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Article

Chewing Gum for The Prophylaxis of Postoperative Nausea and Vomiting Following Laparoscopic Cholecystectomy in Female Patients

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Abstract: PONV remains the most frequent side effect of general anesthesia which contributes significantly to patients' dissatisfactions, complications and costs. Chewing gum potentially can be novel, drug free alternative for PONV . There is a big issue in modern anesthetic practices due to the consequences like unpredicted hospital admission, late work return to ambulatory people, dehydration, wound dehiscence and pulmonary aspiration. A holistic approach can be tried for the high request for ambulatory surgeries prior to and during surgeries for the prevention of PONV. We conduct trial of the efficacy of mint flavored chewing gum as a prophylactic measure to prevent PONV as a part of post anesthesia care. A prospective randomized controlled trial was conducted. 88 female patients of age (37-62 years old) with volatile anesthetic according to general anesthesia for laparoscopic cholecystectomy will be randomized. All randomized patients have grade 3 risk factor for PONV according to APFL score, 44 patients asked for chewing mint flavored gum after having grade 5 OAA/S score (respond to name in normal tone) and the other 44 patients conducted as a control group. Both groups had monitored for PONV for three hours in the postoperative period. In the chewing gum group, nine patients experienced PONV (20.5%), while nineteen patients of the control group had PONV (43.2%). The symbol * indicates a significant difference between percentages was determined by the Pearson Chi-square (χ^2) test at a significance (0.05) and # the Student's t-test at a 0.05 significance level showing significant differences between two independent means. Chewing gum showed a prophylactic efficacy in managing PONV in female patients taking laparoscopic cholecystectomy. Further research with larger sample size and many kinds of surgeries are essential to investigate this therapy.

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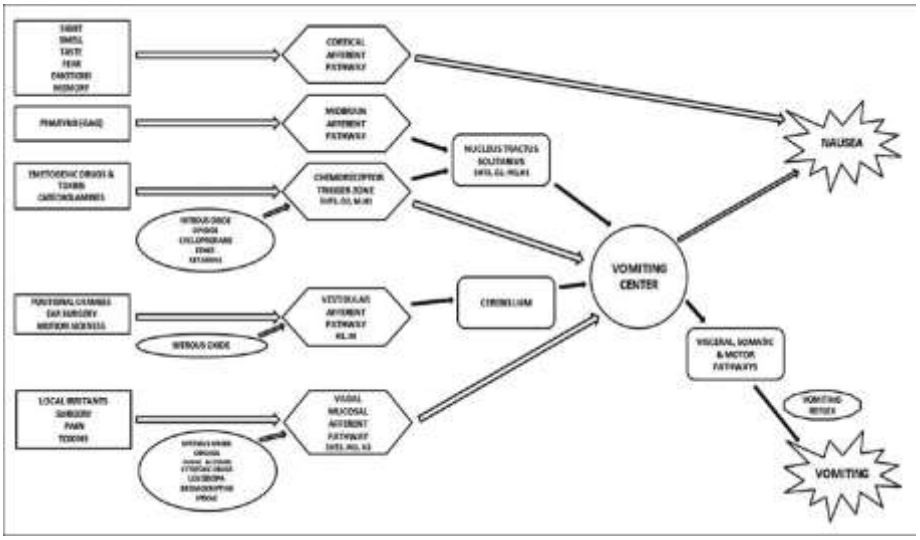
1. Introduction

Postoperative nausea and vomiting (PONV) is the second common complaint. It stays a significant problem in modern anesthetic practice because of the adverse consequences such as unexpected hospital admission, , wound dehiscence, delayed work resuming of ambulatorypeople, pulmonary aspirationand dehydration. [1] In terms of the need for ambulatory surgery. PONV is prevented by the holistic approach should be prior and during surgery . Its prophylaxis decreases PONV thereby patient-related distress and health wellbeing expenses [2,3,4,5], Nausea is not a pleasant feeling of vomiting not linked to expulsive muscular movement [6] forced expelling even some upper gastrointestinal elements by mouth.[6]

POSTOPERATIVE NAUSEA AND VOMITING PHYSIOLOGY

The PONV pathophysiology is compound as in Figure 1 showing a receptors and a pathway.

