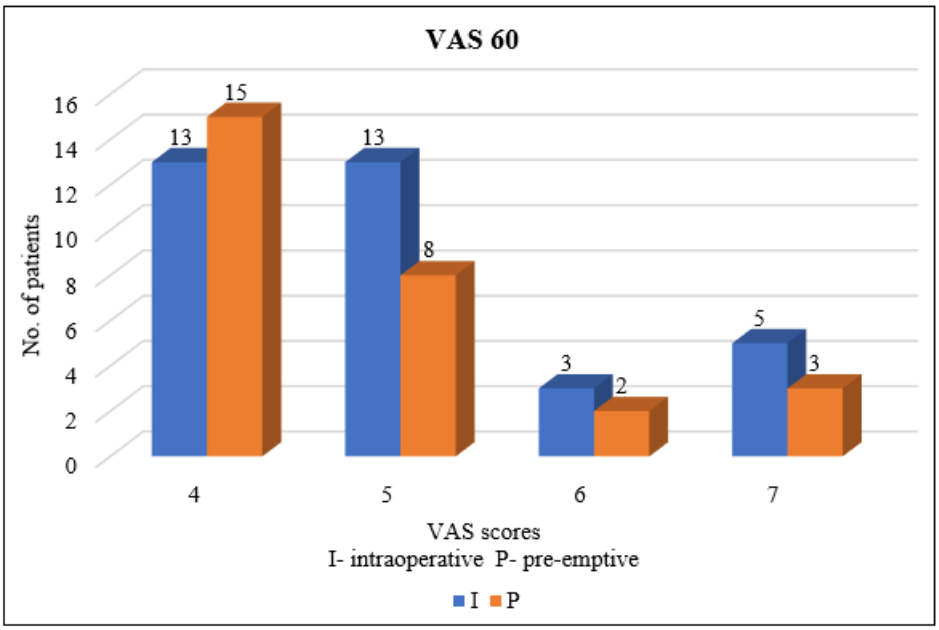


Table 10: Frequency distribution of VAS pain scores at 120 minutes postoperatively among the two groups.

	No: of patients	
VAS score (120min)	Intraoperative paracetamol	Pre-emptive paracetamol
3	5	3
4	19	15
5	7	9
6	2	0
7	1	1
Total	34	28

