Original Article

Citrus reticulata peel improves patient tolerance of low-volume polyethylene glycol for colonoscopy preparation

Hung-Chieh Lan a, Ying Liang b,c, Hsiu-Chuan Hsu b,c, Jiah-Hwang Shu b,c, Chien-Wei Su a,d,e, Hung-Hsu Hung a,d, Ming-Chih Hou a,d,f, Han-Chieh Lin a,d, Shou-Dong Lee d,g,h, Yuan-Jen Wang c,d,*

a Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
b Department of Nursing, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
c Division of Healthcare and Services, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
d Faculty of Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC
e Institute of Clinical Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC
f Department of Endoscopy Center, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
g Department of Medicine, National Defense Medical Center School of Medicine, Taipei, Taiwan, ROC
h Cheng Hsin General Hospital, Taipei, Taiwan, ROC

Received December 9, 2011; accepted April 2, 2012

Abstract

Background: Adequate adjuncts help to reduce the volume of polyethylene glycol-electrolyte lavage solution (PEG-ELS) needed, to ameliorate patient discomfort, and to improve colonic visibility during colonoscopy. This study aimed to assess the effect of Citrus reticulata peel (CRP) as an adjunct to low-volume PEG for colonic preparation.

Methods: A total of 1092 health examination examinees received colonoscopy during the study period. After excluding those who refused to participate and those who did not meet our criteria, 212 examinees were enrolled into this study. They were divided into the PEG group and the PEG + CRP group according to their date of examination. All examinees received 2 L of PEG-ELS one day before colonoscopy. The PEG + CRP group also received additional CRP in the form of a “buccal tablet” between drinks. Tolerance and adverse events were assessed by questionnaire, while the quality of bowel preparation for colonoscopy was scored by an endoscopist.

Results: There were 107 examinees in the PEG group and 105 examinees in the PEG + CRP group. The demographic characteristics of the examinees were comparable between these two groups. Examinees in the PEG + CRP group had a trend of better colonic visibility than those in the PEG group (p = 0.056). Moreover, examinees in the PEG + CRP group had a higher rate of acceptable taste (p = 0.015) and lower rate of difficulty swallowing (p = 0.001). The incidences of adverse events including vomiting (p = 0.045), bloating (p = 0.035), and difficulty sleeping (p < 0.001) were also significantly lower in the PEG + CRP group.

Conclusion: Compared with conventional colonic preparation, the application of CRP as an adjunct could improve examinees’ tolerance, decrease the incidence of adverse events, and maintain the quality of colonic cleansing.

Keywords: adjunct; bowel preparation solutions; citrus; colonoscopy; low-volume polyethylene glycol

* Corresponding author. Dr. Yuan-Jen Wang, Division of Healthcare and Services, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: yjwang@vghtpe.gov.tw (Y.-J. Wang).

Copyright © 2012 Elsevier Taiwan LLC and the Chinese Medical Association. All rights reserved.

http://dx.doi.org/10.1016/j.jcma.2012.06.022
1. Introduction

During colonoscopy, sufficient bowel preparation is essential for detecting small lesions and visualizing the mucosa. However, colonoscopy preparation regimens are either poorly tolerated by patients because of the large volume of polyethylene glycol-electrolyte lavage solution ([PEG-ELS]) or the risk of electrolyte imbalance and hemodynamic instability (from sodium phosphate). Such challenges limit the clinical application of sodium phosphate and full-dose PEG-ELS.1

Low-volume PEG combined with adjunctive laxatives has been shown to be comparable to full-dose PEG in terms of colonic preparation quality and better patient tolerance.2–7 Adjuncts such as ascorbic acid, bisacodyl, and olive oil have been demonstrated in recent trials to be effective in achieving colonic visibility and patient tolerance.2,3,8 However, anorexia, vomiting, bloating, and abdominal pain still affect a substantial number of patients who receive bisacodyl as an adjunct for colonic preparation, and this may compromise the quality of colonic cleansing.