Figure 1. Physiology Of Postoperative Nausea And Vomiting



They are physiological and pharmacological of 5HT3 - serotonin, 5-HT3 = 5-hydroxytryptamine subtype 3H1, H3 - histamine, M, M1, M3 - muscarinic, D2 - dopamine..

There are five main afferent pathways in the stimulation of vomiting:

- Midbrain.
- Neuronal from vestibular system
- The chemoreceptor trigger zone (CTZ(
- Reflexes of afferent from the cerebral cortex
- The vagal mucosal in the gastrointestinal schemes

Stimulation of them can activate vomiting by the receptors of cholinergic, dopaminergic, serotonergic or histaminergic [7]

The nausea and vomiting neuroanatomical site controlling is not clear called "vomiting center" in reticular brainstem forming [8] afferent inputs which these pathways give. More interactions happen "with nucleus tractus solitarius. Neurokinin-1 (NK-1) receptors are" in the postrema and are important in emesis.[8]

CTZ is ouctside blood–brain barrier contacting cerebrospinal fluid (CSF). The CSF enable the blood substances and interaction. Adsorbed toxins or drugs that circulate in the blood could be a reason for nausea and vomiting by stimulating CTZ sending emetogenic initiations to the brainstem's vomiting area for activation of the vomiting reflex.

Vomiting center can also be stimulated by disturbance of the gut or oropharynx, movement, pain, hypoxemia, and hypotension.

Signals directed to the cranial nerves including the glossopharyngeal, trigeminal, hypoglossal, and accessory nerves, along with the spinal segmental nerves.

Contraction of the abdominal muscles while the glottis is closed. This closure increases pressure within the thoracic and abdominal cavities The pyloric sphincter with the esophageal sphincter relax and active antiperistalses in the esophagus expeling the gastric elements due to vagal and sympathetic activities causing, pallor, sweats and bradycardia.

Multiple factors of the patient, surgery, and anesthesia affect PONV requiring releasing 5-hydroxytryptamine (5-HT) in neuronal cascades with the central nervs and gastrointestinal tract operation. The 5-HT subtype 3 receptor (5-HT3) takes place in specific emetic responses.

Regional anesthesia:

PONV risks were 9 times bigger in those getting general anesthesia than those getting regional anesthesia.[19]. In addition, the postoperative emesis after regional nerve blocks is often smaller than those of the general anesthesia.[20] Emesis having central neuraxial block is bigger than the peripheral nerve blocks as the sympathetic nervous system blockades cause postural hypotension ofnausea and vomit.[21,22,23,24]. Nausea on epidural opioid decreases with lipid-soluble opioids like fentanyl and sufentanil, their rostral spread from the lumbar epidural injection site to the chemoreceptor trigger zone (CTZ) and vomiting center is reduced compared to less lipid-soluble opioids like morphine.

POSTOPERATIVE FACTORS

a. Pain: Visceral or pelvic pain s frequently make postoperative emesis[25,26]
b. Ambulation: Abrupt movement, position shifts, transports transitioning from the postanesthetic recovery part to the postsurgical ward can trigger nausea and vomiting in those receiving opioid medications. [25,26,27,28]
c. Postoperative opioids raises PONV vulnerability in manners that depend on doses;[29] lasting for as long because opioids control pain in the postoperative periods.[30] Regardless of administration path, nausea and vomiting do not differ.
d. Employed in perioperative periods for reducing opioid need
e. It is no more advised to use supplemental oxygen for PONV prevention.