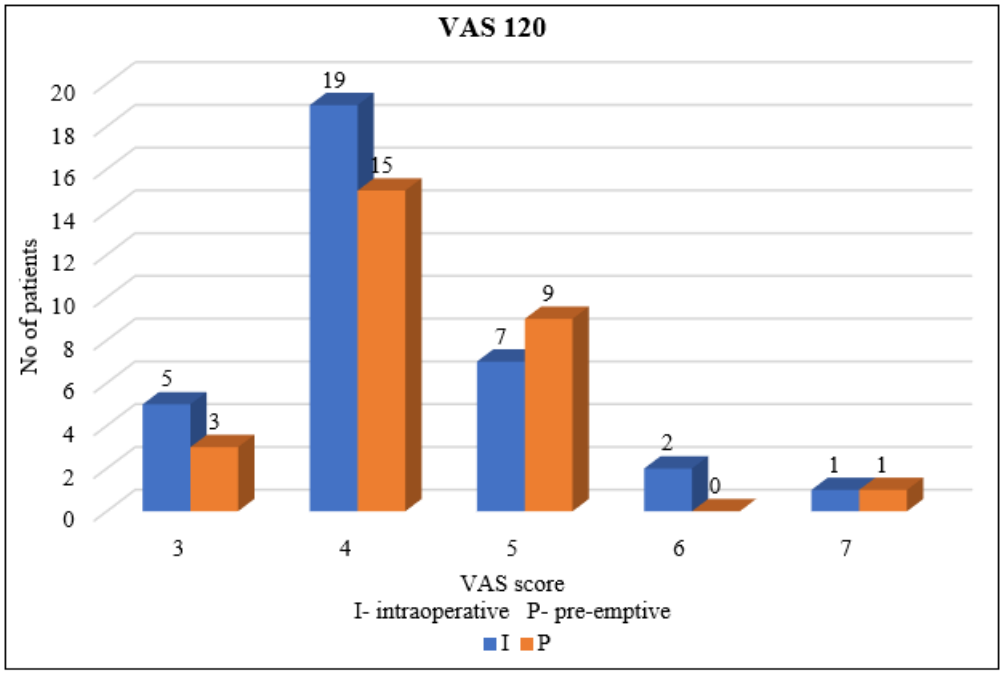
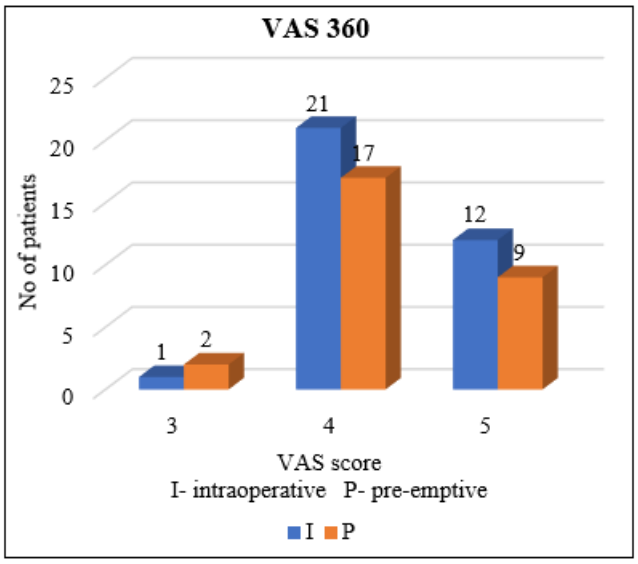


Table 11: Frequency distribution of VAS pain scores at 360 minutes postoperatively among the two groups.

	No of patients	
VAS score (360min)	Intraoperative paracetamol	Pre-emptive paracetamol
3	1	2
4	21	17
5	12	9
6	0	0
7	0	0
Total	34	28



Mann Whitney U test was performed for the assessment of any difference between the two groups (intraoperative and pre-emptive paracetamol administration) as VAS score is an ordinal variable.

Table 12: Comparison of post-operative VAS scores between the two groups (Mann-Whitney U).

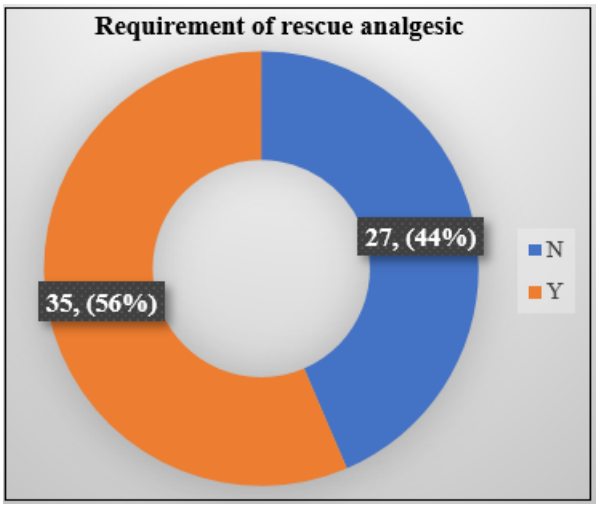
VAS score	15min	30min	45min	60min	120min	360min
Mann-Whitney U	453.500	465.500	408.000	403.000	446.000	448.500
Significance (2-tailed)	0.734	0.876	0.288	0.267	0.639	0.649

Mann Whitney U test done between the VAS scores at 15 min , 30 min, 45 min, 60 min, 120 min and 360 minutes post-operatively failed to show any statistically significant differences between the pain scores of patients given pre-emptive versus intraoperative administration of paracetamol.

