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ORIGINAL ARTICLE

Retrospective Study

Bleeding risk with clopidogrel and percutaneous endoscopic gastrostomy

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Abstract

AIM

To compare bleeding within 48 h in patients undergoing percutaneous endoscopic gastrostomy (PEG) with or without clopidogrel.

METHODS

After institutional review board approval, a retrospective study involving a single center was conducted on adult patients having PEG (1/08-1/14). Patients were divided into two groups: Clopidogrel group consisting of those patients taking clopidogrel within 5 d of PEG and the non-clopidogrel group including those patients not taking clopidogrel within 5 d of the PEG.

RESULTS

Three hundred and nineteen PEG patients were found. One hundred and sixty-eight males and 151 females with mean body mass index 28.47 ± 9.75 kg/m^2 and mean age 65.03 ± 16.11 years were identified. Thirty-three patients were on clopidogrel prior to PEG with 286 patients not on clopidogrel. No patients in either group developed hematochezia, melena, or hematemesis

within 48 h of percutaneous endoscopic gastrostomy (PEG). No statistical differences were observed between the two groups with 48 h for hemoglobin decrease of > 2 g/dL (2 *vs* 5 patients; P = 0.16), blood transfusions (2 *vs* 7 patients; P = 0.24), and repeat endoscopy for possible gastrointestinal bleeding (no patients in either group).

CONCLUSION

Based on the results, no significant post-procedure bleeding was observed in patients undergoing PEG with recent use of clopidogrel.

Key words: Percutaneous endoscopic gastrostomy; Clopidogrel; Bleeding; Complications; Antiplatelets

Core tip: Percutaneous endoscopic gastrostomy (PEG) is a common but invasive procedure. In the past, many medications were held prior to the procedure to reduce the risk of potential bleeding complication, such as clopidogrel. Much debate has been performed regarding the need for cessation of clopidogrel prior to PEG placement with little evidence found in the literature. This manuscript showed that clopidogrel use in patients undergoing PEG placement had no increased early post-procedure bleeding risk.

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INTRODUCTION

Percutaneous endoscopic gastrostomy (PEG) is most commonly performed to provide nutritional support to patients who fail to swallow for a long time requiring tube feeding support[1]. This procedure was first reported by Gauderer *et al*[2] in 1980. Since then PEG has become an important technique for inserting feeding tubes in patients with swallowing difficulties who require long term nutritional support without undergoing laparotomy[2,3]. The placement of PEG tube is classified among high-risk endoscopic procedure because of the risk of associated clinically significant bleeding. The enteric tube can be placed surgically, under radiological guidance or by endoscopic technique. When compared, the endoscopic technique has the least overall risk[4]. Due to having the least overall risk, it is considered to be the technique of choice. However, endoscopic procedures may be low or high risk procedures. High risk endoscopic procedures are ones which are associated with the risk of bleeding being > 1%. PEG is considered a high risk procedure and carries a 2.5% risk of complications[3]. PEG tube is usually required in patients who are elderly and have multiple comorbidities. These patients are usually on antithrombotic agents or anticoagulants and hence are at increased risk of procedure-related bleeding. At the same time, holding the antiplatelet or anticoagulant agents could have potential thromboembolic complications from the underlying pro-thrombotic state. These medications for various cerebrovascular, cardiovascular, and hematological disorders has drastically increased[3]. These agents significantly increase gastrointestinal (GI) bleeding risk. However, a recent study revealed that the incidence of bleeding after a PEG placement appears to be similar at 2.8%[5]. Based on literature review, PEG post-procedure bleeding risk is estimated to be 2%-2.5%[6,7]. According to current guidelines, clopidogrel discontinuation for 7-10 d prior to PEG in patients with underlying low thromboembolic risks is recommended[6-8].

In case of high underlying thromboembolic risk, it is recommended to consider postponing the procedure until it is safe to hold the thienopyridines (clopidogrel, *etc*.). They should be held for 7-10 d when the underlying risk is low. In patients taking dual antiplatelet therapy, it is safe to continue aspirin while holding the clopidogrel. In cases where patients are on monotherapy with thienopyridines, these patients can be started on aspirin during peri-procedure period.

The patterns of clinical practice for the management of these medications differ from these recommendations. Differences also exist in the patterns of practice among gastroenterologists themselves in the use of these agents. An international survey that was conducted in 2008 revealed that differences exist between Western and Eastern countries with regards to management of these agents[9].