In this study, we evaluated Citrus reticulata peel (CRP), dried tangerine peel, as an adjunct for colonoscopy preparation. Citrus peel is commonly used for flavoring food and beverages worldwide. CRP is the dried pericarp of the ripe fruit of Citrus reticulata Blanco, and its main indications in traditional medicine include bloating, anorexia, vomiting.9,10 We deduced that adding CRP to a conventional colon preparation of low-volume PEG-ELS with bisacodyl could improve the quality of colonic cleansing by reducing the side effects produced by the bisacodyl. To validate this hypothesis, we conducted a prospective study comparing the quality of colonic cleansing and examinees’ satisfaction with a conventional low-volume preparation against one with added CRP.

2. Methods

2.1. Examinees

We enrolled examinees who were visiting Taipei Veterans General Hospital for health examination during the period May 22, 2009 to September 25, 2009. The exclusion criteria were: the presence of serious conditions such as severe cardiac, pulmonary, renal, hepatic, or metabolic diseases; active alcoholism, drug addiction, or major psychiatric illness; known allergy to PEG-ELS; and refusal to participate. Oral and written instructions about the colonic preparation were given to all examinees.

After obtaining informed consent, examinees were assigned to either the PEG group (conventional preparation using low-volume PEG-ELS with bisacodyl) or the PEG + CRP group (conventional preparation with additional CRP) according to their date of colonoscopy examination. Examinees in the PEG group were enrolled from May 22, 2009 to July 28, 2009, while those in the PEG + CRP group underwent colonoscopy from July 29, 2009 to September 25, 2009. The hospital’s institutional review board approved the study protocol (98-03-05A).

2.2. Preparation instructions

Each pack of low-volume PEG-ELS (Niflec; China Chemical & Pharmaceutical Co., Ltd. Taiwan, R.O.C.) contained 82.9 g sodium sulfate anhydrous, 21.36 g sodium chloride, 10.83 g potassium chloride, 24.57 g sodium bicarbonate, and polyethylene glycol 4000 for a total of 137.155 g. All examinees received one pack of Niflec in 2 L of water 1 day before the procedure and were asked to drink one glass of solution (250 mL) every 10–15 minutes, starting at 4 PM, until the 2 L had been consumed (within 2 hours). They were also instructed to begin a clear liquid diet on the morning of the day before colonoscopy and to fast after midnight.

The PEG + CRP group received additional CRP between drinks (every 10–15 minutes after completing 250 mL of solution) with one piece (2 g) of CRP (Fig. 1). Examinees were instructed to place the CRP between the hard palate and tongue rather than swallowing it. After 5 minutes with this in place, they had to spit out the remaining CRP and continued with the preparation solution. Eight pieces of CRP were given for every colonoscopy preparation.

All examinees received 15 mg bisacodyl after the first time they had diarrhea or at 8 PM on the same day if there was no bowel movement. All examinees were also asked to drink sports drinks or warm water after completing the entire preparation solution (but not exceeding 3500 mL in total volume).

2.3. Colonoscopy

After the examinee had undergone successful conscious sedation, the endoscopist waiting in the preparing room was informed to perform the colonoscopy. The endoscopist and technicians were blinded to the correlation between the study periods and the preparation regimen. All colonoscopies were performed in the morning, and examinees were continuously monitored (heart rate and oxygen saturation) during the procedure and recovery period. The quality of bowel cleansing was graded by the endoscopist at the end of the procedure according to a previously described scale. (Table 1).11,12

Fig. 1. Citrus reticulata peel in a 2 g piece.
2.4. Study end-points

The primary end-point was overall colon cleansing. Secondary study end-points included adverse events and patient tolerability, which were evaluated at the time before colonoscopy. The onset time (from the first dose of PEG-ELS to the first time the patient had diarrhea) and total duration of preparation solution action (from the time of first diarrhea to the last diarrhea after drinking PEG-ELS) were also calculated.