Rescue analgesic was required in 56% of patients in the study group during the assessment period (6 hrs post procedure)

Table 13: Requirement of rescue analgesic among the entire study group

Requirement of rescue analgesic	No of patients	Percent
No	27	43.5
Yes	35	56.5
Total	62	100.0

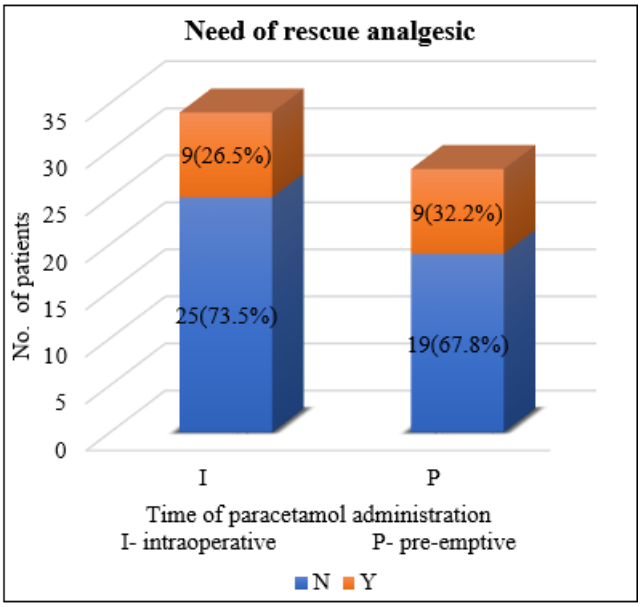


When compared among groups, 26.5% patients in the intra operative group and 32.2% among the pre-emptive group required rescue analgesia which does not amount to any statistically significant difference (chi square value P=0.20)

Table 14: Need of rescue analgesia among the two study groups.

			Time of paracetamol administration		Total
			Intraoperative	Pre-emptive	
No. of patients	Need of rescue analgesic	No	12	15	27
		Yes	22	13	35
	Total		34	28	62

Pearson chi-square value 0.149; p value 0.2

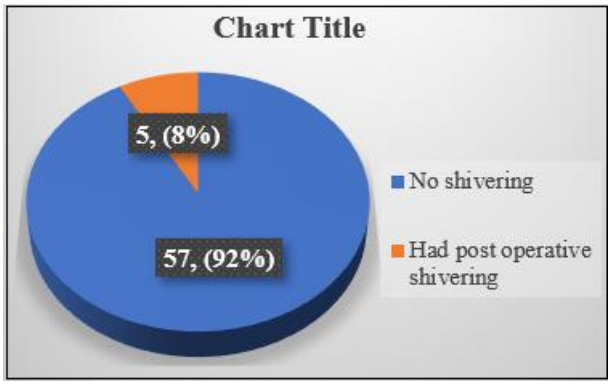


Post-operative shivering was considerably less in the study group as only 8.1% had shivering during the assessment

period. As the overall incidence of post-operative shivering was very less in the study group statistical tests for difference between the groups were not performed.

Table 15: Post-operative shivering in the entire study group

Post-operative shivering	No: of patients	Percentage
No shivering	57	91.9
Had shivering	5	8.1
Total	62	100.0



Among the entire study group 15(24.2%) patients developed a stress response during extubation which could indicate presence of significant pain.

There was no statistically significant difference in the occurrence of stress response during extubation between the two groups (intraoperative versus pre-emptive paracetamol administration). The Pearson chi-square test performed yielded a p value= 0.893

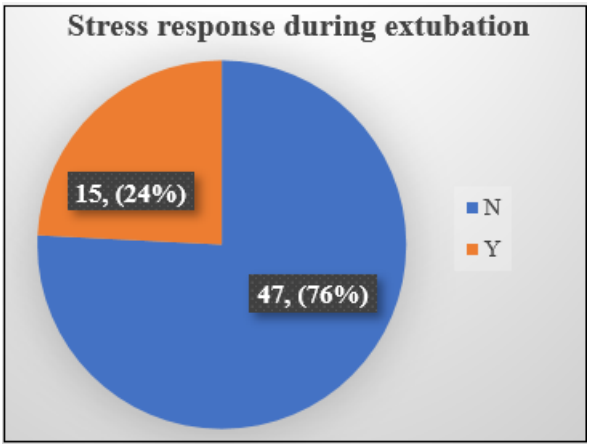


Table 16: Stress response during extubation among the two groups

	Time of paracetamol administration	Stress response during extubation		Total
		No	Yes	
No. of patients	Intraoperative	26	8	34
	Pre- emptive	21	7	28
Total		47	15	62

