Abstract. – Background: The most critical factor determining the quality of colonoscopy results is the extent of bowel cleansing.

Aim: This observational post-marketing study evaluated the efficacy, acceptability and safety of a range of the most commonly used bowel cleansing solutions in routine clinical practice.

Patients: Patients undergoing diagnostic, preventive or follow-up colonoscopy were recruited from 7 centres in Italy, Spain and Greece.

Methods: Quality of bowel preparation was assessed on a 5-point scale and included evaluation of visible bowel surface area and the amount and consistency of residual fluid. Patients evaluated ease of use and palatability.

Results: A total of 437 patients took part. Klean-Prep, the most commonly used preparation in this evaluation, achieved the highest score for quality of bowel cleansing and was rated as good or excellent in 72.0% of patients. In dosage-compliant patients, Klean-Prep showed better results in comparison to Fleet Phosphosoda (p<0.05) in the maximum bowel level reached in the intestine during colonoscopy examinations. All of the bowel cleansing solutions were well tolerated.

Conclusion: The polyethylene glycol-based preparations provided the most adequate cleansing and, of these, Klean-Prep provided the highest “good” or “excellent” level of bowel preparation.

Key Words: Bowel cleansers, Colonoscopy, Polyethylene glycol, Sodium phosphate.

Introduction

Colonoscopy is the gold standard in the detection and diagnosis of colonic disorders such as abnormal polyps and colorectal cancer, as well as in the evaluation of unexplained changes in bowel habits, bleeding or in changes in the lining of the colon (inflammatory disorders). Colonoscopy surveillance is also crucial for follow-up of patients after polypectomy or cancer resection.

Recent efforts to include colonoscopy in colon cancer screening programs for the early detection of a pathology have further enhanced its diagnostic role in gastroenterology. Colorectal cancer is the third commonest form of cancer in industrialised countries with nearly one million new cases diagnosed world-wide each year and half a million deaths. It is known that the incidence and mortality of colon cancer can be effectively lowered by population screening and early diagnosis; in people with an average risk yearly screening should be performed after the 50th birthday. The choice of the applied procedure (endoscopic procedures or fecal blood test) depends on the individual situation of the patient. Complete colonoscopy has the highest sensitivity and specificity for the detection of adenomas or carcinomas and should therefore be offered first.

The most critical factor determining the quality of colonoscopy results is the extent of bowel cleansing, which critically influences the quality, difficulty,
speed and completeness of colonoscopy. Inadequate cleansing impairs visualization and colonicoscopic diagnosis; the procedure may have to be cancelled and rescheduled if preparatory bowel cleansing is inadequate. This raises both discomfort and costs of the procedure. The quality of bowel cleansing may be affected by the choice of product or patient compliance in taking the whole volume of bowel cleansing solution as prescribed.

Several preparations and regimens are available and are currently used for preparatory bowel cleansing. Balanced polyethylene glycol (PEG)-based electrolyte solutions, introduced in the early 1980s, resulted in a significant improvement in both cleansing efficacy and patient compliance with negligible net absorption of water and electrolytes. Alternatively, concentrated low-volume, hyper-osmotic solutions of sodium phosphate (NaP) can be used; these offer the advantage that a smaller volume intake is needed, but they are more frequently associated with electrolyte abnormalities related to the absorption of phosphate.

This observational, prospective survey provides an overview of the efficacy, acceptability and tolerability of the most common bowel cleansing preparations used for colonoscopy.

Materials and Methods

Study Design

The study was an open, multicentre, prospective observational study that included patients who were prescribed a bowel cleansing solution as a preparation for colonoscopy. Patients were enrolled from daily practice by specialists from 7 gastroenterological centres in Italy, Spain, and Greece. All patients undergoing colonoscopy were eligible for the study, but only patients prescribed cleansing solutions such as PEG-based electrolyte solutions and hyperosmotic solutions of NaP were included.

