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Original Article

Outcome of Early Nutrition Support after Perforated Peptic Ulcer Repair

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Abstract

Background: Early nutrition support (ENS) is safe and beneficial for patients undergoing elective upper gastrointestinal tract surgery. However, the value of ENS in perforated peptic repair remains inconclusive.

Objective: The aim of the present study was to investigate the safety, feasibility, and benefits of ENS in perforated peptic ulcer repair.

Methods: Patients with perforated peptic ulcer who underwent repair by simple closure with omental pedicle techniques were randomized into 2 groups. In the ENS group, patients were given an oral diet of congee at will after 24 hours after repair if gastric residual volume was less than 200 mL per 8 hours. In the traditional postoperative care (TPC) group, patients were given liquid diet progressing to congee at will only after 72 hours. The primary outcome was postoperative complications occurring within 30 days after surgery, including surgical site infection (SSI), hospital acquired pneumonia and postoperative repair leakage. Other outcomes included diet intolerance, time to achieve enteral nutrition in the ENS group and length of hospital stay.

Results: One hundred and ten patients were randomly assigned to TPC or ENS (55 patients per group). Baseline and intraoperative clinical characteristics were similar in both groups. Postoperative complications after surgery were seen in 4.6% of patients. The risk of postoperative complications was slightly higher in the TPC group (3 of 55 patients, 5.5 %) versus the ENS group (2 of 55 patients, 3.6%), but the difference was not statistically significant. Superficial SSI was the only postoperative complication. Neither hospital acquired pneumonia nor postoperative repair leakage were observed. Only one patient in the TPC group had diet intolerance, which was successfully managed conservatively. Time to achieve enteral nutrition in the ENS group was 40 hours (almost 2 days) after surgery. The length of hospital stay was similar for both groups.

Conclusions: ENS in patients who underwent perforated peptic ulcer repair appeared to be as safe as, if not clearly superior to, TPC.

Keywords: Peptic ulcer perforation, Perforated peptic ulcer repair, Early nutrition support, Early enteral feeding

Introduction

Perforated peptic ulcer is the second most common complication related to peptic ulcer disease and is associated with 30% to 50% morbidity and 10% to 30% mortality. More than 50% of the morbidity is associated with infection[2]. The use of appropriate antibiotics, adequate fluid resuscitation and early nutrition support can decrease morbidity[17]. The current surgical management of perforated peptic ulcer is mainly confined to simple closure with omental pedicle techniques, as a consequence of major advances in the pharmacologic treatment of peptic ulcer disease[18].

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The postoperative care of the patient is still dominated by the long-held belief that traditional postoperative care (TPC), which requires no oral diet for at least 3 days and a progressive oral diet beginning with liquids, would minimize the risk of diet intolerance, repair leakage and pulmonary aspiration[11]. Even though early nutrition support (ENS) in elective surgery, including non-gastrointestinal, upper gastrointestinal and colorectal surgery, is both beneficial and safe[13,14,15,19,21], the value of ENS in emergency surgery, such as in perforated peptic ulcer repair, is still in doubt due to limited evidence[8]. The aim of the present study was to evaluate the safety, feasibility, and benefits of ENS in patients with perforated peptic ulcer.

Patients and Methods

The present study was a single-center, randomized, single-blind clinical trial. Patients with perforated peptic ulcer diagnosed between August 25, 2018 to October 20, 2019 were recruited into the study. The Khon Kaen Hospital Institutional Review Board at Khon Kaen, Thailand, approved this study (approval ID: KE61026).

Patients who presented with peritonitis and pneumoperitoneum were provided with sufficiently detailed information about the study and was asked to volunteer and sign an informed consent form. Hospital personnel involved in patients' care were informed of the study. Randomization was done via computer-generated blocks of 4, randomly allocating patients into 2 groups, the ENS group and the TPC group. Allocation was concealed in opaque envelopes, which were opened at the end of the surgical procedure. Patients older than 18 years with perforated peptic ulcer who underwent exploratory laparotomy and repair with simple closure with omental pedicle techniques were included in the study.