Pearson chi-square value 0.18; P value – 0.893

The study also looked into any possible adverse effects like nausea, vomiting, drowsiness, giddiness etc., but were not noticed among the study participants in the immediate post-operative period.

4. Discussion

Our study included a total of 62 participants who underwent laparoscopic sterilisation grouped according to the time of administration of intravenous paracetamol with an average age of 27.71 years. The median VAS scores at 15, 30, 45, 60, 120, 360 minutes were 4, 5,5,5,4 and 4 respectively. In comparison, a study by Mesut Polat et al.(Turkey) with an average age of 36.9±4.5 years had mean VAS scores of 7.64, 5.75, 4.99 at 30 , 60, 120 minutes respectively. The lower pain scores during the early post-operative period in our study subjects was possibly related to the practice of using opioids (fentanyl) intraoperatively in our institution [8].

The present study showed a decreasing trend in pain scores as the age of patient increases but a statistically significant difference was seen only in VAS scores at 30 and 60 minutes post-operatively. A study by Jacqueline F. M. et al. which included 11,510 patients with mean age of 62 years who underwent various surgeries also demonstrated a definite decrease in the mean pain scores with age [9]. In contrast our study population includes only a relatively narrow age range of 22-39 years, as the study includes only patients who underwent laparoscopic sterilisation, hence the minimal change with age.

Pain score comparisons against other studies for pre-emptive administration of paracetamol could not be done due to lack of corresponding studies.

The expected benefit of pre-emptive analgesia is in preventing the development of chronic post-operative pain [2]. The lack of demonstrable significant differences between pre-emptive and intraoperative administration of paracetamol in the present study group may be explained by few factors. 1. The routine use of opioids (fentanyl) intraoperatively which ensures good pain control in the immediate post-operative period 2. Due to logistical issues the study could not include longer follow-up assessment for any difference in the development of persistent post-operative pain. 3. The liberal use of NSAIDs in the post-operative ward on a routine basis and not as a rescue agent.

A study by A. Sreenivasalu et al. in their study on effect of pre-emptive intravenous paracetamol in laparoscopy surgery demonstrated significantly less pain in patients receiving paracetamol pre-emptively at 15 minutes and 30 minutes [10]. Similarly Choudhuri and Uppal et al. demonstrated significant opioid sparing effect after administration of pre-emptive intravenous paracetamol in laparoscopic cholecystectomy [10,11]. In a study by Salihoglu et al. demonstrated similar decrease in pain scores and requirement of rescue analgesics in the group receiving pre-emptive paracetamol [10,12]. But both the available comparable studies used paracetamol only in the study group and the control group received placebo. Arici et al showed that patients who received intravenous acetaminophen within 30 minutes of induction of anaesthesia had significantly less postoperative pain and used significantly less opioids [13].

In our study a lack of demonstrable statistical difference in median pain scores may also be attributed to the administration of the same drug pre-emptively and

intraoperatively immediately after start of the surgical procedure in the respective groups.

5. Conclusion

As per our study laparoscopic sterilisation is associated with VAS pain scores of moderate severity in the immediate postoperative period despite use of opioid analgesics. The study could not demonstrate any significant differences between the pain scores, requirement of rescue analgesics, and stress response during extubation, of patients receiving pre-emptive and intraoperative paracetamol intravenously. Pain scores showed decreasing trend with age of the patient, demonstrable at post-operative pain scores of patients at 30 minutes and 60 minutes.

Declaration of interest
None declared.

Funding
None declared.

Ethical approval
The study was approved by the Institutional Ethics Committee.

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