To further evaluate the use of clopidogrel in PEG placement, we performed a retrospective study examining the potential post-procedure risks of bleeding.

MATERIALS AND METHODS

A retrospective study was conducted at a single tertiary-care center on all adult patients having PEG placement (January 2008-January 2014). Institutional review board approval was obtained. PEG was performed by using the standard push or pull technique[2]. The procedure was performed by the attending gastroenterologist and the gastroenterology fellow at our tertiary-care center. All patients were nothing per mouth from midnight to the procedure and received a prophylactic antibiotic 30 min prior to the procedure (if not already receiving antibiotic treatment at the time of PEG insertion for any other reason).

The data pertaining to the several parameters was collected. These included patient demographics, indication for PEG placement, comorbid illnesses, and laboratory data, including hematology profile (hemoglobin, platelets, and coagulation values). The use of each

Table 1 General demographics of patients included in the study

All patients	
Patients (*n*)	320
Age (mean years ± SD)	65.03 ± 16.11
BMI (mean years ± SD)	28.47 ± 9.75
Gender	
Male (*n*)	169
Female (*n*)	151

BMI: Body mass index.

Table 2 Demographics and complications in patients taking clopidogrel *vs* patients not on clopidogrel

Outcome	No plavix	Plavix	*P* value
Patients (*n*)	286	33	-
Age (mean years ± SD)	64.37 ± 16.44	71.21 ± 11.43	0.02
BMI (mean years ± SD)	28.30 ± 9.59	29.25 ± 10.66	0.60
Hgb drop < 48 h	5	2	0.16
Local complications < 48 h	8	2	0.28
Transfusions < 48 h	7	2	0.24
Rescope < 48 h	1	1	0.20

BMI: Body mass index; Hgb: Hemoglobin.

antiplatelet drug was noted and data regarding the timing of the last dose prior to PEG placement and the first dose following PEG was also recorded. Patients were divided into two groups: Clopidogrel group consisting of those patients taking clopidogrel within 5 d prior to the PEG and the non-clopidogrel group including those patients not taking clopidogrel within 5 d of the PEG.

Procedure-related complications, repeat endoscopy, and blood transfusions < 48 h of PEG was collected. The complications were classified as early (< 48 h of PEG placement) *vs* late (> 48 h). GI bleeding was defined as hemoglobin (hgb) drop > 2 g/dL from baseline, observation of GI bleeding (hematochezia, melena, hematemesis), required blood transfusion, and endoscopic hemostasis. The severity of bleeding was defined as mild (clinical evidence of bleeding, no transfusion required), moderate (transfusion required, less than 4 units, but no surgery required) and severe (transfusion of more than 5 units, radiological or surgical intervention).

Statistical analysis was conducted using the following: Descriptive statistics (demographics), two-tailed unpaired *t* test (continuous data), and Fisher's exact test (categorical data). Statistical significance was significant at $P < 0.05$. Statistics were reviewed by two biostatisticians (Matthew L Bechtold and Doug L Nguyen).

RESULTS

Three hundred and nineteen patients with PEG placement were identified, consisting of 168 males, 151 females, mean age 65.03 ± 16.11 years, and mean BMI 28.47 ± 9.75 kg/m^2 (Table 1). Thirty-three patients were using clopidogrel (mean age 71.21 ± 11.43 years). Thirty patients out of these 33 patients received a dose of clopidogrel within 5 d prior to the actual day of the procedure, whereas three patients out of 33 received a dose of Plavix within 7 d prior to the procedure. Two hundred and eighty-six patients were not taking clopidogrel (mean age 64.37 ± 16.44 years). Within 48 h of PEG, no patients in either group developed hematochezia, hematemesis, or melena (Table 2). Within 48 h of PEG, decrease in hgb of > 2 g/dL was identified in 2 patients (clopidogrel group) *vs* 5 patients (non-clopidogrel group) ($P = 0.16$). Blood transfusion within 48 h was necessary in 2 patients (clopidogrel group) *vs* 7 patients (non-clopidogrel group) ($P = 0.24$). No patients underwent repeat endoscopy for GI bleeding.

DISCUSSION

PEG over the years has emerged as a popular method to provide long-term enteral nutrition to patients. A PEG is required in those with inadequate intake of nutrition but have a normally functioning GI tract[1].

