



**ORIGINAL ARTICLE**

## Optimizing peri-operative feeding to decrease post-operative stress response in patients with colo-rectal cancer.

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### ABSTRACT

**Background:** Stress hormones and inflammatory mediators provoked by any injury including surgery catabolise glycogen, fat and protein yielding glucose, free fatty acids, and amino acids in the circulation to be used in the immune response and tissue healing. On the other hand, these catabolic reactions inversely affect the process of post-operative recovery both on the short and long run. Hence nutrition for surgical patient must be properly planned to avoid these consequences.

**Aim of the study:** to prove the alleviating effect of pre-operative carbohydrate load and early post-operative feeding on post-operative catabolic stress response.

**Methods:** This prospective randomized comparative study included patients operated for colorectal cancer ending with anastomosis not stoma. The patients were randomly divided into two groups; with the study group adopted carbohydrate loading pre-operatively and early post-operative feeding, while the control group submitted to the traditional pre- and post-operative feeding protocols.

**Results:** There were statistically significant difference between both groups in which application of study protocol decreases the post-operative ICU stay ( $P = 0.0005$ ) and hence overall hospital stay. On the other hand, postoperative blood glucose level and pH showed significant difference in the study protocol adopting group ( $P = 0.00002$ ,  $0.00004$  respectively), whereas other complications as anastomotic leakage showed no statistically significant difference between the two groups ( $P = 0.552$ ).

**Conclusions:** Pre-operative carbohydrate loading and early post-operative feeding as components of Early Recovery After Surgery (ERAS) have a remarkable improving effect on post-operatives outcomes.

**Keywords:** colo-rectal surgery, enhanced recover after surgery (ERAS), carbohydrate loading, early post-operative feeding.



### INTRODUCTION

Surgical intervention resulting in cellular injury, occurs through dual pathways, direct and indirect injury. Surgical access, organ mobilization, dissection, and excision represent the direct form of injury. On the other hand, blood loss, alterations in perfusion, microvascular changes, and anesthetic techniques are causes of indirect injury [1].

Cellular injury provokes neutrophils and macrophages to produce proinflammatory cytokines, which in turn induce the liver to increase synthesis of acute phase reactants. Level of these acute phase reactants is directly proportional to the magnitude of the stress response and the development of the systemic inflammatory response [2]. On the other hand, activation of the hypothalamic-pituitary-adrenal

axis leads excess release of counter-regulatory hormones including cortisol, growth hormone, glucagon, and catecholamines, resulting in the development of insulin resistance and impaired immune function [3].

Intraabdominal surgery is catabolically burdensome, in particular, with intraoperative blood glucose levels in the non-diabetic patient exceeding 180 mg/L which may remain elevated for days after surgery provoking insulin resistance, and hence persistently elevated blood glucose levels. Organ dysfunction, adverse wound outcomes, and mortality are all more common in those with hyperglycemia [4].

On the other hand, nitrogen after elective abdominal surgery in healthy patients can approximate 40–80 g, which represents a profound loss and potentially catastrophic to the

malnourished patient. Diminished protein stores are associated with delayed mobility, poorer respiratory function, infection from a reduced immunological function, and prolonged recovery [5].

All these adverse events and what is more, are all triggered by the traditional excessive unneeded behaviour of pre-operative fasting which may be continued post-operatively, augmenting surgery induced stress response [6].

#### METHODS

In this study 54 non-diabetic patients were included with final diagnosis colorectal cancer and generally fit for surgery. All patients with inoperable disease or any comorbidity contraindicating surgery were excluded, in addition to diabetic patients whatever being well controlled or not.

The study was approved by the research ethical committee of the local University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The patients were randomly allotted to 2 groups; one destined to follow the protocol of study and the other group followed the traditional protocol.

The patients of both groups were properly counselled and consented regarding their colon cancer surgery and the expected complications of the surgical treatment, and then each group had sufficient explanation regarding the preparation protocol and the post-operative oral intake, outlining and explaining the steps of each protocol.

The group allotted to the study protocol was instructed to stop oral intake of solid food 16 hours preoperatively and continue on clear fluids ***insisting on having 200 ml of a clear sugary beverage 8 hours pre-operatively to be repeated 6 hours later.*** A bowel cleansing solution was introduced 12 hours pre-operatively to be consumed in 2 hours.

On the other hand, the group of the traditional protocol had their preparation started 48 hours pre-operatively in the form of abstaining from all forms of solid food and continuing on clear non-residual fluids up to 6 hours pre-operatively,

giving metronidazole 500 mg and neomycin 500 mg tid, having an enema using 500 ml of saline 0.9% every 8 hours until having clear output, with no sugary drinks pre-operatively.

The radical surgical resection was done according to the site of the primary tumour. The duration of the operation was recorded in addition to estimating the amount of blood loss and the need for blood transfusion.

After the operation ended, the patient was transferred to the ICU for the recovery period until the patient is stable enough to be transferred to the common ward. The patient following the fast-track protocol were given oral fluids starting at the night of the surgery day (day 0) and solid food was introduced at day 2 post-operatively. On the other hand, the patients of the traditional protocol were prevented from having oral feeding up to 5th post-operative day and were put on IV fluids.

