

Conventional regimen versus split-dose regimen in bowel preparation: Results of a randomized controlled trial

Protocole classique versus protocole fractionné dans la préparation colique: Résultats d'un essai contrôlé randomisé

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ABSTRACT

Introduction-Aim: Good bowel preparation is essential for colonoscopies. This study aimed to compare the quality of bowel preparation between the split-dose regimen (SD), recommended by European endoscopy societies, and the conventional regimen (CR) in Tunisia, where SD is not routinely adopted, and to identify factors leading to poor preparation in both groups.

Methods: We performed a randomized controlled trial, spread over four months (January-April 2019). Patients were randomly assigned to two groups at a 1:1 ratio: SD or CR.

Results: One hundred and thirty-three patients were included: 65 in the SD group and 68 in the CR group. SD showed better bowel cleansing than CR by comparing the mean Boston score in the two groups (6.05 versus 4.75, $p < 0.001$). Tolerance of the preparations was comparable between the groups. Factors associated with poor preparation in the SD group were constipation ($p=0.04$) colonoscopy indication (screening) ($p=0.01$) and public transport ($p=0.001$). In multivariate analysis, constipation and public transport were independent factors in poor preparation with a relative risk of 4.9 and 26 respectively. For the CR group, age <65 years ($p=0.022$), low level of education ($p=0.03$) and unemployment ($p=0.015$) were predictive factors for poor preparation. In multivariate analysis the low level of education was an independent risk factor for poor preparation with a relative risk of 20.

Conclusion: Our study showed that SD provides better bowel preparation than CR without altering the tolerance. In addition, factors predictive of poor preparation in the SD group were modifiable, unlike those of CR.

Key words: Colonoscopy, Bowel preparation solutions, Polyethylene glycol

RÉSUMÉ

Introduction-Objectif: Une bonne préparation colique constitue un critère majeur de qualité d'une coloscopie. L'objectif de notre étude était de comparer le protocole splitté (PS) et le protocole classique (PC), et d'identifier les facteurs prédictifs de mauvaise préparation dans chaque groupe.

Méthodes: Il s'agit d'un essai contrôlé randomisé en simple insu, étalé sur 4 mois (Janvier – Avril 2019). Les patients étaient répartis en deux groupes de façon aléatoire selon un ratio 1:1, PS ou PC.

Résultats: Cent trente-trois patients ont été inclus: 65 dans le PS et 68 dans le PC. La tolérance était comparable dans les deux groupes. Le PS a montré sa nette supériorité dans la qualité de préparation par rapport au PC, avec un score moyen de Boston de 6,05 vs 4,75 ($p \leq 0,001$). Les facteurs associés à une mauvaise préparation dans le groupe PS étaient la constipation ($p=0,04$), la coloscopie faite dans le cadre d'un dépistage ($p=0,01$) et le transport en commun ($p=0,01$). En analyse multivariée, la constipation et le transport en commun étaient des facteurs indépendants de mauvaise préparation avec un risque relatif de 4,9 et de 26 respectivement. Pour le groupe PC, l'âge <65 ans ($p=0,022$), le faible niveau d'étude ($p=0,03$) et le chômage ($p=0,015$) étaient des facteurs prédictifs de mauvaise préparation. En analyse multivariée, un faible niveau d'étude était un facteur de risque indépendant de mauvaise préparation avec un risque relatif de 20.

Conclusion: Le PS permettait d'obtenir une meilleure préparation colique que le PC sans altérer la tolérance. Les facteurs prédictifs de mauvaise préparation dans le groupe PS étaient modifiables contrairement à ceux du PC.

Mots clés: Coloscopie, Solutions de préparation intestinale, Polyéthylène glycol.

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INTRODUCTION

Colonoscopy is the gold standard in screening colorectal cancer (CRC). Over the past two decades the increase in the number of colonoscopies performed worldwide led to a decrease in CRC incidence and mortality (1-5).

Its cost-effectiveness depends on the quality of the bowel preparation which is related to several factors. Non-modifiable factors are essentially patient-related, such as obesity, diabetes and neuropathies (3, 6, 7). Modifiable factors include diet and the preparation regimen.