2.5. Data collection

Before the colonoscopy, each examinee was interviewed by our nursing staff to evaluate the acceptability of the preparation (i.e. taste, ease of swallowing, and percentage of incompletely consumed preparation solution) and adverse events, including bloating, nausea, vomiting, abdominal cramps, and sleep disturbances. Our study nurses responsible for data collection were blinded to examinee allocation. After instructing examinees how to fill out the questionnaires, study nurses let examinees rank their discomfort during the preparation (on a scale of 1—5, with 1 representing “Very Difficult” to 5 representing “Very Easy”) and fill out the questionnaires themselves.

2.6. Statistical analysis

Sample size calculation was based on the assumption of a 70% satisfactory preparation (excellent, good, or fair) in the PEG group and 85% in the PEG + CRP group, respectively, by using the Z-statistic to compare dichotomous variables, with $\alpha = 0.05$ (two-tailed) and $\beta = 0.20$. The estimated sample size was 95 examinees per arm. Keeping in mind a likely drop-out rate of 10%, at least 105 examinees were required in each group.

Pearson Chi-square analysis or Fisher’s exact test were used to compare categorical variables, while the Mann—Whitney U test was used to compare continuous variables. A two-tailed $p < 0.05$ was considered to be statistically significant. All statistical analyses and database collection were performed using the Statistical Package for Social Sciences (SPSS 17.0 for Windows; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Demographic characteristics

A total of 1092 health examination examinees received colonoscopy during this study period. After excluding those who refused to participate and those who did not meet our criteria, 212 examinees were enrolled into this study. There were 107 examinees in the PEG group and 105 in the PEG + CRP group (Fig. 2). These two groups were comparable in terms of age, gender, height, body weight, chronic constipation, abdominal surgery, and the co-morbidities of hypertension and diabetes mellitus (Table 2). All colonoscopies were completed to the level of the cecum. The number of examinees with prior colonoscopy and those who had received medication that could interfere with the adequacy of bowel preparation were also similar in both groups (Table 2).

3.2. Onset, action, and tolerance of preparation solution

Compliance with the preparation was better in the PEG + CRP group than that in the PEG group, as demonstrated by significantly higher rates of acceptable taste (85.7% versus 71%; $p = 0.015$) and lower rates of difficulty swallowing (8.6% versus 27.1%; $p = 0.001$) (Table 3). The onset time was similar in both groups (66.4 minutes versus 73.0 minutes; $p = 0.213$). Regarding the mean duration from first diarrhea to last diarrhea after drinking PEG-ELS, a significantly shorter time was noted in the PEG + CRP group, as shown by a statistically lower rate (6.7% versus 34.6%; $p < 0.001$) (Table 3). The onset of vomiting (7.2% in the PEG + CRP group versus 17.8% in the PEG group; $p = 0.045$), lower rate of bloating (81.9% versus 92.5%; $p = 0.035$), and lower rate of difficulty sleeping (6.7% versus 34.6%; $p < 0.001$). Other side effects including nausea, abdominal cramping, headache, and dizziness were comparable between the two groups (Table 4).

3.3. Adverse events

Compared with the PEG group, the incidence of adverse events with colonoscopy preparation was significantly lower in the PEG + CRP group, as shown by a statistically lower rate of vomiting (7.2% in the PEG + CRP group versus 17.8% in the PEG group; $p = 0.045$), lower rate of bloating (81.9% versus 92.5%; $p = 0.035$), and lower rate of difficulty sleeping (6.7% versus 34.6%; $p < 0.001$). Other side effects including nausea, abdominal cramping, headache, and dizziness were comparable between the two groups (Table 4).

3.4. Quality of colonic cleansing

The quality of the colonic cleansing was comparable in both groups with regard to the overall percentage and number of satisfactory preparations (Table 5). In the PEG + CRP group, 95 examinees (90.5%) had a satisfactory preparation (defined as excellent, good, or fair) compared with 86
examinees (80.4%) in the PEG group, with a trend in favor of CRP use \( (p = 0.059) \) (Table 5).