Exclusion criteria included preoperative shock on admission, time to operation of over 24 hours, known malignant gastric ulcers confirmed by histopathology, the presence of neuropsychiatric disease, pregnant and lactating women, predisposing factors for impaired wound healing (e.g., currently using immunosuppressive agents, or chronic use of steroids), the presence of HIV/AIDS, and intraoperative findings consistent with malignant ulcers.

Preoperative preparation was identical in both groups and included the insertion of nasogastric tube, urinary catheter, the administration of balanced crystalloid for fluid replacement, intravenous antibiotics with ceftriaxone (2 grams every 24 hours) and metronidazole (500 mg every 8 hours).

The surgical procedure was done by either the attending staff or a trainee under supervision. Firstly, after exploratory laparotomy, the perforation site was identified by examining the first portion of duodenum and the anterior surface of stomach. If the aforementioned sites were clearly intact, the posterior wall of the stomach and the small bowel were examined. Ulcer biopsy for histopathological examination was mandatory if the ulcer was located at the stomach. Simple closure of the ulcer perforation with omental pedicle technique was the preferred surgical procedure for all cases. This was done by placing 2 or 3 interrupted sutures parallel to the longitudinal axis of the gastrointestinal tract, and an omental pedicle was mobilized and secured over the perforation site with previously placed sutures. The integrity of the repair was tested by filling the stomach with air. If no leak was observed, the peritoneal cavity was irrigated with warm saline. Finally, a Penrose drain was placed at the right subphrenic and subhepatic area, and the abdominal incision was closed.

The nasogastric tube was left in place postoperatively. The urinary catheter was removed on postoperative day 1. Postoperative pain was controlled with morphine (0.1 mg per kilogram, every 4 hours) for the first 2 postoperative days. An intravenous acid – reducing therapy with omeprazole (40 mg every 12 hours) was continued throughout the hospital stay.

In the TPC group, the nasogastric tube was removed 72 hours postoperatively. Oral intake of liquids was started and advanced to congee at will. The Penrose drains were gradually withdrawn every day beginning at 12 hours after initiation of congee.

In the ENS group, the nasogastric tube was removed at 24 hours after operation unless the gastric residual volume was more than 200 mL per 8 hours. Oral intake of congee was started at will. The Penrose drains were gradually withdrawn every day beginning at 12 hours after initiation of congee.

In both groups, oral intake was suspended if the patient was unable to tolerate oral diet. Diet intolerance was defined as postprandial vomiting or abdominal pain (pain score of more than 8 on visual analog scale), and antiemetic drugs were prescribed. If symptoms persisted for over 24 hours, a nasogastric tube was re-inserted. Patients were discharged they were able to tolerate oral diet and defecate, with no drains remaining.

All patients were prescribed oral acetaminophen (500 mg on demand), amoxycillin (2 grams every 12 hours for 14 days), clarithromycin (1 gram every 12 hours for 14 days) and omeprazole (20 mg every 12 hours) for at least 2 months. Patients were advised to have their stitches removed on postoperative day 7 and to return for a follow-up clinical examination on postoperative day 30.

The outcome of the study was the occurrence of 30-day postoperative complications. This included, especially, infection-related postoperative complications such as superficial, deep or organ space SSI, hospital acquired pneumonia, and postoperative repair leakage. Diet intolerance, time to achieve enteral nutrition (especially in the ENS group), and length of hospital stay were also recorded. These complications were defined according to the Clavien-Dindo classification[6]. Postoperative repair leakage was defined as any extraluminal enteric contents detected by drain, at the surgical incision site, or the presence of intraabdominal collection[4,14].

The planned sample size per group was estimated using previous information on 30-day postoperative complications, with a two-sided 5% significance level and a power of 80%. The estimated sample size per group was 250.

Data were collected using data collection forms. These forms were filled by clinicians who were not directly involved in the study, and the collected data were regularly transferred to a computerized database by the researchers.

Categorical variables were compared using the Chi-squared or Fisher's exact test, as appropriate. Student's *t* test, Wilcoxon test or Mann-Whitney U-test was used for continuous data. Statistical significance was defined as a p-value < 0.05.

Results

During the study period, there were 205 eligible patients. Ninety-five patients were excluded for various reasons, resulting in 110 patients who were randomized. The CONSORT flow diagram is shown in Figure 1. No randomized patients dropped out of the study or were lost to follow-up. Baseline clinical characteristics and operative findings of patients in both the ENS and TPC groups are shown in Tables 1 and 2.

