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Use of Drugs for Bowel Preparation for Colonoscopy in Miri General Hospital

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ABSTRACT

Introduction: Malaysian National Cancer Registry Report 2007-2011 has reported that colorectal cancer (CRC) is the second most prevalent cancer in Malaysia after breast cancer. Early detection and removal of precancerous lesions is vital to reduce the chances of late progression of CRC which may increase the likelihoods of survival. Among the screening tools, colonoscopy remains as the current standard method for evaluating the colon. The efficacy of colonoscopy attributed by the adequacy of bowel cleansing using bowel preparation formulations. This study aims to assess the success rates of colonoscopy using the available bowel preparation formulations in Miri General Hospital and to identify the factors to ineffective bowel preparation.

Methods: Inpatient and outpatient data extracted and collected from Pharmacy Hospital Inventory System (PHIS) from January 2017 to December 2017. Defined daily dose (DDD), cost, and rates of successful colonoscopy of each bowel preparation formulation evaluated.

Results: DDD for polyethylene glycol-electrolyte lavage solution (PEG-ELS)-based cleansing agent and sodium phosphate (NaP) solution were 0.0047 and 0.0124 respectively. The cost per bowel preparation course using PEG-ELS is 88.3% higher than NaP. Besides that, PEG-ELS showed higher rates of repeated colonoscopy compared to NaP (28.6% versus 4.6%).

Conclusion: This study reflects the need to enforce constant appropriate counselling among patients in both settings to ensure successful colonoscopy especially patients on PEG-ELS. Comprehension of potential patient-related and procedure-related factors should aid healthcare professionals in selecting proper bowel preparation regimes accordingly, such the quality of colonoscopy performance and delivery of service to patients can be optimized.

Key words: *colonoscopy, colorectal cancer, bowel preparation, risk factors*

INTRODUCTION

Colorectal cancer (CRC) is the second common cancer in Malaysia (13.2%) as reported in Malaysian National Cancer Registry Report 2007-2011 after breast cancer and the first among males and second among females. The overall incidence rate for CRC was 21.3 cases per 100,000 populations according to National Cancer Patient Registry on Colorectal Cancer 2008-2013 (1). Colonoscopy remains as the current standard method for imaging the mucosa of the entire colon (2). It can reduce the risk of CRC through early detection and removal of precancerous lesions. In addition to CRC screening and surveillance, colonoscopy plays an important diagnostic tool for evaluating gastrointestinal symptoms. Regardless of indication, the success of colonoscopy associated closely to the adequacy of pre-procedure colonic cleansing or preparation (3).

Unfortunately, according to the U.S. Multi-Society Task Force on Colorectal Cancer, up to 20-25% of all colonoscopies reported to have an inadequate bowel preparation (4) (5). Bowel preparation for colonoscopy is a complex procedure involving diet modifications and laxative choice according to patient prerequisites (6). The formulation that will optimise the quality of colonoscopy for a particular patient assessed based on their efficacy, safety, and tolerability (3). Given the high prevalence of colonoscopy failure, it is imperative for healthcare professionals to equip themselves with appropriate knowledge in managing pre-colonoscopy bowel preparation to ensure a successful colonoscopy. Additionally, it is essential to identify possible patient-related or procedure-related factors that may influence the quality of bowel preparation (7). This leads to the design of our study which aims to assess the success rates of colonoscopy using the available bowel preparation formulations and to identify factors that may contribute to ineffective bowel preparation in Miri General Hospital.

METHODS

Sample and setting

Data extracted from Pharmacy Hospital Inventory System from January 2017 to December 2017, including both outpatient and inpatient data in Miri General Hospital, Sarawak. The data collected processed and consolidated into one single dataset. ATC code set by World

Health Organisation (WHO ATC) assigned to each medicine based on generic name and drug class. Subsequently, the accompanying defined daily dose (DDD) of each ATC code and unit of measurement for DDD assigned to respective medicine based on route of administration.

Data analysis

Medication utilisation data analysed using a two-step analysis.

First step: To calculate total dose for each bowel cleansing product in one full year (total number of doses administered multiply by the dose per pack). This is followed by summation of total dose for all bowel cleansing agents according to ATC code.