The "split-dose" regimen (SR) has been shown to be associated with better bowel preparation and a higher rate of detection of polyps and adenomas than the conventional regimen (CR) (8-10). SR is now recommended by European societies of endoscopy (23). However, it has several drawbacks, which probably explain why it is not systematically adopted worldwide. The disadvantages include sleep quality alteration, risk of having a bowel movement during the journey to the endoscopy unit on the day of the examination and finally risk of inhalation of gastric residue when the colonoscopy is performed under anesthesia. There is a lack of Tunisian data thus we decided to evaluate the feasibility and the results of the SR by comparing it to the CR in a Tunisian population.

METHODS

It was a prospective comparative study. We included all patients aged between 18 and 85 registered for morning colonoscopy (8:00am-1:30pm) in our Department between January and April 2019.

The secretary of the endoscopy unit randomly (one by one) distributed to the patients one of the two bowel preparation regimens (SR versus CR) previously written in the form of two prescriptions. The SR consists of splitting the preparation solution of Polyethylen Glycol (PEG) in two parts: the day before (2 litres from 8 to 10pm) and the morning of the examination (2 litres from 3 to 5 am), with a minimum delay of 2 hours before anaesthesia for clear liquids (11,12). The CR (One Day Before) regimen consists of administering the entire dose of preparation the day before the examination: 2 litres from 4 to 6 pm and 2 litres from 8 to 10 pm. This prescription was accompanied by a 3-day residue-free diet. The distribution was not communicated to the physician performing the colonoscopy thus it was a simple blind study.

Prior to the colonoscopy we collected, through a questionnaire, patient informations and informations on bowel preparation. At the end of the procedure, we assessed the tolerance using the visual analogue scale (VAS) (13). An examination was considered well tolerated if the VAS was between 0 and 3. Tolerance was considered average if the VAS was between 4 and 6 and poor if the VAS was > 6.

The Quality of preparation was determined by the endoscopist according to the Boston score (14, 15-18). A good bowel preparation is defined by a score ≥ 7 , a so-called average preparation if the score is equal to 5-6 and poor if <5.

The quality of sleep was assessed as follows: mild disturbance (one or no nocturnal awakenings), moderate disturbance (multiple nocturnal awakenings), severe disturbance (complete sleep deprivation).

The data were analyzed using SPSS version 19.0 software. In all statistical tests, the significance level was set at 0.05. We received a favorable response from the hospital's ethics committee. Patient anonymity was respected.

RESULTS

We included 133 patients over a period of 4 months (January-April 2019): 68 in CR group and 65 in SD group. Demographic and clinical features in each group are described in Tables 1 and 2 respectively. The two groups were comparable in terms of demographic and socioeconomic characteristics, lifestyle, colonoscopy indications, co-morbidities, family history of CRC and BMI.

Table 1. Demographic features in each study group

Parameters	Conventional regimen n=68	Split-dose regimen n=65	P
Gender			0.455
Female	26 (38%)	29 (45%)	
Male	42 (62%)	36 (55%)	
Smoking	16 (23%)	17 (26%)	0.726
Alcohol	5 (7%)	11 (17%)	0.09
Marital status			0.634
Married	60 (88%)	59 (91%)	
Education			0.947
Illiterate	20 (31%)	21 (32%)	
Primary	17 (26%)	19 (29%)	
Secondary	17 (26%)	16 (25%)	
University	11 (17%)	9 (14%)	
Working status			0.832
Housekeeper	22 (34%)	23 (36%)	
Unemployed	5 (8%)	5 (8%)	
Self-employed	11 (17%)	13 (20%)	
Employed	9 (14%)	12 (18%)	
Retired	17 (27%)	12 (18%)	
Medicaid	8 (12%)	10 (15.4%)	0.588

Table 2. Clinical parameters in each study group

	Conventional regimen n=68	Split-dose regimen n=65	P
Family history of CRC	5 (7%)	7 (11%)	0.5
Comorbidities	43 (63%)	38 (58%)	0.573
Abdominal-pelvic surgery	29 (43%)	33 (51%)	0.348
Colonoscopy indication			0.761
Symptoms	49 (72%)	45 (69%)	
Screening	19 (28%)	20 (31%)	
Psychotropic drug			
Neuroleptics	2 (3%)	2 (2%)	0.974
Tricyclics	2 (3%)	1 (1%)	0.578
Opioids	4 (6%)	3 (3%)	0.589
Poly medication	13 (20%)	19 (30%)	0.2
World Health Organization (WHO)			0.111
WHO=0	55 (81%)	60 (92%)	
WHO=1	11 (16%)	5 (8%)	
WHO=2	2 (3%)	0 (0%)	

The preparation was well tolerated in half of the cases (50% in CR group versus 55% in SR group).