Some of the common indications for placement of a PEG include: Neurological disorders that impair the normal physiology of swallowing, malignancies involving the oropharynx or the esophagus and facial trauma[10-12]. There are several options available when considering placement of a gastrostomy tube. However, the endoscopic technique is preferred due lower incidence of complications and is more cost effective than open surgical gastrostomy[13]. Even though the incidence is less, there are still several complications reported that are secondary to PEG placement[14-17]. In a meta-analysis performed by Wollman *et al*[18], the procedure-related mortality was noted as 0.5% and the 30-d all-cause mortality was 15%. Bleeding is one of the complicating factors contributing to mortality.

Our study focused on the risk of post-PEG placement early bleeding in patients that were already on clopidogrel as compared to those not taking clopidogrel. The study did not reveal any significant increase in the risk of early post-procedure bleeding (occurring within 48 h after the procedure) in patients who were taking clopidogrel. When the data was analyzed according to age (above and below the age of 60) and body mass index (BMI) (more than or less than BMI of 30), there was also no significant differences in the bleeding risks or need for blood transfusions. With this data, the use of clopidogrel should not be considered a contraindication to PEG placement. However, other parameters must be considered prior to PEG in this patient population.

First, prior to performing any endoscopic procedure, the risks and benefits should be thoroughly reviewed, including risk of bleeding[6,7]. Second, careful consideration to the clinical impact of withholding an antithrombotic agent must be performed. Hence, each case

should be individually evaluated and the decision made after evaluating the pros and cons of proceeding with procedure and holding any antithrombotic agents.

As with any study, strengths and limitations were observed. The strengths include a large amount of patients undergoing PEG placement at a single tertiary-care center over 6 years. However, limitations are observed as well and should be considered when interpreting the results. First, this is retrospective study and not a randomized controlled trial. Certain biases may be involved in accordance to a retrospective study but efforts were done to try to minimize those biases. Second, given the small sample size of patients undergoing PEG while on clopidogrel (n = 33), a type II statistical error may be present which indicates the study lacked the power to detect a significant difference between the two groups. However, given that PEG placement has traditionally been withheld on patient who have been on recent clopidogrel, a limited number of patients underwent PEG with clopidogrel over the 6-year period and all of those patients were included in the study. Based on this possibility, results should be interpreted with caution and further larger studies are required to evaluate the overall effect of clopidogrel and PEG placement.

In conclusion, bleeding is a potential complication of PEG placement. Our retrospective study demonstrated no statistically significant increase in bleeding risk or requirement of blood transfusions in patients who were on clopidogrel for PEG placement. Therefore, clopidogrel did not increase bleeding risk despite cessation for a shorter time period as recommended by current guidelines.

COMMENTS

Background

Percutaneous endoscopic gastrostomy is a common procedure for patients who require enteral supplemental nutrition. In the past, any medications that could lead to increased bleeding risk were held prior to the percutaneous endoscopic gastrostomy (PEG) placement. However, recently, this practice has been challenged, especially with clopidogrel with little evidence in the literature.

Research frontiers

Little evidence is in the literature regarding the use of clopidogrel during PEG placement. This retrospective study evaluates the use of concomitant clopidogrel and PEG placement in a tertiary-care hospital in regards to post-procedure bleeding. Very few publications are available in the literature to evaluate this subject. Two publications that are related are below. Lucendo AJ, Sánchez-Casanueva T, Redondo O, Tenías JM, Arias Á. Risk of bleeding in patients undergoing PEG tube insertion under antiplatelet therapy: a systematic review with a meta-analysis. *Rev Esp Enferm Dig* 2015; 107: 128-136; Richter JA, Patrie JT, Richter RP, Henry ZH, Pop GH, Regan KA, Peura DA, Sawyer RG, Northup PG, Wang AY. Bleeding after percutaneous endoscopic gastrostomy is linked to serotonin reuptake inhibitors, not aspirin or clopidogrel. *Gastrointest Endosc* 2011; 74: 22-34.e1.

Innovations and breakthroughs

This is a rare study evaluating the use of clopidogrel with PEG placement. Very few studies have evaluated this subject. This study shows that clopidogrel may not require cessation prior to PEG placement which is a change in current and past practice.

Applications

For PEG placement, clopidogrel does not require cessation prior to procedure. This will allow patients to continue their much needed clopidogrel for PEG placement.

Terminology

PEG placement is a common procedure performed on patients who require supplemental enteral nutrition. Clopidogrel is also a common medication for antiplatelet properties.

Peer-review

The manuscript is provided useful information that clopidogrel discontinuation before PEG is not necessary in case of urgent need for such procedure.

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