Second step: To determine statistics on medicine use in terms of number of Defined Daily Dose (DDDs) per-1,000 inhabitant's per-day for every ATC code.

$$\text{DDDs per-1,000 inhabitants per-day} = \frac{T \times 1,000}{\text{DDD} \times P \times 365}$$

T : An estimate of total dose of the bowel cleansing agent by ATC code utilized in 2017

DDD : DDD assigned for the drug according to WHO ATC/DDD system

P : Total inpatient and outpatient population that visited Miri General Hospital in 2017

365 : Refers to 365 days in a year

In this analysis, the total inpatient and outpatient population taken for 2017 in Hospital Miri is 212,595.

The following DDDs are used in this research:

ATC code	Name	DDD	U	Route of administration
A06AD15 (8)	Macrogol	10	g	Oral (O)
A06AD17 (9)	Sodium Phosphate	50	g	Oral (O)

Macrogol is the international non-proprietary name for Polyethylene glycol (PEG)-based laxative.

Cost of bowel preparation formulations and rates of successful colonoscopy (clean colonoscopy) analysed using the following methods:

- I. Cost of bowel preparation formulations: Each formulation evaluated based on respective stock keeping unit (SKU) followed by total cost per one complete bowel preparation course.
- II. Rates of successful colonoscopy: The number of patients that require a repeated colonoscopy within one week from initial scheduled colonoscopy considered as inadequate bowel preparation pre-colonoscopy (unsuccessful colonoscopy).

RESULTS

Two colon cleansing agents and schedules have been utilised and studied for bowel preparation during colonoscopy. The commonly used agents in Miri General Hospital are Polyethylene glycol-electrolyte lavage solution (PEG-ELS), which is a non-absorbable solution, and aqueous sodium phosphate (NaP), which is a low-volume hyperosmotic solution (7). PEG-ELS contain 64g of macrogol 4000 per sachet whereas NaP contains 48g (400 mmol) of monobasic sodium phosphate and 18g (130 mmol) of dibasic sodium phosphate per 100 mL.

663 patients underwent colonoscopy in Miri General Hospital in 2017. Out of 663 colonoscopies carried out, only 14 patients (2%) used PEG-ELS as bowel cleansing agent pre-colonoscopy (Figure 1). This further supported by medication utilization analysis. The total utilization of both bowel cleansing agents is 0.0171 DDD/1,000 inhabitants/day. The total utilisation of NaP and PEG-ELS is 0.0124 and 0.0047 DDD/1,000 inhabitants/day respectively (Table 1). Based on total utilisation, NaP is most commonly prescribed for bowel preparation compared to PEG-ELS.

Selection of drugs for bowel preparation, cost of each bowel preparation formulation is taken into consideration. A complete course and dosing of bowel preparation practiced in Miri General Hospital demonstrated in Table 2. One bottle of NaP (90 mL) and three sachets of PEG-ELS required for a complete course of bowel preparation respectively. Each bottle of NaP costs MYR19.50 while each sachet of PEG-ELS costs MYR12.24. Therefore, the cost of NaP per course is MYR19.50 while the use of PEG-ELS will sum up to MYR36.72 per course. In short, one course of PEG-ELS is 88.3% more expensive than NaP. The total

expenditure of NaP and PEG-ELS is MYR15795.00 and MYR697.68 respectively. These data are summarized in Table 3.

According to the analysis, 28.57% of patients who were previously on PEG-ELS for their initial scheduled colonoscopy had a repeated colonoscopy within one week due to poor bowel preparation (Figure 2). Meanwhile, only 4.62% of patients who prescribed with NaP had a recurring colonoscopy.