RISK SCORING SYSTEM

A patient's PONV baseline danger is accurately tested by a validated grade according to independent variables.[7] The two most frequent risks for inpatient with an inhaled anesthesia balance are, the first is Apfel with another risk called Koivuranta.[32,33]

The first accords with: history of PONV, female, no smoking , and/or motion sickness, and postoperative opioids use.[33] The PONV with 0, 1, 2, 3, and 4 risks of 10%, 20%, 40%, 60%, and 80%, in respect.[33] Patients are with"low," 0–1, "medium," "high".[2 or 3, and more risks 7]

Also, other clinically related elements are considered, if vomiting may cause important medical risks, such as, in those suffering wired jaws, higher pressure of intracranial, and post gastric, or esophageal surgeries.[7]

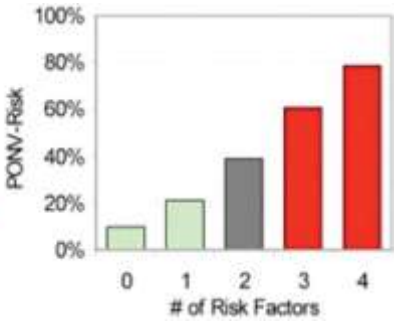
INCLUSION CRITERIA:

- Female sex
- Age > 30 years old
- Apfel score = 3
- ASA score < 3 (1 or 2)
- Laparoscopic cholecystectomy
- Volatile anesthetic based general anesthesia

EXCLUSION CRITERIA:

- Planned propofol maintained general anesthesia
- ASA score > 2
- Apfel score not equal to 3
- Contraindication for chewing:
- Full upper or lower dentures
- Impaired laryngeal or esophageal function (bulbar palsy)

Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV	1
Postoperative Opioids	1
Sum =	0 ... 4



- Conversion from laparoscopic to open cholecystectomy.

Tabel 1: Apfel Score [65].

ASA classification	Description
1	A normal, healthy patient
2	A patient with mild systemic disease
3	A patient with severe, systemic disease
4	A patient with severe, systemic disease that is a constant threat to life
5	A moribund patient who is not expected to survive without the operation
6	A declared brain-dead patient whose organs are being removed for donation

PONV adult risks.

Simplified risk score from Apfel et al.9 to show the patient's risk for PONV. If 0, 1, 2, 3, and 4 risks appear, PONV risk is about 10%, 20%, 40%, 60%, and 80%, in respect. PONV

Tabel 2: ASA and grade of physical status [66].

INTRA OPERATIVE MANAGEMENT

Antiemetic prophylaxis, 4mg IV dexamethasone and 10 mg IV metoclopramide were administered prior to induction. Midazolam was given prior to or in the induction. Propofol, ketamine and an opioid (tramadol) induced general anesthesia was with co-induction by sevoflurane.

Neuromuscular block is given, then anesthesia maintained by sevoflurane with oxygen. Endotracheal tube placement was done, further non opioid analgesia (paracetamol vial) is given and intravenous fluid given according to protocols.

The neuromuscular block inverted at the surgery end by neostigmine and atropine with endotracheal extubation then the patient transferred to the recovery rooms.

POST OPERATIVE MANAGEMENT

Score	Responsiveness
5	Responds readily to name spoken in a normal tone
4	Lethargic response to name spoken in a normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Responds only after painful trapezius squeeze
0	No response after painful trapezius squeeze

At the recovery room and after having an OAA/S (Observer Assessment of Alertness / Sedation) rating equaling 5 (answering immediately t o name spoken in normal tone), the patients of chewing gum group are asked for chewing a mint flavored gum for 20 minutes then transferred to the surgical word. The control group patients were transferred to the surgical word after having OAA/S score of 5 excluding those with less than OAA/S of 5.

Both groups were observed for three hours of the postoperative period. They were asked every 30 minutes if they have any nausea and monitored if they develop any reaching or vomiting.

Any event in the observation period was marked in designated monitoring list. If any patient developed reaching orvomiting a rescue medication of 4mg IV on danseron was given.