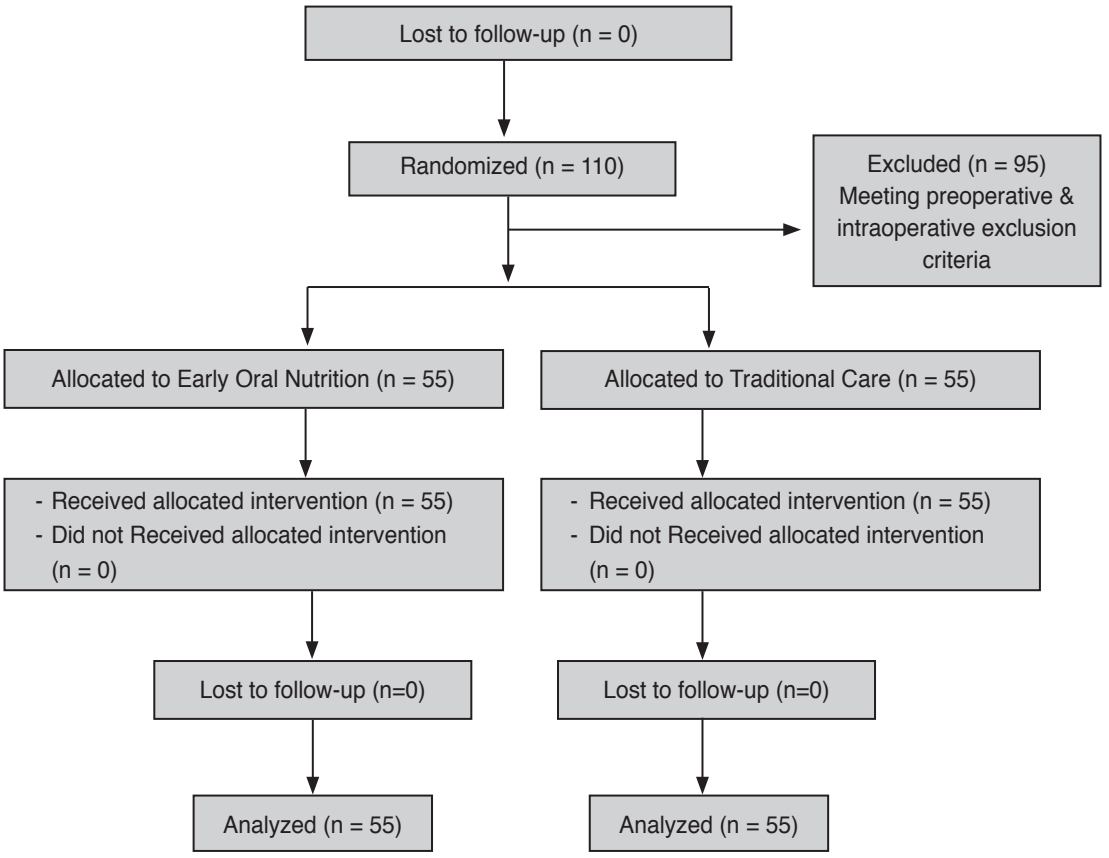

Figure 1 The CONSORT flow diagram for the present study

Table 1 Baseline characteristics of patients in the ENS and TPC groups

	ENS group N = 55	TPC group N = 55
Male: number (%)	51 (93)	50 (91)
Age, years: mean (SD)	58.1 (11.9)	50.6 (15.6)
BMI: median (IQR)	20.8 (19.2, 23.3)	21.3 (20,23)
Underlying disease: number (%)	14 (25)	9 (16)
Diabetes mellitus	2 (4)	4 (7)
Hypertension	6 (11)	7 (13)
Chronic obstructive pulmonary disease	3 (6)	1 (2)
Liver cirrhosis	2 (4)	0
Heart disease	1 (2)	0
Chronic kidney disease	4 (7)	1 (2)
NSAID use: number (%)	39 (71)	38 (69)
ASA class: number (%)		
I	4 (7)	2 (4)
II	32 (58)	41 (75)
III	19 (35)	12 (22)
Smoking: number (%)	32 (58)	31 (56)
Duration before surgery, hours: mean (SD)	13.9 (6.1)	12.2 (4.8)