Table 1. Use of Drugs for Bowel Preparation for Colonoscopy in Miri General Hospital in 2017

ATC	Therapeutic Group/ Drug	2017
A06	Drugs for Constipation	
A06A	Drugs for Constipation	
A06AD	Osmotically acting laxatives	Total 0.0171
A06AD15	Macrogol (PEG-ELS)	0.0047
A06AD17	Sodium phosphate	0.0124

Table 2. Dosing and total units per course practiced in Miri General Hospital

Agent	Dosing	Total units per course
PEG-ELS	250 mL every 15 minutes or 1000 mL over 1 hour for 3 schedules	1 sachet in 1 L of water for a total of 3 L per course (3 sachets of PEG-ELS)
Aqueous sodium phosphate	Two doses of 45 mL sodium phosphate with 250 mL of clear liquid 10-12 hours apart	90 mL (1 bottle of NaP)

Table 3. Total expenditure of drugs used for bowel preparation in 2017

Agent	PEG-ELS	Aqueous sodium phosphate (NaP)
Quantity dispensed	57 sachets	810 bottles
Cost per unit (MYR)	12.24	19.50
Total cost per course (MYR)	36.72	19.50
Total cost per year (MYR)	697.68	15,795.00

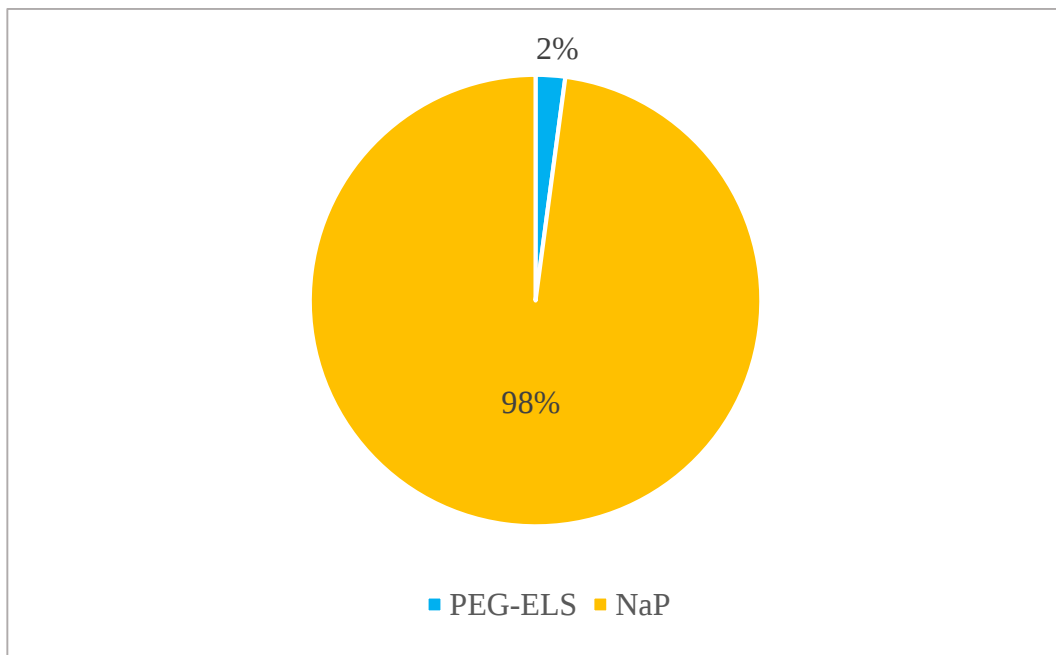