Tabel 3:(OAA/S)

2. Materials and Methods

The current work is prospective randomized controlled clinical test with patients randomized which is equal to chewing gum and control groups.

The two groups designed to be comparable regarding "body mass index (BMI). The second is while third is age followed by American Society of Anesthesiologists (ASA)" physical status arrangement score and anesthesia duration.

Randomization done by generating a random allocation sequence, odd sequence patient randomized as control and even sequence for chewing gum group. Informed and written consent were taken from the patients undergoing the trial.

3. Results

This study enrolled 88 patients and followed up for the last examination, 44 randomized to chewing gum and 44 as a control group between 5 November 2019 and 24 September 2020.

The study violated no protocols. The two groups had the same PONV risks and were comparable regarding patient features (age, BMI and ASA score), and surgery and anesthesia details (Table 4,5,6 and 7).

After operation nausea and vomiting occurred in 19 (43.2%) of the controls and 9 (20.5%).

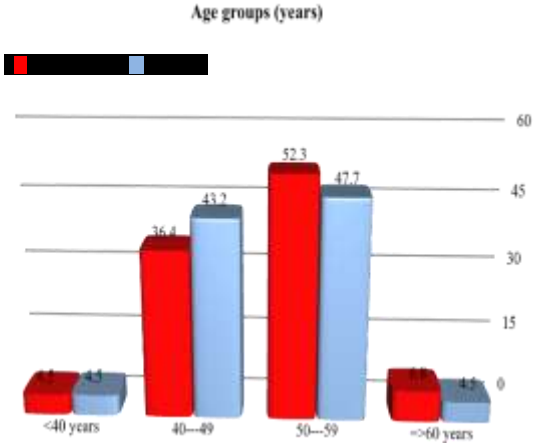
The PONV incidence and the efficacy of chewing gum prophylaxis was increased with higher BMI and longer duration of anesthesia. (table 8and 9).

Nausea statistically and significantly reduced in the chewing gum group (20.5%) in comparison to the controls (43.2%) with significant P value (P=0.22).

Although vomiting in the chewing gum group reduced, 3 patients developed vomiting (6.8%) as compared to 7 (15.9%) in the control group-a statistically insignificant, because the P value was more than the significance limit (P=0.179, >0.05) (Table 7).

Table 4:

		Chewing gum		Control		P value
		No	%	No	%	
Age (years)	<40 years	2	4.5	2	4.5	0.908
	40---49	16	36.4	19	43.2	
	50---59	23	52.3	21	47.7	
	=>60 years	3	6.8	2	4.5	
	Mean±SD	50.4±6.1		49.7±5.0		0.567
	(Range)	(37-62)		(38-62)		



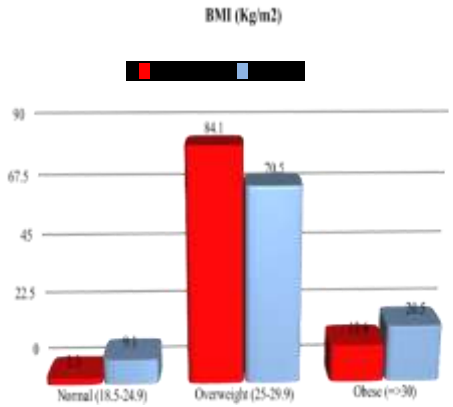
Both Group sare comparable in mean age with insignificant p value (p=0.908).