4. Discussion

Colorectal cancer is the second leading cause of cancer mortality worldwide and accounts for approximately 9% of overall cancer mortality.\(^13\)\(^-\)\(^15\) It is estimated that attaining the goals for population colorectal cancer screening can save 18,800 lives per year in the United States.\(^13\) Colonoscopy is considered the standard against which the sensitivity of other colorectal cancer screening tests should be compared.\(^15\) Thorough colonoscopy depends on adequate bowel preparation, and around one-fifth to one-third of failed procedures are due to poor preparation.\(^16\),\(^17\) The quality of bowel preparation also has a direct impact on the adenoma detection rate.\(^18\)-\(^20\) However, during colonic preparation, colonic visibility, patient tolerance, and safety are often difficult to achieve. According to the American Society for Gastrointestinal Endoscopy consensus statement, “Physicians favor preparations associated with best patient compliance in order to achieve the best results. Patients favor preparations that are low in volume, palatable, and have easy to complete regimens.”\(^21\) Unfortunately, such conflicts limit the clinical application of preparation solutions.

Standard full-dose PEG-ELS has little effect on electrolytes, but patients have to tolerate the abdominal fullness, nausea, and vomiting associated with the large lavage volume. Sodium phosphate solution, although much smaller in volume, is not suggested for the elderly or those with heart failure, impaired renal function, uncontrolled hypertension, or ascites due to risk of electrolyte imbalance and hemodynamic

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Demographic data of the study examinees.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td>PEG group ((n = 107))</td>
</tr>
<tr>
<td>Age (y)</td>
<td>55.5 ± 10.1</td>
</tr>
<tr>
<td>Sex male/female</td>
<td>64/43 (59.8/40.2)</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>164.1 ± 8.5</td>
</tr>
<tr>
<td>Body weight (before preparation) (kg)</td>
<td>68.0 ± 14.1</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>25.11 ± 4.13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33 (30.8)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (8.4)</td>
</tr>
<tr>
<td>Abdominal surgery(^a)</td>
<td>30 (28)</td>
</tr>
<tr>
<td>Chronic constipation(^b)</td>
<td>18 (16.8)</td>
</tr>
<tr>
<td>Medication may alter preparation adequacy(^b)</td>
<td>9 (8.4)</td>
</tr>
<tr>
<td>Prior colonoscopy</td>
<td>33 (31.0)</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as mean ± SD; categorical variables are expressed as numbers (%).

CRP = *Citrus reticulata* peel; PEG = polyethylene glycol; SD = standard deviation.

\(^a\) Includes cholecystectomy, gastrectomy, appendectomy, and total hysterectomy with bilateral salpingo-oophorectomy.

\(^b\) Includes insulin, narcotics, hypoglycemic agents, and antidepressants.
To improve patient tolerance to full-dose PEG, one of the strategies is to add an adjunct to reduce the PEG volume. Low-volume PEG combined with adjunctive laxatives is shown to have comparable colonic preparation quality and better patient tolerance than full-dose PEG.6–7 This strategy is recommended by current guidelines.21,22

Another reason for choosing reduced PEG plus bisacodyl in health examinations is its ease of dosing and the greater convenience it affords to patients.23 Adjuncts such as ascorbic acid, olive oils, and reduced dose bisacodyl are all proven to have sufficient efficiency.2,3,8 However, in clinical practice, even patients who receive reduced PEG-ELS with bisacodyl still suffer from nausea, vomiting, bloating, and abdominal pain. Consequently, it has become necessary to evaluate the efficacy of Citrus reticulata peel as an additional adjunct for colonoscopy preparation.

