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ORIGINAL RESEARCH

Prophylactic isopropyl alcohol inhalation and intravenous ondansetron versus ondansetron alone in prevention of post operative nausea and vomiting in patients undergoing laparoscopic surgeries- a prospective randomised comparative study

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ABSTRACT

INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most common problems after general anaesthesia causing post operative surgical complications, delayed discharge, psychological and physiological distress for the patients[1].

There are many predictive Risk factors that contribute to PONV like Female gender, history of motion sickness, history of PONV[2] ,Age, Menstruation, non smoker, general anaesthesia, opioids, Duration of surgery, Laparoscopic and gynaecological surgeries.

These patients are routinely screened to reduce the morbidity associated with PONV.[2,3]

The Mechanism of PONV is complex as there are 3 major pathophysiological pathways involved in PONV, CTZ, vestibulocochlear pathway and gastrointestinal pathway.

The specific neurotransmitters serotonin and dopamine have been identified to trigger the emesis in CTZ.

Many medications and Multimodal antiemetic therapy have been implemented in the treatment of PONV.[3]

Serotonin receptor antagonist, ondansetron has been shown to be effective at treating and preventing PONV[4].It inhibits the serotonin receptors in the gastrointestinal tract and causes selective antagonism of the serotonin receptor sites and the vagal afferent nerves and blocks the 5HT3 binding sites at the gastrointestinal tract. and CTZ[5,6].

Current pharmacological antiemetic agents are not without potential adverse effects. Recent studies have suggested the use of aromatic inhalation of 70 % isopropyl alcohol which is known to interfere or influence neurotransmitters at CTZ[6].

Therefore, the purpose of this study is to evaluate the effectiveness of inhaled 70% isopropyl alcohol with ondansetron versus ondansetron alone in controlling PONV in patients undergoing laparoscopic surgeries under general anaesthesia.

AIM OF THE STUDY

• To determine the effectiveness of combining prophylactic inhalation of isopropyl alcohol with iv ondansetron versus ondansetron alone in prevention of PONV.

METHODOLOGY

Approval from the institutional ethical committee obtained for the prospective randomized study. A sample size of 80 patients was computed using power analysis based on a previous study with 40 in each group. These patients were either ASA 1 OR 2 category posted for elective laparoscopic surgeries.

Patients were excluded if the surgical time exceeded 2 hours, any intraoperative event such as hypotension or bleeding, known smokers, pregnant females, history of PONV or menstruating females.

Following the written informed consent, all the patients received detailed information on treatment and the requirements of the study. In addition, the patients were instructed on the use of the VNRS scale (0-10). A baseline VNRS was obtained in which 0 indicated no nausea and 10 indicated worst imaginable nausea.

Demographic data was noted during the pre-anaesthesia evaluation.

On arrival to the operation room the anaesthesia provider applied standard monitoring devices like NIBP, ECG, SPO_2.

We used a computer-generated random sampling method to process and assign patients to either group A or group B.

Both the anaesthesiologist and the patient were blinded.

Group A received isopropyl alcohol vapors from a commercially available 70% isopropyl alcohol pad immediately prior to pre oxygenation.

The anaesthesia provider removed the isopropyl alcohol pad from the package and held it approx. 0.5 inch from the nares and instructed the patient to take 3 deep nasal inhalation of the isopropyl alcohol vapors.

The group B patients received a normal saline soaked gauze as a control with the same procedure.

Both the groups followed the same preoperative and postoperative instruction and drug protocol except the test drug. A 4mg IV dose of injection ondansetron was administered 15 to 20 mins prior to induction in both the groups. The anaesthesiologist recording the post operative VNRS scale was blinded.

Induction of general anaesthesia was performed. Patient premedicated with glycopyrrolate and midazolam, pre induction with inj.fentanyl 2µg/ml IV. Induction with intravenous lidocaine (0.5-1mg/kg) and propofol (1.5 -2mg/kg), injection vecuronium 0.1 mg/kg IV and intubation done by an expert anaesthesiologist with an experience of 5 years in clinical anaesthesia.

Maintenance was done with oxygen, air and Isoflurane (0.2-0.8%).

Intra operative analgesics were administered as per the anaesthesia provider's choice.