The table presents a comparison of BMI categories between chewing gum and control groups. The majority of participants were overweight (84.1% in the chewing gum group vs. 70.5% in the control). Mean BMI values were similar (28.2±1.3 vs. 28.0±2.2, p=0.751), indicating no significant difference between groups. (Table 5)

Table 5:

		Chewing gum		Control		P value
		No	%	No	%	
BMI (Kg/m2)	Normal (18.5-24.9)	1	2.3	4	9.1	0.231
	Overweight (25-29.9)	37	84.1	31	70.5	

	Obese (=>30)	6	13.6	9	20.5	
	Mean±SD	28.2±1.3		28.0±2.2		0.751
	(Range)	(24.5-31)		(23.8-33)		

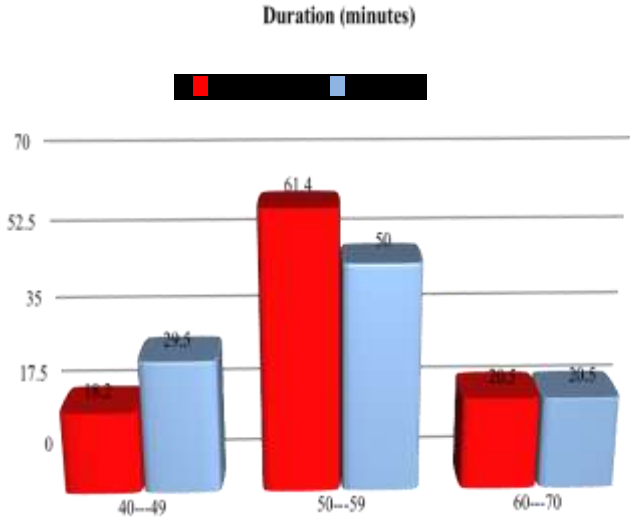


Both groups are comparable in mean BMI with insignificant P value (P=0.231).

The table compares the duration (minutes) between the chewing gum and control groups. The majority of participants in both groups had durations between 50–59 minutes (61.4% vs. 50%). Mean durations were 53.1±6.4 and 51.0±7.2 minutes, respectively, with no significant difference (p=0.163), indicating comparable distributions across groups. (Table 6)

Table 6:

		Chewing gum		Control		P value
		No	%	No	%	
Duration (minutes)	40---49	8	18.2	13	29.5	0.427
	50---59	27	61.4	22	50.0	
	60---70	9	20.5	9	20.5	
	Mean±SD	53.1±6.4		51.0±7.2		0.163
	(Range)	(40-70)		(35-65)		

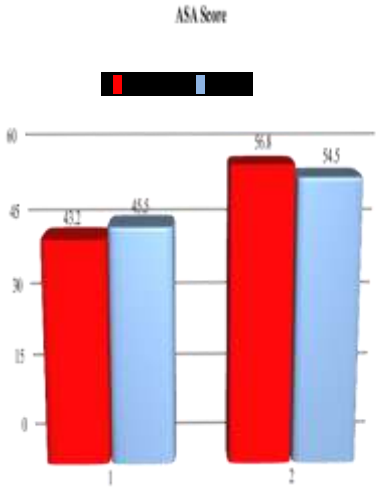


Both groups are comparable in mean duration of anesthesia with insignificant p value (p=0.427).

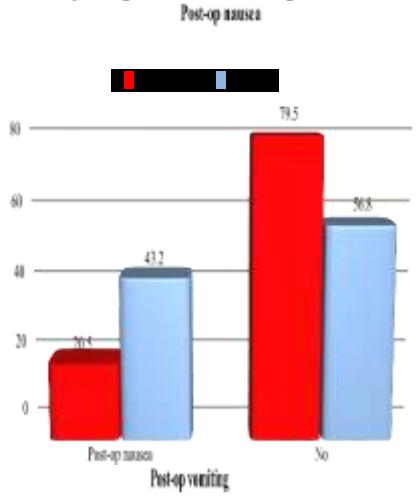
The table presents ASA scores and postoperative nausea and vomiting between the chewing gum and control groups. ASA scores were comparable (p=0.830). Postoperative nausea was significantly lower in the chewing gum group (20.5% vs. 43.2%, p=0.022). No significant difference was observed in postoperative vomiting (p=0.179), indicating a potential benefit in nausea reduction. (Table 7)