Citrus peel is widely used for flavoring food and beverages worldwide.24,25 According to one report in the US state of Arizona, in people that had the habit of regularly consuming citrus fruits or citrus juice, peel consumption itself was also relatively common, at around 34.7%.26 Citrus peel is rich in flavonoid glycosides that have a wide range of biological effects in vitro and in vivo, including antioxidant, anti-inflammatory, and anti-carcinogenic properties.27 Epidemiological evidence suggests that citrus peel consumption may provide protection against coronary heart disease28–31 and stroke.32 Citrus flavonoids include hesperidin, neo-hesperidin, nobiletin, tangeritin and so on.33 Like other fruits, citrus peel is rich in electrolytes, minerals, and vitamins, especially vitamin C.34

In East Asia, citrus peel has been used in traditional herbal medicines for a long time.35 CRP is well documented for its prokinetic, anti-bloating and appetite-improving effects.36–38 In previous clinical studies, it significantly improved cancer patients’ appetite and effectively relieved delayed gastric emptying.39,40 Based on those background data, we decided to conduct this prospective study to compare the conventional preparation solution (PEG group) against one with CRP (PEG + CRP group) in terms of the quality of colonic cleansing, compliance, and adverse effects.

Using a rating questionnaire, significantly more examinees accepted the taste (85.7% versus 71%; p = 0.015) and fewer examinees had difficulty in swallowing (8.6% versus 27.1%; p = 0.001) in the PEG + CRP group. Also, the side effects and discomfort were significantly reduced in the PEG + CRP group, as evidenced by the lower rates of vomiting (p = 0.045), bloating (p = 0.035), and difficulty sleeping (p < 0.001). Taken together, this suggests that CRP could serve as an adjunct to reduce the discomfort of patients receiving colonic cleansing.

Is it the flavor, the taste or CRP’s prokinetic effect that directly impacts on the preparation result? There are a number of factors that may explain this phenomenon. First, during bowel preparation, the unpleasant salty taste (mostly related to sodium phosphate) and large volume (mostly PEG related) are the major causes of side effects (nausea and vomiting).22 In clinical settings for PEG preparation, patients were encouraged to consume the solution completely with a flavored clear liquid diet. Some commercial preparation solutions also come in a form with different types of flavor for patients. However, most of these patients still suffered from abdominal fullness, bloating, nausea, and vomiting despite alteration of the unpleasant taste.21 Thus, it would appear that the side effects from PEG are often volume-related and could not be improved by flavor in our clinical observation.

### Table 3
Comparison of adverse events in colonic preparations between the PEG group and the PEG + CRP group.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>PEG group (n = 107)</th>
<th>PEG + CRP group (n = 105)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>20 (18.7)</td>
<td>18 (17.1)</td>
<td>0.909</td>
</tr>
<tr>
<td>Vomiting</td>
<td>19 (17.8)</td>
<td>8 (7.2)</td>
<td>0.045</td>
</tr>
<tr>
<td>Abdominal cramping pain</td>
<td>4 (3.7)</td>
<td>11 (10.5)</td>
<td>0.100</td>
</tr>
<tr>
<td>Bloating</td>
<td>99 (92.5)</td>
<td>86 (81.9)</td>
<td>0.035</td>
</tr>
<tr>
<td>Headache</td>
<td>24 (22.4)</td>
<td>29 (27.6)</td>
<td>0.475</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6 (5.6)</td>
<td>13 (12.4)</td>
<td>0.137</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>37 (34.6)</td>
<td>7 (6.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as number (%).

CRP = Citrus reticulata peel; PEG = polyethylene glycol.

---

### Table 4
Comparison of colonic preparation solution between the PEG group and the PEG + CRP group.

<table>
<thead>
<tr>
<th>Grade</th>
<th>PEG group (n = 107)</th>
<th>PEG + CRP group (n = 105)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfactory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>11 (10.3)</td>
<td>9 (8.6)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>40 (37.4)</td>
<td>44 (41.9)</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>35 (32.7)</td>
<td>42 (40.0)</td>
<td></td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pool</td>
<td>21 (19.6)</td>
<td>10 (9.5)</td>
<td></td>
</tr>
<tr>
<td>Failed</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as number (%).

p = 0.059, satisfactory versus unsatisfactory.