ENS: Early nutrition support; TPC: Traditional postoperative care; IQR: interquartile range, SD: standard deviation

Table 2 Intraoperative findings of patients in the ENS and TPC groups

	ENS group N = 55	TPC group N = 55
Operative time, minutes: median (IQR)	59 (48,71)	56 (48,81)
Intraoperative diagnosis: number (%)		
Duodenal ulcer	43 (78)	53 (96)
Site of perforation: number (%)		
Prepyloric	6 (11)	1 (2)
Antrum	3 (5)	0
Body of stomach	3 (5)	1 (2)
First part of duodenum	43 (78)	53 (96)
Size of perforation, mm: median (IQR)	5 (3,5)	5 (3,6)
Peritoneal contamination: number (%)		
Clear	1 (2)	2 (4)
Cloudy, purulent	54 (98)	53 (96)
Feculent	0	0
Operative procedure: number (%)		
Graham technique	2 (4)	5 (9)
Cellen-Jones technique	4 (7)	1 (2)
Omentoplasty	49 (89)	49 (89)

ENS: Early nutrition support, TPC: Traditional postoperative care; IQR: interquartile range

Table 3 Comparison between outcomes of patients in the ENS and TPC groups

Outcomes (summarized as number (%), unless stated otherwise)	ENS group N = 55	TPC group N = 55	Risk ratio	95% CI	*p*-value
Overall complications	2 (4)	3 (6)	1.5	[0.26-8.63]	0.999
Superficial surgical site infection	2 (4)	3 (6)	1.5	[0.26-8.63]	0.999
Organ Space infection	0	0	–	–	–
Hospital acquired pneumonia	0	0	–	–	–
Postoperative repair leakage	0	0	–	–	–
Diet intolerance	0	1 (2)	–	–	0.999
LOH, days: median (IQR)	7 (6,7)	7 (6,8)	–	–	0.052
Time to enteral nutrition in ENS, hours: median (IQR)	40 (36,53)	–	–	–	–

ENS: Early nutrition support; TPC: Traditional postoperative care; LOH: length of hospital stay; IQR: interquartile range

Although there were significant differences between the two groups in terms of age, intraoperative diagnosis, and site of perforation, these were likely due to chance.

Overall, 5 of 110 patients (5%) had postoperative complications after surgery. There were no significant differences in terms of complications between the 2 groups (Table 3). Infection (superficial SSI) accounted for all postoperative complications. Neither hospital acquired pneumonia nor leakage after repair were found. One patient in the TPC group had diet intolerance and responded to conservative treatment. The average time to achieve enteral nutrition in the ENS group was 40 hours after operation (almost 2 days). The median length of hospital stay in the TPC group was 7 days (IQR, 6 to 8 days) versus 7 days (IQR, 6 to 7 days) as well in the ENS group, which were not significantly different (p-value = 0.052). Table 3 details the outcomes of the present study.

Discussion

The present study showed that ENS in patients who underwent perforated peptic ulcer repair did not increase the risk of postoperative complications within 30 days after surgery, although no clear benefit of ENS was demonstrated. However, the present study has several limitations. There were some differences in baseline and intraoperative characteristics of patients between the 2 randomized groups. Blinding the surgeons and patients was not possible for obvious reasons. The study as it currently stands lacked statistical power because the planned sample size has not been reached. But the strength of the present trial included a complete follow-up with no missing data, and the adherence to the principle of intention-to-treat analysis.

ENS has been shown to be safe, feasible, and beneficial in elective gastrointestinal surgery[13,14,15,19,21], but there is a lack of such evidence in the emergency setting. Advantages of early nutrition in emergency gastrointestinal surgery have been suggested. A few RCTs have indicated that early tube feeding in nontraumatic gut perforation might offer advantages with regards to wound complications and hospital stay[11,12]. Only one RCT has shown that early oral feeding in an Enhanced Recovery Pathway in laparoscopic perforated peptic ulcer repair might provide such advantages[9]. According to a long-held belief, traditional postoperative care in emergency abdominal surgery should prevent anastomotic complications, prevent postoperative ileus and vomiting, and lung aspiration[24]. The present study aimed to challenge this belief, by examining the safety, feasibility, and benefits of ENS in the emergency setting, specifically in patients undergoing surgery for perforated peptic ulcer.