Figure 1. Number of patients underwent colonoscopy in 2017

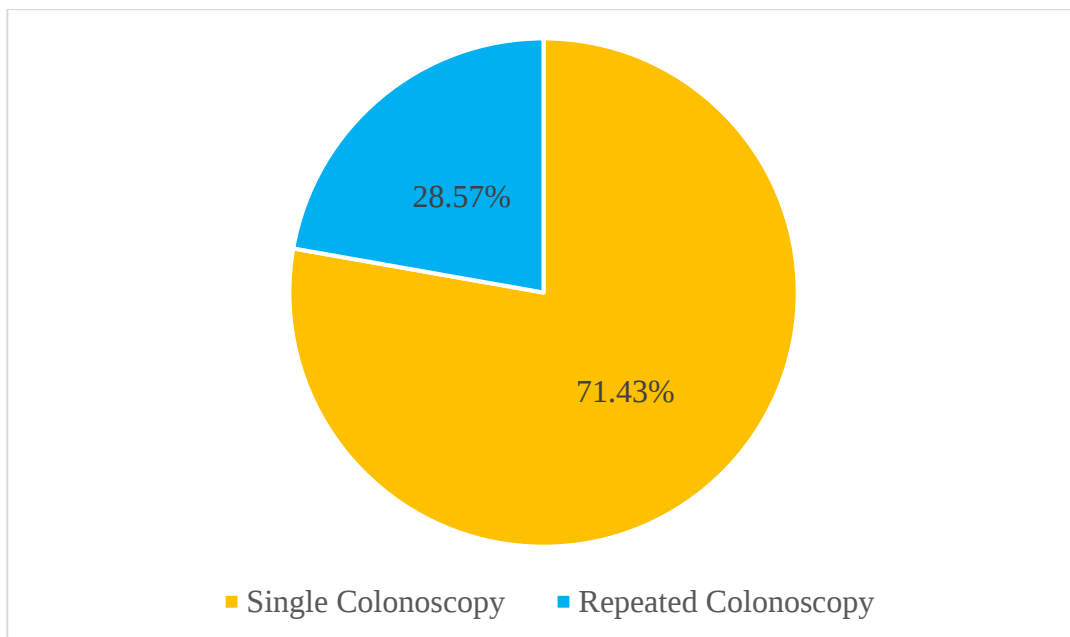


Figure 2. Percentage of repeated colonoscopy for patients on PEG-ELS

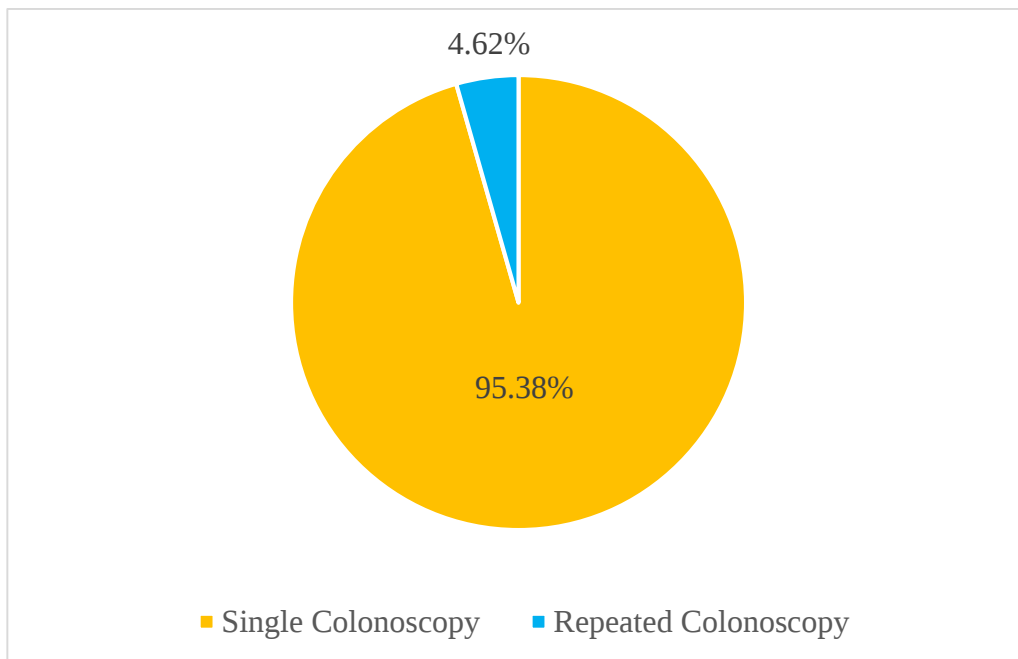


Figure 3. Percentage of repeated colonoscopy for patients on aqueous sodium phosphate (NaP)

DISCUSSION

A successful colonoscopy requires an adequate preparation of the large bowel that facilitates clear visualisation of the mucosal surface. The effectiveness of the bowel preparation is a critical factor related to the safety, diagnostic accuracy, quality, difficulty and speed of the examination (10). An ideal oral bowel preparation agent takes into consideration of its convenience to administer, price, safety, efficacy with an acceptable side-effect profile (11). Based on multiple studies, all the available preparations can produce adequate cleansing results with acceptable tolerance although results for individual patients are variable (10).