CRP = Citrus reticulata peel; PEG = polyethylene glycol.
Second, Hayes et al compared the efficacy of bowel preparation quality between flavored and unflavored PEG solution. They did not mention whether the flavored group had less discomfort and fewer side effects. Third, the PET + CRP group in fact showed a significantly shorter duration of action than the PEG group (p = 0.001), indicating that the prokinetic effects of CRP rather than the flavor may better explain the decreasing duration of action of the preparation solution, reducing the volume-related side effects and facilitating the smoother consumption of PEG.

The high percentage of bloating rate in both groups (81.9–92.5%) may be due to the usage of bisacodyl at a dose of 15 mg. The symptoms improved for examinees in the PEG + CRP group when CRP was applied. Moreover, examinees in the PEG + CRP group showed a much shorter duration of action of the preparation solution compared with those in the PEG group (p = 0.001). Although CRP has not been reported to have an indication for insomnia, it also improved difficulty sleeping during colonoscopy preparation in this study. This effect may directly result from the shorter duration of action in the PEG + CRP group, thus not depriving examinees’ of their sleeping time.

Additionally, the effect may be indirect through less vomiting and bloating. Vomiting is an important and critical issue. The salty taste, large volume of solution applied, and patients’ underlying disease are all common causes of vomiting. It should be noted that it is difficult to calculate the volume of vomitus in these studies. Thus, patients who suffer from severe vomiting may be left with under the recommended dose of PEG-ELS, which in turn lowers the quality of preparation.43

There was no statistically significant difference in colonic visibility between the two groups. However, there was a trend favoring CRP use when the results were dichotomized as satisfactory (excellent, good, and fair results together) or unsatisfactory (poor and very poor results together) for colonic visibility (90.5% versus 80.4%; p = 0.059). This trend may be due to the summation of the prokinetic effects of CRP9,10 and improved examinee tolerance and compliance. In comparison, the percentage of good to excellent preparations in our cohort (47.7% for PEG versus 50.5% for PEG + CRP) is inferior to the results of previous reports (86.2–88.0%).2,6

In those studies, investigators started their PEG-ELS treatment from 6–9 PM, and patients received colonoscopy the following morning. However, after considering examinees’ compliance and convenience when undergoing such health examinations, our examinees received their PEG-ELS dosing at 4 PM. Consequently, the duration from PEG-ELS dosing time to colonoscopy initiation time was around 15–18 hours, which is longer than the times applied in the previous studies (9–12 hours). This may greatly influence the preparation quality as a result of intestinal shedding, which may explain the difference between current and previous studies. Furthermore, the effect of CRP might have been countervailed by the long duration of bowel preparation prior to examination.

Our study had a number of limitations that should be noted. First, it was difficult to establish a placebo that resembled the appearance, smell, and texture of CRP in this study. The lack of a placebo group in order to detect a placebo effect could be a weakness. Second, this study was not a double-blinded randomized controlled study; although we had objective evidence (quality of preparation) as our primary end-point, patients in the PEG + CRP group may have been influenced by the Hawthorne effect. However, the endoscopists were also blinded to the grouping of colonoscopy preparation. This may have helped to reduce the bias in assessing the degree of colon cleansing, which was the primary end-point of our current study. Third, the component of CRP responsible for the gastrointestinal prokinetic effects remains unknown. To quantify these findings with regard to clinical practice, further study may be required to investigate which component is responsible for this effect.

In conclusion, when compared with conventional colonic preparation, the use of CRP as an adjunct can improve examinee tolerance, decrease the incidence of adverse events, and maintain the quality of colonic cleansing.

Acknowledgments

This study was supported by grants from Taipei Veterans General Hospital (V98A-154), Taipei, Taiwan.

References