In the present study, perforated peptic ulcer was more common in men than in women. There was a difference in the mean age between the ENS and TPC groups, but this might not be clinically significant as all patients could be considered middle-aged. There was also a difference in the site of perforation, the duodenum being the more common site in the TPC group (TPC group, 96% versus ENS group, 78%). But because other sites of perforation were almost all located in the prepyloric region, and both prepyloric gastric ulcer and duodenal ulcer share the same pathophysiology of ulcer development,[5] the difference in location of perforation between the 2 groups should not be clinically important.

The overall postoperative complication rate in the present study was 5%, less than that previously reported in the literature[8,16].

A possible explanation might be that high-risk patients were excluded from the present study. The TPC group tended to have a higher risk of postoperative complications, but this was not statistically significant. Perhaps a longer period of routine nasogastric decompression, which has been shown to increase the risk of diet intolerance, lung aspiration, and time to resume oral diet after surgery, might be the explanation for this[9].

In the present study, all postoperative complications were superficial SSI. A superficial SSI rate of 5% was also less than that reported previously. The wound type for perforated peptic ulcer surgery is regarded as contaminated or dirty, which should have an SSI rate between 15% to 40 %[6]. The much lower rate of SSI in the present study could be explained by our excluding high-risk patients, and the extensive use of antibiotics during the perioperative period[8,23]. None of the patients in both groups developed organ space SSI, hospital acquired pneumonia or postoperative repair leakage. Only one patient in TPC group had diet intolerance. Emergency abdominal surgery, especially in the presence of peritonitis, might account for this. The intestinal mucosa usually heals within 24 hours, but gastrointestinal motility and gastric function mainly return within 24 to 48 hours after surgery. Prolonged nasogastric decompression also increases the duration of diet intolerance, and hence the length of time to resuming oral diet after surgery.

The most appropriate time to start oral feeding in patients under the ENS regimen is 40 hours after surgery, and patients are not expected to have diet intolerance. Perhaps by allowing oral congee only after evidence of a sufficiently low residual gastric volume, which is a good predictor of returning stomach function, we prevented diet intolerance[7]. The length of hospital stay in both groups was 7 days, on average, and this was probably due to the requirement that all peritoneal drains be removed prior to home discharge.

The present study suggests that ENS in perforated peptic ulcer repair does not increase the risk of postoperative complications. However, this might not apply to high risk patients, such as those with late presentation, or with preoperative shock.

Conclusion

Early nutrition support in perforated peptic ulcer repair does not seem to increase the risk of postoperative complications, especially SSI and repair leakage. The appropriate time to start oral nutrition if ENS were to be implemented, to minimize diet intolerance, is 40 hours after surgery. There was no significant difference between ENS and TPC groups in terms of length of hospital stay, which might be because of the requirement to remove all drains before discharge. Thus, while ENS might be as safe as TPC, it might not clearly be more beneficial.

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บทคัดย่อ **การเริ่มให้อาหารทางปากเร็วในกลุ่มผู้ป่วยที่ได้รับการผ่าตัดกระเพาะอาหารและลำไส้เล็กส่วนต้นทะลุ**

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กลุ่มงานศัลยศาสตร์ โรงพยาบาลขอนแก่น

ความเป็นมา: การเพิ่มให้อาหารทางปากเร็วในผู้ป่วยที่ได้รับการผ่าตัดแบบไม่เร่งด่วน (Elective surgery) ช่วยลดภาวะแทรกซ้อนลงได้ภายใน 30 วัน (Morbidity) โดยเฉพาะภาวะแทรกซ้อนที่มีความสัมพันธ์กับการติดเชื้อ อีกทั้งยังช่วยลดระยะเวลาการนอนโรงพยาบาล แต่ผลของการเริ่มให้อาหารทางปากเร็วในผู้ป่วยที่ได้รับการผ่าตัดฉุกเฉิน (Emergency surgery) โดยเฉพาะภาวะกระเพาะอาหารและลำไส้เล็กส่วนต้นทะลุนั้นยังสรุปได้ไม่ชัดเจน