All the intra operative medications were recorded.
A nausea VNRS score was obtained for all the patients on arrival to PACU and at arrival to the postoperative surgical ward which is ideally 2 hours after arrival to PACU.
For purposes of the study an emetic event was considered vomiting or retching. Nausea was defined as an unpleasant sensation associated with awareness of urge to vomit.
VNRS scores were also obtained at the onset of any episode of nausea and inj.Metoclopramide 10mg IV SLOW was given as a rescue antiemetic.
Subsequent VNRS was recorded at 15 minutes and 30 minutes after the nausea event.
Further patients were assessed every 4 hours for 24 hours.
Additional data collected included time spent in PACU, time spent in postoperative surgical ward, incidence of pain and rescue analgesic given.
The patients were provided with a data collection proforma and instructions. They rated their satisfaction with nausea control at the end of 24 hours using a satisfaction assessment scale called Likert's scale and scores were given as follows:
1.Totally dissatisfied, 2. Dissatisfied, 3. Somewhat satisfied, 4. Satisfied, 5. Totally satisfied
Statistical analysis was performed using SPSS software. Data was analyzed using a student's *t* test for parametric data and Mann Whitney *U* test for a non parametric data. Incidental data were analyzed using chi square test. A *P* value of 0.05 or less was considered significant.

RESULTS

A total of 80 patients were recruited for the study (40 in each group). Both the groups were similar with respect to age, risk of PONV, type of surgery, duration of anaesthesia and surgery.

TABLE 1: Age

Age in years –Frequency distribution of patients in two groups studied

Age in Years	Group A	Group B	Total
<40	9(22.5%)	4(10%)	13(16.3%)
40-50	20(50%)	13(32.5%)	33(41.3%)
50-60	5(12.5%)	11(27.5%)	16(20%)
>60	6(15%)	12(30%)	18(22.5%)
Total	40(100%)	40(100%)	80(100%)
Mean ± SD	46.97±9.48	53.42±10.30	50.20±10.36

Demographic data and perioperative information.
No significant difference in the distribution of PONV were determined between groups
P value significant Only at 4th hour

TABLE 2: Gender

Frequency distribution of patients in two groups studied:

Gender	Group A	Group B	Total
Female	19(47.5%)	19(47.5%)	38(47.5%)
Male	21(52.5%)	21(52.5%)	42(52.5%)
Total	40(100%)	40(100%)	80(100%)

P=0.823, Not Significant, Chi-Square Test

TABLE 3:

Weight

Weight (Kg)- Frequency distribution of patients in two groups studied

Weight(Kg)	Group A	Group B	Total
50-60	3(7.5%)	3(7.5%)	6(7.5%)
61-70	17(42.5%)	12(30%)	29(36.3%)
>70	20(50%)	25(62.5%)	45(56.3%)
Total	40(100%)	40(100%)	80(100%)
Mean ± SD	72.42±9.56	73.47±10.34	72.95±9.91

P=0.639, Not Significant, Student t Test

TABLE 4:
Smoking Status- Frequency distribution of patients in two groups studied

Smoking Status	Group A	Group B	Total
No	35(87.5%)	34(85%)	69(86.3%)
Yes	5(12.5%)	6(15%)	11(13.8%)
Total	40(100%)	40(100%)	80(100%)

P=1.000, Not Significant, Chi-Square Test

TABLE 5:
PONV risk factors- Frequency distribution of patients in two groups studied

PONV risk factors	Group A	Group B	Total
1	0(0%)	0(0%)	0(0%)
2	0(0%)	0(0%)	0(0%)
3	7(17.5%)	2(5%)	9(11.3%)
4	13(32.5%)	13(32.5%)	26(32.5%)
5	13(32.5%)	16(40%)	29(36.3%)
6	7(17.5%)	9(22.5%)	16(20%)
Total	40(100%)	40(100%)	80(100%)

P=0.342, Not Significant, Chi-Square Test

TABLE 6:
Surgery time and anaesthesia time (mins)-
Frequency distribution of patients in two groups studied