The most popular and currently used regimes in Miri General Hospital are PEG-ELS and NaP. Based on the analysis done, it shown that a major proportion of patients that underwent colonoscopy used NaP (98%). This may be attributed to the widely available stock and comparatively lower cost of NaP to PEG-ELS. Besides that, PEG-ELS listed as a restricted medication that is reserved solely for patients with fluid restriction such as those with chronic kidney disease stage two and above and patients with underlying heart failure.

PEG is a non-absorbable solution that should pass through the bowel without any net absorption or secretion. Significant fluid and electrolyte shifts are therefore avoided but large

volumes (3 - 4 L) still required to achieve a cathartic effect. On the other hand, sodium phosphate osmotically draws plasma water into the bowel lumen to promote colonic cleansing and as a result, significant fluid and electrolyte shifts can occur (7). Even though studies have shown that PEG-ELS and NaP were comparable for effectiveness in producing satisfactory bowel cleansing effect, the side effect profile for PEG-ELS is more favourable. In two years (January 2006 - December 2007), 171 and 10 cases of renal failure reported to the United States Food and Drug Administration (FDA) following administering NaP and PEG-ELS respectively. In 2008, FDA has issued a safety warning for NaP-containing product about the risk of acute phosphate nephropathy, a rare but serious adverse effect that may result in permanent loss of renal function. According to European Society of Gastrointestinal Endoscopy (ESGE) Guideline, routine use of NaP for bowel preparation should be avoided due to its safety concerns. It suggests the use of NaP only in cases where alternative products may not be tolerated or in selected individuals who are at low risk of developing NaP-related side effects (6). Caution should be used in prescribing NaP to young patients, elderly (>55 years old), patients with dehydration, pre-existing kidney disease, bowel obstruction, inflammation of bowel, hypertension or patients who are taking angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs, or diuretics (3). Blood investigation and adequate hydration recommended before administering NaP-containing products which warrants hospital admission. These would indirectly translate into extra costs, hence increased overall cost for NaP even it was demonstrated that NaP is of lower cost per course.

Based on our study, it reported that both agents linked to rate of repeated colonoscopy. This can be attributed by patient-related and procedure-related factors. Patients in our study setting are mainly elderly and of lower socioeconomic background. This is in line with recent studies conducted in which it demonstrated that age ≥ 60 years and poor understanding of bowel preparation process was predictive factors of poor bowel preparation (7). Adherence to bowel preparation instructions remain as the main procedure-related challenge in our setting. According to several studies, it shown that regardless of the formulation used, non-adherence has been shown to affect the quality of bowel preparation (7). Additionally, PEG-ELS have shown to have higher rate of repeated colonoscopy compared to NaP. This may be contributed by greater non-compliance to large volume of solution to be taken especially in patients with fluid restriction. This result also demonstrated in Nguyen et al study whereby 86.7% of patients failed to complete the bowel preparation

that results in poor or inadequate bowel cleansing (12). This finding further supported by Ness et al and Chan WK et al. (13) (14).

LIMITATIONS

As the data extracted from Pharmacy Hospital Inventory System, the number of bottles of NaP dispensed may not accurately present the actual usage in Miri General Hospital due to duplicated prescriptions on the same day. Besides that, PEG-ELS was a restricted item for specific population in 2017 which may not represent real usage as some patients self-purchased the medication and hence not being prescribed in the system.

CONCLUSION

In conclusion, we identified that 98% of our population used NaP as the choice of bowel preparation pre-colonoscopy due to limited access to PEG-ELS. PEG-ELS also linked to higher rates of repeated colonoscopy because of old age, lower socioeconomic status, and poor adherence to instructions. This highlights the need to enforce appropriate counselling among patients in both inpatient and outpatient settings to ensure successful colonoscopy. Comprehension of risk factors identified in this study should aid healthcare professionals in selecting suitable bowel preparation regimes accordingly, such the quality of colonoscopy performance and delivery of service to patients can be optimised.

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