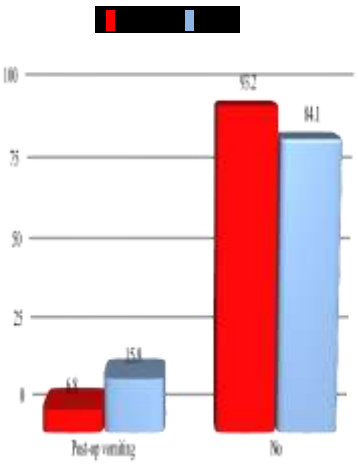
Table 7:

		Chewing gum		Control		P value
		No	%	No	%	
ASA Score	1	19	43.2	20	45.5	0.830
	2	25	56.8	24	54.5	
Post-op nausea	Yes	9	20.5	19	43.2	0.022*
	No	35	79.5	25	56.8	
Post-op vomiting	Yes	3	6.8	7	15.9	0.179
	No	41	93.2	37	84.1	



Both groups have comparable ASA scores with insignificant p value (p=0.830).





The tables examine postoperative nausea and vomiting in relation to age, BMI, duration, and ASA score across chewing gum and control groups. Significant associations were found for ASA score (p=0.005, p=0.008) and duration (p=0.001) in the control group. No significant differences were observed in other variables, suggesting selective postoperative effects. (Table 8)

Table 8:

		Chewing gum				Control			
		Post-op nausea				Post-op nausea			
		Yes		No		Yes		No	
		No	%	No	%	No	%	No	%
Age (years)	<40 years	-	-	2	100	-	-	2	100
	40---49	2	12.5	14	87.5	9	47.4	10	52.6
	50---59	7	30.4	16	69.6	9	42.9	12	57.1
	=>60 years	-	-	3	100	1	50.0	1	50.0
	P value	0.345				0.638			
BMI (Kg/ m2)	Normal (<25)	-	-	1	100	-	-	4	100
	Overweight	8	21.6	29	78.4	13	41.9	18	58.1
	Obese (=>30)	1	16.7	5	83.3	6	66.7	3	33.3
	P value	0.843				0.079			
Duration (minutes)	40	-	-	8	100	3	23.1	10	76.9
	50	5	18.5	22	81.5	8	36.4	14	63.6
	60	4	44.4	5	55.6	8	88.9	1	11.1
	P value	0.071				0.006*			
ASA Score	1	2	10.5	17	89.5	4	20.0	16	80.0
	2	7	28.0	18	72.0	15	62.5	9	37.5
	P value	0.155				0.005*			

		Chewing gum				Control			
		Post-op vomiting				Post-op vomiting			
		Yes		No		Yes		No	
		No	%	No	%	No	%	No	%
Age (years)	<40 years	-	-	2	100	-	-	2	100
	40---49	-	-	16	100	3	15.8	16	84.2
	50---59	3	13.0	20	87.0	3	14.3	18	85.7
	=>60 years	-	-	3	100	1	50.0	1	50.0

	P value	0.401				0.540			
BMI (Kg/ m2)	Normal (<25)	-	-	1	100	-	-	4	100
	Overweight	3	8.1	34	91.9	4	12.9	27	87.1
	Obese (=>30)	-	-	6	100	3	33.3	6	66.7
	P value	0.737				0.222			
Duration (minutes)	40	-	-	8	100	-	-	13	100
	50	1	3.7	26	96.3	2	9.1	20	90.9
	60	2	22.2	7	77.8	5	55.6	4	44.4
	P value	0.113				0.001*			
ASA Score	1	2	10.5	17	89.5	-	-	20	100
	2	1	4.0	24	96.0	7	29.2	17	70.8
	P value	0.395				0.008*			

STATISTICAL ANALYSIS

The statistical package SPSS-27 was utilized for analysis. Data analysis included frequencies percentages, means, standard deviation, and ranges (minimum- maximum values).

Students-t-test was used for the means difference significance (quantitative data) for the differences between two independents while the difference significance (qualitative data) by Pearson Chi-square test (χ2-test) applying Yate's corrections or Fisher Exact tests if valid. The study considered statistical significance if the P value was equal or lower than 0.05.