In the SR group, the sleep quality was more impacted with more sleepless nights and more important discomfort compared to the CR group (42% and 19% respectively, $p=0.014$). The majority of the participants expressed however their acceptability to repeat the preparation in both groups (93% in CR group and 98% in SR group). The trip to the hospital was not interrupted due to a bowel movement under any regimen (Table 3).

Table 3. Compliance and tolerance in each study group

	Conventional regimen n=68	Split-dose regimen n=65	P
History of poor preparation	27 (41%)	33 (54%)	0.158
Residue free diet			0.92
No	10 (15%)	8 (12%)	
<3 days	9 (13%)	7 (11%)	
≥3 days	49 (72%)	50 (77%)	
Compliance			0.829
3-4L	9 (13%)	11 (17%)	
>4L	59 (87%)	54 (83%)	
Tolerance			0.518
Nausea	16 (25%)	19 (29%)	
Vomiting	15 (23%)	10 (15%)	
Incontinence	9 (13%)	10 (15%)	
Willingness to re-preparation	63 (93%)	64 (98%)	0.157
Quality of sleep			0.014
Sleepless night	13 (20%)	27 (43%)	
Moderate gene	38 (58%)	28 (44%)	
Light gene	15 (23%)	8 (13%)	
Distance to endoscopy center			0.548
<1h	49 (91%)	52 (88%)	
1-2h	3 (6%)	6 (10%)	
>2h	2 (4%)	1 (2%)	
Transport			0.097
Car	36 (53%)	34 (52%)	
Public transport	15 (22%)	19 (29%)	
On foot	2 (3%)	6 (9%)	
Inpatient	15 (22%)	6 (9%)	
Interrupted trip for bowel movement			
No	68 (100%)	65 (100%)	

When comparing the mean Boston score in the two groups, the SR showed a clear superiority in preparation quality over the CR (6.05 ±1.136 versus 4.75±1.297, $p<0.001$) (Shown in Figure 1). A Boston score ≥7 was significantly more frequently found in patients prepared according to SR (32.3% versus 8.8%, $p=0.001$). However, there was no significant difference in terms of Polyp detection rate (PDR) (41.17% for CR vs 41.53% for SR).

We did not calculate adenoma detection rate (ADR) which is one of the main quality criteria for colonoscopy.

The time between the last dose of PEG and the colonoscopy was as follow: less than 5 hours (0% in the CR group and in 22% of in the SR group), between 5 and 10 hours (12% in the CR group and 77% in the SR group) and superior to 10h (88% in the CR group and 1% in the SR group). There was a significant difference between the 2 groups in terms of time between the last dose of PEG and the colonoscopy ($p<0.001$). A Delay of less than 5 hours between the last dose and the colonoscopy was not associated with better preparation. The residue-free diet did not impact bowel preparation quality in either group.

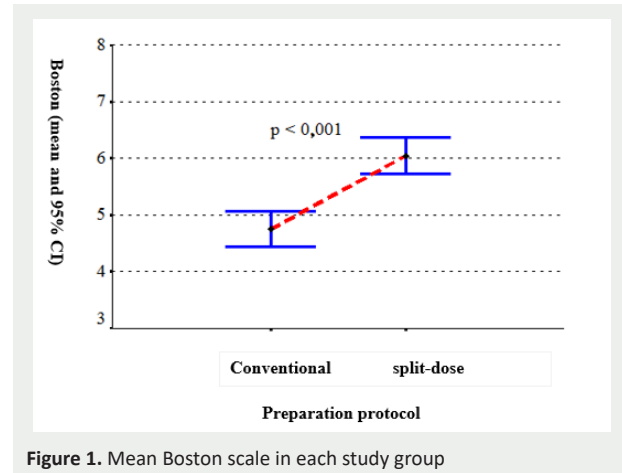


Figure 1. Mean Boston scale in each study group

Factors associated with poor preparation in the SR group were constipation ($p=0.04$), screening as an indication for colonoscopy rather than symptoms ($p=0.01$) and using public transportation on the day of the examination ($p=0.001$). The quality of preparation did not depend on age or the presence of co-morbidities in this group. In multivariate analysis, constipation and public transit were independent risk factors of poor preparation with a relative risk of 4.9; 95% CI [1.1-21.7] and 26; 95% CI [2.6-264.5] respectively.