The length of the ICU stay, the emergence of any post-operative complications, and the post-operative laboratory results were all recorded.

#### RESULTS

##### *Statistical analysis*

All patients' data were collected, checked, and analyzed by using (SPSS version 20). Data were expressed as mean  $\pm$  SD and number with (%) according to type of variable. Chi-square test ( $\chi^2$ ) or Fischer's exact t test or Mann-Whitney was used when appropriate. P value  $<0.05$  was considered statistically significant.

The total number 54 patients were included in the study. Their data either in the pre-operative or intra-operative stage is presented in table (1)

Concerning the postoperative follow-up, the length of ICU stay was significantly shorter in study protocol adopting group (1.48 days) compared to traditional protocol adopting group (2.59). Also, the blood glucose level was significantly lower, and the pH was significantly optimal in the study protocol adopting group compared to the second group. However, the rate of ileus, wound infection and other complications were quite similar in both groups with no significantly statistical difference between both groups. All are shown in table (2)

**Table 1:** Containing patients’ personal data, co-morbidities, tumour site, pre-operative risk factors, and their operative recordings.

Data type		Study protocol N (27)	Traditional protocol N (27)	P Value
<i>Sex of patients</i>	Male	18 (67%)	16 (59%)	0.573
	Female	9 (33%)	11 (41%)	
<i>Mean age (years)</i>		56.59 ± 8.32	58.59 ± 7.82	0.298
<i>Hypertension (the only recorded co-morbidity)</i>		15 (56%)	11 (41%)	0.276
<i>Site of the primary tumor</i>	Right colon	8	10	0.819
	Left colon	4	3	
	Sigmoid colon	15	14	
<i>Pre-operative risk factors</i>	Hb < 10 gm%	6	6	1.0
	Alb <3 gm%	8	4	0.190
<i>Duration of the operation(min)</i>		154.44 ± 15.43	157.78 ± 12.67	0.1252
<i>Amount of blood loss (ml)</i>		355 ± 88.66	377.78 ± 98.32	0.331
<i>Amount of transfused blood</i>	2 units transfused	10	11	0.948
	1 unit transfused	9	8	
	Nothing transfused	8	8	

**Table 2:** Postoperative follow-up and complications data.

Post-operative follow-up and complications	Study protocol N (27)	Traditional protocol N (27)	P Value
<i>ICU stay (days)</i>	1.48 ± 0.43	2.59 ± 0.86	0.0005
<i>Blood sugar (mg%)</i>	139.63 ± 17.36	238.41 ± 21.64	0.00002
<i>pH</i>	7.4 ± 0.01	7.25 ± 0.05	0.000048
<i>Ileus</i>	4	8	0.19
<i>Wound complications</i>	2	3	0.638
<i>Specific cardio-respiratory complications, urinary infections, or anastmotic leakage</i>	No case recorded in either group		1.0

**DISCUSSION**

It is essentially established that a successful surgical intervention is not only a matter of properly done surgical procedures, but also is a correct metabolic control, understanding post-injury metabolic consequences to provide appropriate nutritional support [7].

This work targeted to study the effect of carbohydrate loading as a component of ERAS protocol compared to the traditional one in patients submitted to colo-rectal surgery.

It is well shown from the above-mentioned data in table (1), that the characters of the two studied groups are quite comparable focusing on the element of the study.

Following the patient up in both groups during the immediate post-operative period, the patients of the study group showed significantly lower blood glucose level post-operatively compared to the group of the traditional protocol. This can favour the effect of pre-operative load which lessened the stress response caused by release of stress agents

(cytokines and hormones). On the other, this provides considerable evidence about the effect of this study protocol in decreasing the other elements of post-operative catabolic response.

Moreover, the pH was considerably optimum in the study group compared to the traditional one and explaining the significantly shorter ICU stay in this group, and this brought another strong evidence for the relieving effect of the pre-operative load on the post-operative catabolic response.

Few cases in both groups had other complications as ileus, surgical site infection and other ones without favouring either of the two protocols, this may need further studies to establish it definitely. These findings are supported by *Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations: 2018*, which encouraged Patients undergoing elective colorectal surgery should be allowed to eat up until 6 h and take clear fluids including CHO drinks, up until 2 h before initiation of anaesthesia with high level of evidence and showed moderate level of evidence regarding improving well-being and insulin resistance. So, this protocol was strongly recommended [8].

#### Conclusions

Based on this study, we conclude that pre-operative carbohydrate loading, and early post-operative feeding has a promising effect on the post-operative recovery and functional outcomes in colo-rectal surgery and that will consequently affect early post-operative morbidity. This protocol is considered a safe one and easily applicable especially in the non-diabetic patients; but still studies to be done to prove its efficacy in diabetics and those with other advanced comorbidities compromising wound healing.

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#### Conflict of interests:

The authors state that there is not any conflict of interests to disclose.

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