Patients were provided with detailed instructions about dietary measures to be taken for the examination and about the consumption of the investigational treatments. The treatments were prescribed in strict adherence with the prescription information for each preparation, as listed in relevant Summary of Products Characteristics (SmPCs).

The study received approval from the Ethics Committee of each Clinical Centre, and all patients provided written informed consent prior to participation in the trial.

A total of 437 patients (51% males, 49% females; mean age 59.2 years) were enrolled in the study, 210 (48%) from Italy (3 centres), 107 (24.5%) from Spain (2 centres) and 120 (27.5%) from Greece (2 centres).

The majority of patients (63%) were undergoing colonoscopy for diagnostic reasons, while the remainder were having follow-up procedures (28%) or preventive screening tests (9%). The examinations were mainly requested by a specialist, namely gastroenterologists, internists, oncologists and surgeons (74%), followed by the general practitioner (25%); 1% of cases did not record the origin of the request.

Treatments

Routine clinical practice was followed for patients undergoing diagnostic, preventive, or follow-up colonoscopy. Patients enrolled in the study were prescribed the following bowel cleansing solutions in each country:

**Italy**: Klean-Prep (PEG 3350 + electrolytes), Isocolan (PEG 4000 + electrolytes), Selg 1000 (PEG 4000 + electrolytes), Selg-S 1000 (PEG 4000 + electrolytes + simethicone), Fleet Phosphosoda (sodium phosphate).

**Spain**: Klean-Prep, Solucion Evacuante Bohm (PEG 4000 + electrolytes), Fleet Phosphosoda.

**Greece**: Klean-Prep, Fleet Phosphosoda.

In 4.3% of patients, other preparations, mainly galenics, were prescribed, herewith nominated as “Others”.

There were no indications or restrictions on the doses to be administered other than those reported in the SmPC of each prescribed preparation. The usual volume of water (or fluids) to be consumed with the preparations was 4 litres for PEG preparations and 2 litres for NaP preparations.

For each patient, the prescribed dose, as well as the actual dose, was recorded in the case report form in order to evaluate patient compliance with the prescribed preparations.

Data Collection

At entry into the study, the following data were recorded for each patient: patient demographics, reasons for colonoscopy (prevention, diagnosis, follow-up), physician who asked for colonoscopy (specialist or general practitioner), bowel cleansing preparation used and dosing.
The efficacy of the bowel cleansing preparation was evaluated by assessing both the adequacy of the bowel preparation and the maximum bowel level that was reached during colonoscopy.

The adequacy of bowel preparation was evaluated according to the following 5-point scale: 1 = excellent (completely clear); 2 = good (small amount of yellow or light brown fluid, easily sucked away); 3 = satisfactory (large amount of watery yellow or brown fluid, tedious to suck away); 4 = poor (semisolid stool that cannot be sucked away); 5 = failed (solid stool). The colonoscopist was also asked to record the maximum bowel level reached during the examination according to the colon area achieved, namely: 1 = caecum; 2 = ascending colon; 3 = transverse colon; 4 = descending colon; 5 = sigmoid colon.

The overall acceptance of the prescribed bowel cleansing solutions by the patients was also assessed through an evaluation of the ease of use, according to the following scale: easy to use, acceptable to use, slightly difficult to use, extremely difficult to use, unable to finish. The patients were also asked to provide an assessment about the palatability of the product, scoring the taste as: pleasant taste, acceptable taste, poor taste, unpalatable.

The tolerability of each prescribed preparation was evaluated by recording any adverse events reported by the patients. During the visits the incidence of any adverse event was ascertained by asking standard questions regarding the occurrence of any new medical problem during the treatment period. Any event was recorded by the physician who was also asked to give an assessment of the causal relationship with any drug taken in the surveyed period.

**Statistical Analysis**

Final analysis was performed in SAS 8.2. The data were tabulated as frequency tabulations and descriptive statistics together with more detailed statistical analysis for subgroups and/or including co-variables were performed and reported.