Subgroup analyses are including assessment by age (<40, 40-49,50-59, = or >60), Body Mass Index (<25, 25-30, >30) and duration of anesthesia (40-50, 50-60, 60-70).

4. Discussion

In this randomized control trial we tested the effectiveness of the chewing gum as a prophylactic measure for PONV in female patients experiencing laparoscopic cholecystectomy.

Chewing gum is hypothesized to reduce postoperative ileus and PONV by stimulating early recovery of gastrointestinal (GI) function, through cephalo-vagal stimulation.

Chewing gum could induce increased salivation and swallowing frequency, thus improving the clearance rate of reflux within the esophagus and decreasing the esophageal PH which has an effect in decreasing PONV.

Following the results obtained in this study, there is a statistically significant reduction in the incidence of nausea in the chewing gum group(43.2% in control group and 20.5% in chewing gum group) with P-value 0.022 and reduction in incidence of vomiting (15.9% in control group and 6.8% in chewing gum group) with P-value 0.179. Although there is a decrease in the vomiting incidence but it did not reached the statistical

significance value (P-value > 0.05), probably due to limited number of cases who developed vomiting in both groups.

J. N. Darvall, M. Handscombe and K. Leslie in 2017[66], conducted a pilot randomized control trial by comparing chewing gum vs ondansetron for PONV cure in patients undergoing laparoscopic or breast surgery.

They randomized 94 females taking laparoscopic or breast surgery to ondansetron 4 mg i.v. or chewing gum if PONV was experienced in the postanaesthesia care unit (PACU).

Postoperative nausea and vomiting in the PACU occurred in 13 (28%) ondansetron patients and 15 (31%) chewing gum patients (P1⁄40.75).

Full resolution of PONV in five of 13 (39%) ondansetron vs nine of 12 (75%) chewing gum patients (risk differences 37%,P=0.07). Chewing gum is superior to ondansetron in treatment of PONV in laparoscopic and breast surgery in female patients.

Despite using chewing gum as a treatment for PONV, this study supports our trial results regarding the efficacy of chewing gum in management of PONV.

Another randomized controlled trial by Yunhui Gong , Qianwen Zhang And Lin Qiao In 2015 [67], evaluated Xylitol Gum Chewing to Achieve Early Postoperative Restoration of Bowel Motility After Laparoscopic Surgery.

Overall, 120 patients experiencing elective gynecologic laparoscopy were randomly classified into final numbers: 53 controls, 56 patients. Controls underwent a routine postoperative regimen. Starting 6 hour after surgery, study patients chewed mint-flavored, sugarless xylitol gum until flatus occurred thrice a day.

Other postoperative management was routine. First bowel sounds, first flatus, first bowel movement, and discharge times. First flatus and first bowel sounds occurred significantly (P<0.001) earlier in the study patients. No significant differences were found for first defecation time, hospitalization duration, or mild/severe intestinal obstruction (all P>0.05).

They concluded that xylitol gum chewer after laparoscopy save times to first flatus helping with curing postoperative gastrointestinal functional It was easy, suitable, and tolerated.

The current study confirms the hypothesis of chewing gum after recovery of gastrointestinal function, but it did not test it's efficacy regarding PONV prevention.

The meta analysis of Chao Xu, Jie Peng and Su Liu's [68] and their systematic literature review of 10 randomized controlled trials evaluated whether chewing enhance postoperative gastrointestinal function and decreased complications (nausea, vomiting and ileus) after gynecological surgery. The study used Weighted mean difference (WMD). In addition, it also utlized odds ratios (ORs) The experimental groups experienced a significant reduction in nausea (OR 0.45, 95% CI: 0.29–0.69) and vomiting (OR 0.38, 95% CI: 0.22–0.68). Additionally, postoperative ileus was decreased (OR 0.25, 95% CI: 0.14–0.44), with shorter times to aerofluxus (WMD −7.55, 95% CI: −10.99 to −4.12), first intestinal sounds (WMD −6.20, 95% CI: −8.14 to −4.27), first defecation (WMD −12.24, 95% CI: −18.47 to −6.01), and overall hospitalization duration (WMD −0.72, 95% CI: −1.19 to −0.25).