Variables	Group A	Group B	Total	P Value
Surgery time(hrs)				
• 1-30	0(0%)	0(0%)	0(0%)	0.928
• 31-60	23(57.5%)	22(55%)	45(56.3%)	
• 61-90	14(35%)	16(40%)	30(37.5%)	
• 91-120	2(5%)	1(2.5%)	3(3.8%)	
• 121-150	1(2.5%)	1(2.5%)	2(2.5%)	
Anaesthesia time(min)				
• 1-30	0(0%)	0(0%)	0(0%)	0.216
• 31-60	9(22.5%)	5(12.5%)	14(17.5%)	
• 61-90	25(62.5%)	24(60%)	49(61.3%)	
• 91-120	3(7.5%)	9(22.5%)	12(15%)	
• 121-150	3(7.5%)	2(5%)	5(6.3%)	
Total	40(100%)	40(100%)	80(100%)	

Chi-Square Test/Fisher Exact Test

TABLE 7:

Incidence of post operative nausea and vomiting and rescue antiemetic requirement - Frequency distribution of patients in two groups studied

Variables	Group A	Group B	Total	P Value
Incidence of PONV				
• No	32(80%)	32(80%)	64(80%)	0.773
• Yes	8(20%)	8(20%)	16(20%)	
Rescue antiemetic				
• No	35(87.5%)	32(80%)	67(83.8%)	0.543
• Yes	5(12.5%)	8(20%)	13(16.3%)	
Total	40(100%)	40(100%)	80(100%)	

Chi-Square Test/Fisher Exact Test

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TABLE 8:

VNRS SCORE- Frequency distribution of patients in two groups studied

VNRS SCORE	Group A	Group B	Total	P Value
ON ARRIVAL TO PACU				
• 1-3	0(0%)	0(0%)	0(0%)	0.062+
• 4-6	10(25%)	19(47.5%)	29(36.3%)	
• 7-10	30(75%)	21(52.5%)	51(63.8%)	
4HRS				
• 1-3	0(0%)	0(0%)	0(0%)	0.021*
• 4-6	3(7.5%)	12(30%)	15(18.8)	
• 7-10	37(92.5%)	28(70%)	65(81.3%)	
8HRS				
• 1-3	0(0%)	0(0%)	0(0%)	0.068+
• 4-6	3(7.5%)	10(25%)	13(16.3%)	
• 7-10	37(92.5%)	30(75%)	67(83.8%)	
12HRS				
• 1-3	0(0%)	0(0%)	0(0%)	0.193
• 4-6	3(7.5%)	8(20%)	11(13.8%)	
• 7-10	37(92.5%)	32(80%)	69(86.3%)	
16HRS				
• 1-3	0(0%)	0(0%)	0(0%)	0.431
• 4-6	2(5%)	5(12.5%)	7(8.8%)	
• 7-10	38(95%)	35(87.5%)	73(91.3%)	
2OHRS				
• 1-3	0(0%)	0(0%)	0(0%)	0.431
• 4-6	2(5%)	5(12.5%)	7(8.8%)	
• 7-10	38(95%)	35(87.5%)	73(91.3%)	
24HRS				
• 1-3	0(0%)	0(0%)	0(0%)	0.358
• 4-6	1(2.5%)	4(10%)	5(6.3%)	
• 7-10	39(97.5%)	36(90%)	75(93.8%)	

Total	40(100%)	40(100%)	80(100%)	

Chi-Square Test/Fisher Exact Test

The simplified PONV score was significantly lower in group A(IPA) at 4th hour postoperatively.
VNRS score was also significantly lower in group A(IPA) only at the 4th hour postoperatively.
The number and percentage of patients in both the groups requiring rescue antiemetic were not significant.
No adverse effects noted. No significant difference observed between the groups.
Patient satisfaction score was significantly higher in group A(IPA).
The difference in between groups was not significant other than at the 4th hour.

TABLE 9
VNRS SCORE- A COMPARISON IN TWO GROUPS OF PATIENTS STUDIED

VNRS SCORE	Group A	Group B	Total	P Value
ON ARRIVAL TO PACU	8±1.1	8.6±1.17	8.3±1.17	0.027
4HRS	7.32±0.89	8.23±0.99	7.77±0.98	0.006
8HRS	7±0.91	7.13±0.99	7.06±0.99	0.07
12HRS	6.5±0.98	6.7±0.98	6.6±1.02	0.08
16HRS	5.4±0.95	5±1.03	5.2±1.03	0.06
2OHRS	4±1.01	4.2±1.03	4.1±1.08	0.12
24HRS	3±0.9	3±1.09	6±1.04	0.6

TABLE 10
SATISFACTION SCORE-
Frequency distribution of patients in two groups studied

