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Original Article

Impact of Chewing Gum Protocol on Delayed Gastric Emptying Following Pancreaticoduodenectomy

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Abstract

Introduction: Delayed gastric emptying (DGE) is one of the most troublesome post-operative complications following pancreatic resection. Not only does it contribute considerably to prolonged hospitalization but it is also associated with an increased cost of treatment, necessitates the use of additional investigations and procedures, and can cause life-threatening complications.

Aim: This study aims to study the feasibility of implementing chewing gum protocol in pancreaticoduodenectomy (PD) with pancreaticogastrostomy, using historical control for comparison.

Materials and Methods: Patients having pancreatic, periampullary cancer and other diseases who were planned for elective PD procedures were included in the study. Patients were divided into two groups, control group: Traditional protocol and intervention group: Chewing gum intervention. The primary endpoint for this study was fixed as the occurrence of DGE following PD.

Results: Statistical analysis showed significant differences in the occurrence of DGE and its related parameters such as time for the removal of nasogastric tube (NGT) and time to start an oral solid diet. It also showed a significant difference in secondary parameters such as time to first flatus, time to stools, and post-operative hospital stay. Multivariate analysis also showed a significant beneficial effect of chewing gum.

Conclusion: In patients undergoing PD, implementing gum chewing in the early post-operative period is easy, inexpensive, and without any adverse events. Gum chewing has significantly reduced the incidence of DGE and its parameters such as time to the removal of NGT, resumption of solid diet, time to the passage of first flatus, time to the passage of first stool, and thereby reduced the post-operative hospital stay significantly.

Key words: Chewing gum, Delayed gastric emptying, Pancreaticoduodenectomy

INTRODUCTION

Pancreaticoduodenectomy (PD) is the standard approach for pancreatic cancers and certain benign pancreatic diseases. Pancreatic cancers are one of the major health concerns throughout the world. Pancreatic cancer is one of the leading causes of cancer death in the world. PD is technically a major demanding procedure. With careful patient selection and preparation, advanced operative techniques, ever-advancing principles of intensive care, post-operative comprehensive care, and advanced radiological interventions – perioperative mortality of pancreatic surgery has decreased markedly over the decades to <5% in high-volume centers.[1,2] Despite this, the post-operative morbidity due to complications remains still high (30%–50%).

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In present, the major morbidity following PD is delayed gastric emptying (DGE) and rates of 19–57% are reported even from centers specializing in pancreatic surgery.[3,4] DGE is one of the most troublesome post-operative adverse outcomes following PD. It contributes considerably to prolonged hospitalization and also associated increased cost of medical treatment, necessitates additional investigations and procedures, and might lead to life-threatening major complications. In spite of immense advances in surgical care and techniques, DGE following PD is still a major

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morbid complication in modern surgery. It seems difficult to ascertain the exact incidence of DGE due to variations in definitions. Many groups have proposed definitions of DGE based on time of nasogastric tube (NGT) removal, emesis after NGT removal, need for prokinetics, need of NGT reinsertion, and failure to progress with diet.

In an attempt of developing an objective, universally acceptable, consensus definition for DGE after major PD, the International Study Group of Pancreatic Surgery had developed a generally applicable, objective definition with three grades of DGE based on severity and its clinical impact primarily.[5]

The factors causing DGE are still unclear and are multifactorial.[1,6-10] The potential explanations for DGE after PD include altered neurohumoral pathways, decreased in plasma motilin concentrations due to resection of the duodenum, physiological responses to any collection and sepsis, extended nodal dissection along the common hepatic vessel with disruption of innervation to antrum pyloric region, systemic inflammatory mediators released during surgery and stress, intra-abdominal complications leading to gastroparesis and ileus, devascularized or denervated pylorus after PD, disruption of the pancreatic anastomosis, post-surgical transient acute pancreatitis, disrupted neuronal and hormonal homeostatic mechanisms, and obstruction mechanical or functional by addition of feeding jejunostomy. Various strategies were tried in the past to decrease DGE (DGE) incidence. Pharmacologic manipulations such as the addition of motilin stimulants – erythromycin and prokinetic drugs were tried.[10] Many refinements and modifications in surgical techniques such as pylorus-preserving resections, antecolic versus retrocolic gastrojejunostomy (GJ), the addition of a Braun enteroenterostomy, and uncut Roux-en-Y gastrojejunal reconstructions were also tried in the prevention of DGE.[3,4,11]

Aim

This study aims to study the impact of the implementation of chewing gum protocol in the early post-operative period following PD and evaluating its effects on DGE.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Institute of Surgical Gastroenterology and Liver Transplantation, Stanley Medical College, Chennai, India, from April 2014 to October 2014. All patients suffering from pancreatic, periampullary, and other diseases, planned for PD, were prospectively included in this study.

Inclusion Criteria

- Patients having pancreatic, periampullary cancer and other diseases who were planned for elective PD procedure were included in the study
- All adults aged between 18 and 75 years having good performance status (performance score of more than 80).