Chewing gum has appeared as an effective measure for the amelioration of gastrointestinal activities and reduces problems post gynecological surgery.

This review supports our study results regarding nausea (OR 0.45) and vomiting (OR 0.38) and emphasized the chewing gum roles in recovering GIT function postoperatively.

n 2014, Y-P Zhu's meta-analysis of 939 women assessed gum chewing's impact on postoperative bowel motility after cesarean section. Results showed gum chewers had shorter times to first flatus (6.42 hours), bowel sounds (3.62 hours), stool (6.58 hours), and hospital stay (5.94 hours) with no side effects. The study supports gum chewing as a safe, effective method for accelerating gastrointestinal recovery post-surgery.

Amelia M. Jernigan, Chi Chiung Grace Chen, and Catherine Sewell conducted a randomized trial evaluating chewing gum as a preventive strategy for postoperative ileus following laparotomy in benign gynecologic surgeries[70].

The study assigned 109 patients in a random manner who are considered gum chewer (n=51) or follow-up cares (n=58) and less gum chewers than routine cares with postoperative nausea (16 [31.4%] in contrast to 29 [50.0%]; P=0.049) and postoperative ileus (0 vs. 5 [8.6%]; P=0.032). The postoperative antiemetics needs were similar to postoperative vomiting episodes.

Although it supports our results regarding the reduction of nausea incidence in chewing gum group, this study came against to our study results regarding reduction of vomiting and subsequent antiemetic use in chewing gum patients.

Qing Liu,Honglei Jiang and Dong Xu in 2017 had a similar stud on ameliorating ileus postcolorectal surgery effect [71]. They used 18 RCTs, 1736 patients. In comparison to the standardized postoperative cares, the trial reduced time to first flatus (P = 0.0002), earlier recovery of bowel motion (P < 0.00001), and a reduction in length of hospital stay (P = 0.03). In addition, this chewing reduces postoperative ileus (OR = 0.41,P=0.003). Significant benefits were not approved in the general postoperative complication, nausea, vomiting and bloating.

The results of of this study is against our results. Despite showing shorter gastrointestinal recovery, this review showed no significant reduction regarding post operative nausea and vomiting.

Chewing gum is not a universally appliction to postoperative patients. While chewing gum showed a prophylactic measure for PONV in this trial, it suits patients with key surgeries, with higher opioid obligation and possibly longer emergence times, needs more studies.

5. Conclusion

These findings indicate that, during surgical procedures under general anesthesia, there is a high prophylactic efficacy of chewing gum with regard to reducing postoperative nausea and vomiting (PONV) in female patients who undergo laparoscopic cholecystectomy. A remarkable reduction in incidence of nausea in the chewing gum group (20.5%) vs. control (43.2%), with statistically significant differences, were reported by the study. However, although both vomiting incidence was also lower in the chewing gum group (6.8% vs. 15.9%) this difference did not reach statistical significance. These results indicate that the chewing gum can be a non pharmacological and cost effective adjunctive intervention for PONV management in clinical practice. The implications of this study go beyond enhancing patient comfort and reducing the use of antiemetic drugs and may include reduction in healthcare costs as a result of the reduction in prolonged hospital stays. While further research with larger sample size and area of surgical procedures is needed to validate the generalizability and benefit of chewing gum in PONV prevention.

RECOMMENDATIONS

Chewing gum can be used as a safe, well tolerable prophylactic measure after operative vomiting and nausea in those with laparoscopic cholecystectomy.

Larger sample size studies with different types of surgeries are recommended to examine chewing gum efficacy for PONV management in wider range of patients and surgical interventions.

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