SATISFACTION SCORE	Group A	Group B	Total
1	0(0%)	0(0%)	0(0%)
2	0(0%)	0(0%)	0(0%)
3	1(2.5%)	5(12.5%)	6(7.5%)
4	11(27.5%)	18(45%)	29(36.3%)
5	28(70%)	17(42.5%)	45(56.3%)
Total	40(100%)	40(100%)	80(100%)

P=0.035*, Significant, Fisher Exact Test

DISCUSSION

PONV is a frequent, unpleasant event and avoidance of this is of greater concern than the postoperative pain for patients.
PONV continues to be a persistent problem following general anaesthesia and it also can influence the duration of recovery from anaesthesia and the time needed for patients to return to their routine. Therefore numerous studies have been done making efforts to reduce PONV.
Prophylactic inhalation of IPA vapors in combination with i.v ondansetron had significant P value at 4 hours post-operatively and was not efficacious than ondansetron alone in the prevention of PONV in the present study similar to the study conducted by L.T Kenett et al[(1)].

Verma et al in their study evaluated the effectiveness of inhaled 70 % IPA in controlling PONV in oral maxillofacial surgeries concluded that inhalation of 70% IPA every hour was associated with significant PONV control.[2]

Taj Lara Teran et al in their study found no difference between 70% IPA and 0.1 mg granisetron as a pre-operative antiemetic similar to our study with no positive correlation. [3].

Garett k et al in their study described the patterns of anticipatory nausea and vomiting with appropriate treatments of acute nausea and vomiting with pharmocological agents that block serotonin and dopamine neurotransmitters.[4]

Tramer et al in their systematic review on omitting antagonism of neuromuscular block : effect on PONV concluded that omitting neostigmine may have a clinically relevant antiemetic effect when high doses are used.[5]

Jonathan W et al in their comparative analysis of isopropyl alcohol and ondansetron found that using IPA as a safe mode to control PONV in the PACU and at home and action of IPA is more faster than ondansetron which took mean average time of 30 min as proven by Winston et al in their study.[6]

Kovac et al in their study concluded that combination antiemetic therapy improves efficacy in the difficult to treat PONV patients and suppression of numerous emetogenic peripheral stimuli and central neuroemetic receptors.[7]

Michael D et al in their study found that subjects who received IPA had greater nausea relief at 30mins in contrast to our study which had VNRS score significantly lower in IPA group only at 4th hour.[8]

Bret A Merritt et al in their study concluded IPA to be more cost effective and recommended to evaluate the length of effectiveness, standard dose recommended, most effective mode of inhalation and factors affecting IPA effectiveness.[9]

Peter veldhuis et al in their study concluded that implementation of IPA as the first line nausea treatment in the ED is both viable and practically feasible which can be an added advantage in the management of patient.[10]

Joseph pellegrini et al in their study reported a faster time to 50% reduction in vnrs scores and overall antiemetic requirement in patients associated with high risk for development of PONV unlike our study which did not emphasis on enrolling in patients with high risk for development of PONV.[11]

Mohamed Gaber et al in their study concluded that inhalational isopropyl alcohol and super hydration both had the same antiemetic effect as ondansetron with no side effects.[12]

Simin atashkhoel et al in their study concluded that preventive ondansetron is more effective than preemptive ondansetron in reducing the incidence of PONV and may also shorten the recovery and length of the hospital stay.[13]

Mathew B kiberd et al in their study found that aromatherapy had a small non -significant effect in the management of PONV in comparison with control group which is in coherent with our present study and suggested to consider exploring aromatherapy on patients anxiety ,and pain in the extended period.[14]

Lois M Stalling -weden et al in their study found no significant difference in comparing aromatherapy to standard care.[15]

There were some limitations to the present study. We were unable to blind the study because of the anaesthesia provider to open the pre packed isopropyl alcohol package before administration and the isopropyl alcohol odour was exposed to the patient via inhalation.

Our recommendation to future studies are to include higher sample size and diverse surgical population.

CONCLUSION

Further studies to be encouraged that allows patients to self manage symptoms of PONV in the PACU and home with use of IPA which does not need any formal training.

Education on use of aroma therapy which is a promising alternative to medications with low cost and minimal side effects are needed.

Prophylactic inhalation of IPA in combination with ondansetron was not beneficial than iv ondansetron alone in the prevention of PONV in patients undergoing laparoscopic procedures.

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