**Results**

The total number of patients receiving each bowel cleansing solution is shown in Table I. The results showed that the majority of patients were prescribed with PEG-based preparations and, among them, Klean-Prep was the most commonly prescribed preparation (37.5%); Fleet Phosphosoda (the only NaP preparation prescribed) was used in only 6.2% of patients. General compliance was good for all bowel cleansing solutions evaluated.

All of the PEG-based preparations were shown to be more effective in providing adequate bowel cleansing compared with Fleet Phosphosoda. In particular, Klean-Prep was associated with the highest percentage of patients (72.0%) reporting good/excellent bowel preparation (Figure 1), achieving significantly better results compared with Fleet Phosphosoda (72.0% vs 44.4%, \( p < 0.05; \) Fisher's exact probability). The significantly better results achieved by Klean-Prep for bowel cleansing were also observed in patient compliance to the prescribed dosage; in these patients, Klean-Prep showed significantly better results (\( p < 0.05; \) Cochran-Mantel-Haenszel test) not only in comparison to Fleet Phosphosoda but also to the PEG-based preparation Selg 1000.

PEG preparations achieved better results in comparison to Fleet Phosphosoda for the maximum bowel level reached during colonoscopy, which could represent an indirect measurement of bowel cleansing. In this respect, in the subgroup of compliant patients, Klean-Prep, which achieved the highest scores for bowel cleansing, also showed significantly better results compared with the NaP solution for the maximum bowel level reached during colonoscopy (Figure 2) (\( p < 0.05; \) Cochran-Mantel-Haenszel test).

In terms of ease of use, the PEG-based solutions showed a wide range of variability with the score “easy/acceptable” ranging from 42.4% to 93.3% of patients for the different products (Fig-

---

**Table I. Number of patients receiving each type of bowel cleansing solution.**

<table>
<thead>
<tr>
<th>Product</th>
<th>Volume of solution prescribed (L)</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fleet phosphosoda</td>
<td>2</td>
<td>27 (6.2%)</td>
</tr>
<tr>
<td>Isocolan</td>
<td>3-4</td>
<td>87 (19.9%)</td>
</tr>
<tr>
<td>Klean-prep</td>
<td>4</td>
<td>164 (37.5%)</td>
</tr>
<tr>
<td>Selg 1000</td>
<td>4</td>
<td>33 (7.6%)</td>
</tr>
<tr>
<td>Selg-S 1000</td>
<td>4</td>
<td>45 (10.3%)</td>
</tr>
<tr>
<td>Solucion evacuante</td>
<td>3-4</td>
<td>62 (14.2%)</td>
</tr>
<tr>
<td>Bohm</td>
<td>na</td>
<td>19 (4.3%)</td>
</tr>
</tbody>
</table>

na = not applicable.
Figure 1. Quality of bowel cleansing achieved by each preparation, assessed on a 5-point.

Figure 2. Maximum bowel level reached during colonoscopy following the use of different bowel cleansing preparations.
A total of 20 patients (4.6%) out of the 437 enrolled experienced adverse events, namely nausea, vomiting and abdominal pain, which were mainly of mild to moderate intensity. None of them was classified as serious. All preparations were well tolerated and no significant differences were observed.

**Discussion**

Colonoscopy is the gold standard in the detection and diagnosis of abnormal polyps and colorectal cancer\(^1,12\), the third most common cancer in men, after prostate and lung cancer, and in
women, after breast and lung cancer. With early
detection and treatment the 5-year relative sur-
vival rate for colorectal cancer is 90%.