Exclusion Criteria

The following criteria were excluded from the study:

- Deeply sedated patients
- Patients on mechanical ventilator support
- Edentulous patients who cannot chew gum
- Presence of intestinal obstruction
- Presence of post-operative bleed, vomiting, and major reoperation
- Who refused to participate in the study trial
- Emergency surgery procedures
- Patients having cerebral disorders – danger of aspiration
- Any contraindications for enteral feeding.

Consecutive patients of PD were included in this study, and the parameters analyzed and compared with an equal number of matched historical controls were operated and treated as per the traditional post-operative treatment protocol following classic PD.

Control group

This group comprised a consecutive equal number of comparable patients who were treated as per the traditional protocol in the historical period – just before the study period.

Intervention group

This group also received treatment identical to the control group, but with the only difference being, patients received chewing gum intervention as specified in the protocol mentioned earlier.

Along with traditional post-operative protocol, patients in the intervention group were allowed to chew sugarless chewing gum for 30 min, 3 times a day. From the 1st post-operative day, until they were tolerating a solid diet. During the administration of chewing gum, both patient and nursing staff were required to report any potential side effects/adverse events. The criterion to stop the study was either withdrawal of consent by the patient and/or any serious adverse events due to the administration of chewing gum.

The primary endpoint for this study was fixed as the occurrence of DGE following PD.

Descriptive statistics were done for all data and suitable statistical tests of comparison were done. Continuous

variables were analyzed with the unpaired *t*-test and categorical variables were analyzed with Fisher's exact test. Statistical significance was taken as $P < 0.05$. The data were analyzed using Epi Info software (7.1.0.6 version; Center for Disease Control, USA) and Microsoft Excel 2010.

RESULTS

All the 40 patients {control group (n=20) and test group (n=20)} completed the study. Both the groups were homogenous with regard to demographic data, with no differences in age and gender. The two groups were comparable in operative parameters, with no differences in etiology, presence of diabetes, total operating time, consistency of pancreas, and GJ type. The other post-operative data in both groups: Blood transfusion, pancreatic fistula, enteric/biliary fistula, collections, post-pancreatectomy hemorrhage, need for reoperations/interventions – were comparable in both groups and the difference was not statistically significant. On the statistical analysis of pre-operative parameters by conventional criteria, the association between site of tumor, the status of diabetes, pre-operative sepsis status, duration of surgery, blood loss/transfusions required, type of GJ, and chewing gum intervention groups is considered to be not statistically significant since $P > 0.05$ [Tables 1 and 2].

On analysis of post-operative variables statistically by conventional criteria, the association between the presence of collection, pancreatic fistula, post-pancreatectomy hemorrhage, presence of post-operative sepsis, need for reintervention/reoperation, mortality, and chewing gum intervention groups is considered to be not statistically significant since $P > 0.05$. On analysis of DGE-related parameters by conventional criteria, the association between emesis/distension, reinsertion of NGT, and chewing gum intervention groups is considered to be not statistically significant since $P > 0.05$ [Table 3].

After adjusting for age and gender, chewing gum intervention group demonstrated that the association between DGE, NGT removal, time to pass first flatus, time to first stools, time to resumption of oral solid diet, duration of post-operative stay, and chewing gum intervention groups is considered to be statistically significant since $P < 0.05$ [Tables 4 and 5].

Table 1: Demographic and operative parameters

Variables	Control group	Test group	*P*-value
Age	47.6	52.45	0.252
Gender			
Male	10	9	0.999
Female	10	11	
Etiology			
Pancreatic	7	10	0.659
Periampullary	11	7	
Solid pseudopapillary neoplasm	1	1	
Duodenal	1	1	
Duodenal neuroendocrine tumors	0	1	
Diabetes	9	9	0.999
Duration of surgery	361.5	365.5	0.815
Pancreas consistency			
Firm	14	13	0.504
Soft	5	7	
Hard	1	0	
Gastrojejunostomy type			
Retrocolic	12	8	0.749
Antecolic	8	12	

Table 2: Post-operative parameters

Parameter	Control	Test group	*P* value
Pancreatic fistula			
Grade A	9	6	0.576
Grade B	1	2	
Grade C	0	1	
Collections	1	2	0.548
PPH			
Grade A	1	2	0.513
Grade B	0	0	
Grade C	1	0	
Reoperation/intervention	3	2	0.34
Blood transfusion	9 (2 units)	13 (1.6 units)	0.204
Post-operative sepsis	5	6	0.74

Table 3: DGE parameters

Parameter	Control (n=20)	Test group (n=20)	*P* value
NGT removal (days)	5	3.6	0.0005
Resumption of oral solids (days)	12	8.65	0.006
Emesis/distension	4	4	0.999
NGT reinsertion	4	4	0.999
Need for prokinetics	4	4	0.999
DGE			
Grade A	14	9	0.031
Grade B	4	3	
Grade C	1	0	

DGE: Delayed gastric emptying, NGT: Nasogastric tube

DISCUSSION

Whipple PD is the standard procedure of choice for the treatment of benign diseases such as chronic pancreatitis as well as for the treatment of malignancies (carcinoma of the pancreatic head, neck, or uncinate process, distal common bile duct, ampulla of Vater, duodenum, solid pseudopapillary neoplasm, and neuroendocrine tumors).[6,12]