วัตถุประสงค์: เพื่อศึกษาผลของการเริ่มให้อาหารทางปากเร็วในผู้ป่วยที่ได้รับการผ่าตัดกระเพาะอาหารและลำไส้เล็กส่วนต้นทะลุ

วิธีการศึกษา: ผู้ป่วยหลังได้รับการผ่าตัดกระเพาะอาหารและลำไส้เล็กส่วนต้นทะลุทั้งหมด 110 รายแบ่งเป็นกลุ่มที่เริ่มให้อาหารทางปากเร็วภายในระยะเวลาไม่เกิน 72 ชั่วโมงหลังผ่าตัด (กลุ่ม ENS) กับกลุ่มที่เริ่มให้อาหารทางปากแบบดั้งเดิม (หลัง 72 ชั่วโมง) (กลุ่ม TPC) โดยเปรียบเทียบอัตราการเกิดภาวะแทรกซ้อนภายใน 30 วัน หลังการผ่าตัด อัตราการเกิดภาวะแทรกซ้อนที่สัมพันธ์กับการติดเชื้อภายใน 30 วันหลังผ่าตัด อุบัติการณ์ของภาวะรอยต่อลำไส้รั่ว อาการอืดแน่นท้องและอาเจียนหลังเริ่มให้อาหารทางปากและเวลาที่ได้เริ่มอาหารทางปากในกลุ่มที่เริ่มให้อาหารทางปากเร็วระยะเวลาการนอนโรงพยาบาล

ผลการศึกษา: พบภาวะแทรกซ้อนภายใน 30 วันหลังการผ่าตัดกระเพาะอาหารและลำไส้เล็กส่วนต้นทะลุ ทั้งหมด 5 ราย (ร้อยละ 4.54) โดยกลุ่ม TPC มีโอกาสเกิดภาวะแทรกซ้อนภายใน 30 วัน หลังผ่าตัดมากกว่ากลุ่ม ENS 1.5 เท่า (ร้อยละ 5.5: ร้อยละ 3.6, $P < 0.999$) พบว่าการติดเชื้อแผลผ่าตัดชั้นตื้น เป็นภาวะแทรกซ้อนที่สัมพันธ์กับการติดเชื้อภายใน 30 วันหลังการผ่าตัดที่พบมากที่สุด โดยกลุ่ม TPC มีโอกาสเกิดการติดเชื้อแผลผ่าตัดชั้นตื้นมากกว่า กลุ่ม ENS 1.5 เท่า (ร้อยละ 5.5 ; ร้อยละ 3.6 , $P > 0.999$) และไม่พบรอยรั่วของรอยต่อลำไส้ในผู้ป่วยทั้งสองกลุ่ม ทั้งนี้ พบว่ามีผู้ป่วย 1 รายที่ในกลุ่ม TPC มีอาการอืดแน่นท้องและอาเจียนหลังเริ่มให้อาหารทางปาก แต่เริ่มรับประทานอาหารดีขึ้น หลังการรักษาโดยการประคับประคอง นอกจากนี้พบว่าระยะเวลา 40 ชั่วโมงหลังผ่าตัดเป็นระยะเวลาที่ผู้ป่วยในกลุ่ม ENS สามารถเริ่มให้อาหารทางปากได้ และระยะเวลาการนอนโรงพยาบาล ในกลุ่ม TPC และกลุ่ม ENS คือ 7 วัน

สรุปผลการศึกษา: การเริ่มให้อาหารทางปากเร็วในกลุ่มผู้ป่วยที่ได้รับการผ่าตัดกระเพาะอาหารและลำไส้เล็กส่วนต้นทะลุ พบว่ามีแนวโน้มที่จะสามารถลดภาวะแทรกซ้อนภายใน 30 วัน และภาวะแทรกซ้อนที่สัมพันธ์กับการติดเชื้อภายใน 30 วัน และภาวะแทรกซ้อนที่สัมพันธ์กับการติดเชื้อภายใน 30 วันหลังการผ่าตัดลงได้ โดยไม่พบว่าเพิ่มภาวะรอยต่อลำไส้รั่วและอาการอืดแน่นท้องและอาเจียนหลังเริ่มอาหารทางปาก เมื่อเทียบกับการเริ่มให้อาหารทางปากแบบดั้งเดิม