The most critical factor determining the quali-
ty of colonoscopy results is the extent of bowel
cleansing. Available bowel cleansing agents are
PEG-based preparations, NaP solutions or sodi-
um picosulphate. A number of comparative stud-
ies generally show that these agents have similar
bowel cleansing efficacy\textsuperscript{2,13-16}. A recent meta-
analysis showed that NaP solutions were more
effective than PEG-based preparations\textsuperscript{17}. Howev-
er, this result needs to be balanced against the ev-
idence that NaP is more often associated with
electrolyte disturbances, including hyperphos-
phataemia\textsuperscript{14,18}. Indeed, as a result of safety con-
cerns, the US FDA issued a safety alert in De-
cember 2008, stating that oral NaP preparations
should only be available via prescription; oral
NaP products have subsequently been withdrawn
from the USA market\textsuperscript{19}.

In this observational post-marketing study, the
efficacy, acceptability and tolerability of the
most commonly used bowel cleansing prepara-
tions for colonoscopy were evaluated in patients
undergoing colonoscopy for diagnosis, preven-
tive screening or follow-up procedures. The re-
results showed that the quality of bowel cleansing
was rated as “good” or “excellent” in 72.0% of
patients treated with Klean-Prep. This result is
higher than for all the other bowel cleansing
agents in the study and, in particular, significant-
ly higher in comparison to the only NaP-based
preparation prescribed, Fleet Phosphosoda. This
is consistent with results from other clinical
studies that have also demonstrated the efficacy
of Klean-Prep in gastrointestinal lavage\textsuperscript{2,5,13,18}. In
the study carried out by Ell et al\textsuperscript{5} in 2003, which
compared Klean-Prep with a sulphate-free
PEG/electrolyte solution and an NaP solution,
Klean-Prep was found to provide significantly
more effective bowel cleansing than the other
preparations, and was rated consistently higher
for quality of colonoscopic visualization. Fur-
thermore, the results of the present study show
that, in compliant patients, Klean-Prep also
scored significantly better in comparison to the
NaP solution in the bowel level reached during
colonoscopy.

In general, the evaluation of the ease of use
and palatability of the products showed a great
variability among the PEG-based solutions, but
although patient acceptability in terms of taste
needs and handiness should be taken into consid-
eration, this also needs to be carefully balanced
against the high bowel-cleansing efficacy
reached by some of the PEG-based solutions and
the consequent quality of colonoscopic visualiza-
tion. Colonoscopy is the most commonly used
technique for inspection of the colonic mucosa.
The safety and effectiveness of colonoscopy in
identifying important colonic pathology is direct-
ly impacted by the quality of the bowel prepara-
tion before the procedure.

Due to the observational nature of the design
of our study, there are a number of important
study limitations that need to be taken into con-
sideration. There was no collaboration amongst/
across various centres and, therefore, a lack of
overall control for how each centre performed
the study and gathered data. This presents a chal-
lenge in assessing any inherent bias between
study sites. Furthermore, given the observational
nature of the investigation, it must be emphasised
that no treatment randomization occurred within
the study as data were collected from patients
based on “current best clinical practice” at repre-
sentative colonoscopy sites in Italy, Spain and
Greece. Nevertheless, the benefit of this type of
observational study is that the data obtained rep-
resent a real-life overview based on actual clinical
practice\textsuperscript{20}.

Within the observational design of the study
and considering the non-homogeneous size of
the different treatment groups, the results con-
firm the efficacy of Klean-Prep in bowel prepa-
ratio for colonoscopy, with the highest rating
for quality of bowel cleansing compared with
all other agents evaluated in this study, particu-
larly when compared to the only non-PEG for-
matation that was prescribed, with a good tol-
erability profile.

Consistent with previous observations, this
study provides some interesting results and con-
firmation of published outcomes which highlight
Klean-Prep as a first choice preparation for effec-
tive bowel cleansing before colonoscopy.

\textbf{Acknowledgements}

This research project was supported by a grant from
Helsinn Birex Pharmaceuticals Ltd, Damastown, Mul-
huddart, Dublin 15, Republic of Ireland. Editorial sup-
port was provided by in Science Communications (a
Wolters Kluwer business), with funding from Helsinn
Birex Pharmaceuticals Ltd.
An observational comparison of bowel cleansing solutions

References