PD was selected as a target surgery for some important reasons. PD involves major resection of pancreaticoduodenal complex and complex reconstructions

Table 4: Secondary endpoints

Parameter	Control (*n*=20)	Test group (*n*=20)	*P* value
Passage of first flatus (days)	3.55	3.25	0.135
Passage of first stools (days)	5.6	4.7	0.007
Resumption of oral fluids (days)	8.65	5.84	0.005
ICU stay (days)	8.2	6.05	0.053
Post-operative stay (days)	20.35	15	0.005

Table 5: Multivariate logistic regression analysis

Variable	Odds ratio	95% CI	*P* value
NGT removal	10.18	1.09–94.73	0.042
Passage of first flatus	1.8	0.4130–8.0745	0.042
Passage of first stool	15	0.8232–273.3360	0.007
Resumption of oral fluids	4.72	0.243–0.918	0.027
Resumption of solid diet	10.1	1.09–94.73	0.042
Delayed gastric emptying	71.8	3.8448–1342.3922	0.004
Length of ICU stay	0.5	0.0250–10.9591	0.676
Length of post-operative stay	1.3	0.2880–6.1286	0.015

NGT: Nasogastric tube

involving gastrointestinal, biliary, and pancreatic continuity. PD is associated with considerable rates of mortality (up to 5%) and morbidity (reported up to 30%–50%)[1,2] even in high-volume centers specialized in pancreatic surgeries. Many reports suggest that other post-operative complications increase the incidence of DGE. Despite innumerable attempts to prevent or treat it, DGE continues to be a major troublesome clinical problem following PD, especially with pancreaticogastrostomy reconstruction.

DGE is an independent predictor of the prolonged hospital stay after PD. DGE is associated with considerable morbidity to the patient and causes major financial and psychological implications for the patient and health-care system and decreases the quality of life.

Any reduction in post-operative complications, especially DGE, and its associated morbidity in these patients undergoing PD will be beneficial to the patient, healthcare, and society in general. Impact of chewing gum in preventing/treating post-operative ileus following major abdominal surgeries such as gastric, colorectal, gynecological, obstetric, urological, and other procedures was proved by multiple trials including randomized control trials in the past, which was discussed in detail during the review of the literature.[13-20]

The pathophysiology behind the effect of chewing gum is mainly a sham feeding effect causing cephalovagal stimulation and possible neurohormonal stimulation of gastrointestinal motility and function without any additional risks involved. Implementation of the easily available gum chewing protocol in the early post-operative period following PD involves no dangerous side effects, inexpensive, and easy.

At present, even if fast-track recovery and reduced hospital stay are becoming increasingly common, the occurrence of DGE and prolonged hospital stay is causing a substantive economic impact. International differences in post-operative hospital stay must also be acknowledged while considering this study. The average post-operative hospital stay after PD is 14–21 days in Western Europe,[11,21] in recent reports, it averages 7–14 days in the United States,[6,9,22] and in most of the Asian countries, it remains longer, ranging from 19 to 28 days. In this study, we used sugar-free commercially available chewing gum with acceptable texture and flavor. All the patients were very positive and interested in participating in our study. This study clearly demonstrated that in the chewing gum group, the rate of all the grades of DGE was significantly lower and the average time to remove NGT, the start of a solid diet is shorter in the intervention group and the difference is significant. The same effect is also observed in the time to pass first flatus a first stools and the time to start an oral fluid diet, which indicates early recovery from post-operative paralytic ileus. While the post-operative hospital stay is significantly reduced in the chewing gum group, this study failed to demonstrate any significant effect on ICU stay. This study shows that gum chewing in the early post-operative recovery period following PD, significantly decreased the rate of DGE without any adverse effect. Gum chewing also resulted in a significant reduction in time to removal of an NGT, time to start oral fluids, and solid diet. It also resulted in an early passage of first flatus, first stools, and reduced post-operative stay in the hospital.

Limitations of this Study

- Non-randomized trial
- Historical control population
- Small sample size.

The main aim of this study is the effect of chewing gum on DGE and other secondary factors. We have done multivariate analysis using critical variables, instead of looking into each factor's effect on DGE. The quality in the selection of controls is also proven by comparability between groups statistically. A larger sample will surely improve the quality of the study by reducing the bias, but we have incorporated correction methodologies in statistical analysis to overcome the low sample size. Furthermore, we have performed a power analysis to decide the minimum sample size and/or study involved more than the required sample size.

CONCLUSION

In patients undergoing PD, implementing gum chewing in the early post-operative period is easy, inexpensive, and without any adverse events. Gum chewing has significantly reduced the incidence of DGE and its parameters such as time to the removal of NGT, resumption of solid diet, time to the passage of first flatus, time to the passage of first stool, and thereby reduced the post-operative hospital stay significantly. This has resulted in enhancing the confidence and well-being of the patient after this major surgery and reduced the cost of healthcare. Gum chewing did not influence vomiting/abdominal distension, reinsertion of NGT, and length of ICU stay.

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