For the CR group, in uni-variate analysis, age < 65 years ($p=0.022$), low education ($p=0.03$) and unemployment ($p=0.015$) were predictive factors of poor preparation. In multivariate analysis, low education was an independent risk factor for poor preparation with a relative risk of 20; 95% CI [1.1-499].

DISCUSSION

In our study, SR demonstrated its superiority in the quality of bowel preparation but not in the polyp detection rate (PDR). SR group was significantly associated with altered sleep quality, however there was no difference in term of tolerance and acceptability to repeat the preparation. Besides, the trip to the hospital was not interrupted due to a bowel movement under any regimen.

Multiple studies worldwide have compared the effectiveness of SR and CR regimen (9, 19-25). To our knowledge, this is the first North-African study. Having a local study is important since the lifestyle and the diet which are different from one region to another are important factors in bowel preparation.

Radaelli et al in a prospective multicenter study involving 1447 patients comparing two groups (CR vs. SR) concluded that SR was an independent factor associated with good bowel preparation (OR =3.34; 95% CI [2.4-4.63]), an increased PDR (OR=1.46; 95% CI [1.11-1.92]) and an increased rate of cecal intubation (8).

These data were consistent with the results of a meta-analysis (47 RCTs, 13,478 patients) that found that SR was associated with good bowel preparation more frequently than CR (OR = 2.51; 95% CI [1, 86-3, 39]). These results were valid for PEG (OR =2.6; 95% CI [1.46-4.63]), sodium phosphate (OR =9.34; 95% CI [2.12-41.11]), and picosulfate (OR =3.54; 95% CI [1.95-6.45]) (19).

This could be explained by the fact that the second dose of PEG during SR is administered closely to the time of the colonoscopy, which allows better mobilization of the fluid accumulated in the hours following the administration of the first dose (22, 24, 26). In fact, it is recommended that the second part of the preparation should ideally be done 4 to 5 hours before colonoscopy as it is the "five golden hours" that directly impact the quality of preparation (9, 24, 27, 28).

In our study, a maximum delay of 5 hours between the last dose and the colonoscopy was not associated with better preparation. This could be explained by the small number of patients meeting this criterion since they did not have fixed appointments, given that the administrative system is a "first come, first served" system.

In the literature, SR was significantly better tolerated than CR as the fractionation of the preparation facilitates the intake of clear fluid and ensures better hydration (8, 27, 29, 30).

The tolerance of the colonoscopy was comparable in the two groups in our study (76% in the CR vs. 71% in the SR; $p=0.518$). The acceptability of re-preparation was also similar (93% in the CR vs. 98% in the SR; $p=0.157$). However, sleep quality was impaired in the SR group.

Our main reluctance to prescribe SR when it had already demonstrated its superiority in the Western series was the risk that the patient might have a transit during the trip to the hospital. Indeed, a part of the patients consulting the hospital come from another governorate and travel a long way, which is different from Western countries where sectorization is usual. In our study, the trip to the hospital was not interrupted due to a bowel movement under any regimen. These results will encourage us to prescribe SR.

Strengths of our work

- It is single-blinded, randomized controlled trial.
- It is a Tunisian study that deals with the problem of bowel preparation by comparing the CR used until now in most of our hospitals and the SR recommended since many years by the different international societies of endoscopy.

Limitations of our work

- Monocentric study with a small number of participants compared to the international series.
- Non-calculation of the adenoma detection rate (ADR).

CONCLUSION

In our study, we showed that SR was superior to CR in bowel preparation and was not influenced by age and socio-economic conditions, unlike CR. Moreover, tolerance to this protocol does not appear to be inferior to CR, apart from altering the quality of sleep. It did not expose patients to a risk of transit during the journey to hospital.

In the light of these results, we can recommend SR as a bowel preparation for our population.

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