



Safety and Efficacy of adding intravenous N-acetylcysteine to parenteral Dipeptiven in hospitalized patients undergoing colon surgeries

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدقة الله العظيم

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List of Abbreviations

8-ODG	: 8-oxo-2'-deoxyguanosine
ACCP	: American College of Clinical Pharmacy
AGA	: American Gastroenterological Association
AL	: Anastomotic leakage
ALT	: Alanine aminotransferase
BMI	: Body mass index
BT	: Bacterial Translocation
CAT	: Catalase
CIN	: Contrast-induced nephropathy
CRP	: C-reactive protein
EN	: Enteral nutrition
ESPEN	: European Society for Clinical Nutrition and Metabolism
Gln	: Glutamine
GPX	: Glutathione peroxidase
GSH	: Glutathione
GSSH	: Glutathion disulfide
Hb	: Hemoglobin
HNPCC	: Hereditary nonpolyposis colon cancer
LDL	: Low density lipoproteins
MDA	: Malondialdehyde
NAC	: N-acetyl-L-cysteine
NF-κB	: Nuclear factor kappa light chain enhancer of activated B cells
NRS2002	: Nutritional risk screening 2002
PAMPS	: pathogen-associated molecular patterns
POI	: Postoperative ileus
PRRs	: pattern recognition receptors
RME	: Resting metabolic expenditure

List of Abbreviations

ROS	: Reactive oxygen species
SIRS	: Systemic inflammatory response syndrome
SOD	: Superoxide dismutase
SSIs	: Surgical site infections
TLRs	: Toll-like receptors
TNF-α	: Tumor necrosis factor-α
TPN	: Total parenteral nutrition

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Pharmacist/ Ghada Hussein Ahmed El-Adly

Abstract

Introduction

Nowadays, there is a recent trend towards the use of antioxidant agents in the prevention or alleviation of the severity of postoperative systemic inflammatory response syndrome (SIRS) after colon surgeries.

Aim of the work

The aim of the study was to investigate the efficacy of perioperative intravenous administration of N-acetyl cysteine (NAC) as an antioxidant and anti-inflammatory agent in patients undergoing colonic surgeries, in addition to the tolerability of its administration.

Patients and methods

The study was carried out on 60 patients who were admitted to the surgical intensive care unit, Ain Shams specialized hospital, Cairo, Egypt, following colon surgeries. They were randomized to either Group I received a loading dose of NAC followed by continuous infusion started one hour prior to induction of anesthesia, and continued over 48 hours, or Group II received the same volume of dextrose 5%. Clinical and laboratory evaluation for manifestations of SIRS, marker of inflammation (tumor necrosis factor alpha) and oxidative stress marker (malondialdehyde), as well as demonstration of the occurrence of side effects within Group I.

Results

There was a significant difference in the serum levels of both haemoglobin (P value = 0.017), and ALT (P value=0.028) in Group I versus Group II postoperatively, with a non-significant difference in the serum level of tumor necrosis factor alpha, and malondialdehyde between the two groups. There was no statistical significant difference regarding the clinical data and laboratory parameters within the Group I prior and following NAC administration (P value >0.05), and only 6.6 % of the patients of the Group I experienced few and mild side effects.

Conclusion

It is safe to administer NAC perioperatively. However, its efficacy as an antioxidant and anti-inflammatory agent is not significant in the present study, and requires further investigations.

Keywords: Malondialdehyde, perioperative care, systemic inflammatory response syndrome, tumor necrosis factor alpha, acetylcysteine.



Review of Literature

Colon surgeries

Colonic surgeries are among the most frequently performed major abdominal surgical procedures. Colonic surgeries are performed for both benign diseases such as diverticular disease, inflammatory bowel disease, and malignant disease such as colon cancer (*Weinstein et al., 2013*). Colon cancer is considered the third common type of cancer worldwide (*Gandomani et al., 2017*). Surgery for benign diseases includes resection of the affected bowel segment, leaving healthy, well vascularized tissue to be connected together to bowel ends for which a complete resection is done, coupled with regional lymphadenectomy (*Weinstein et al., 2013*).

Indications of colon surgeries:

1. Inflammatory bowel disease

a- Crohn's disease:

Colectomy is indicated in the fibrotic strictures with obstructive symptoms, fistulizing disease with or without abscess, and medically refractory diseases (*Parray et al., 2011*).

b- Ulcerative colitis:

Colectomy is indicated in case of medical therapy failure, high grade dysplasia or malignant transformation, uncontrollable bleeding, and toxic megacolon (**Bennis and Tired, 2012**).

2. Diverticulitis

In the past, it was recommended to do a prophylactic resection after second attack of acute diverticulitis. The current American Gastroenter-ological Association (AGA) guidelines recommend an individualized approach for the surgical management for those patients (**Rezapour et al., 2018**).

3. Gastrointestinal stromal tumors

Either open or laparoscopic surgery for the removal of lesion is considered a first line therapy for any resectable lesion (**Sanchez-Hidalgo et al., 2018**).

4. Colon cancer

Colon cancer is one of the most common indications for colonic surgery. It is observed that about 11% to 43% of colon cancer cases presented as surgical emergencies (**Weixler et al., 2016**).

Classification of colon surgeries:

A. Colectomy:

Colectomy is the removal of any part of the colon beginning from the last part of the ileum to the recto-sigmoid part. Colectomy is classified according to the part that will be removed and depending on the location of the disease into either, total colectomy, right hemicolectomy, left hemicolectomy, or sigmoid colectomy (*Kwok and Hung, 2015*).

I. Total colectomy:

Total abdominal colectomy is the surgical procedure of choice for multiple conditions requiring complete resection of the colon with preservation of the rectum. Patients who are candidate for the removal of the whole colon are multiple and are listed below:

- 1) Familial adenomatous polyposis.
- 2) Some cases of crohn's disease and mucosal ulcerative colitis.
- 3) Hereditary nonpolyposis colon cancer (HNPCC)
- 4) Colon cancer (*Wexner and Fleshman, 2011*).

II. Right hemicolectomy:

It is the surgical resection of the right colon which is performed for benign or malignant lesions of the right colon and cecum. Patients who are candidates for benign hemicolectomy include Crohn's disease, ischemia, trauma, diverticulitis and cecal volvulus. Whereas, for malignant or premalignant diseases who need right hemicolectomy, include adenocar-cinomas or colonoscopically unresectable adenomas, appendicular neoplasms such as adenocarcinoma or carcinoid tumors more than 2cm (*Terrah et al., 2016*).

III. Left hemicolectomy:

Left colon resection is performed for the treatment of benign or malignant diseases of colon. Left hemicolectomy is performed as a single procedure or as a part of complex resection like total colectomy (*Wexner and Fleshman, 2011*). Benign diseases include the removal of certain benign conditions of the descending and sigmoid colon e.g. arterio-venous malformations, diverticular disease and ischemic strictures, removal of sigmoid volvulus and left colon polyps. Malignant disease includes cancer in the left colon (*Jamali, 2012*).

IV. Sigmoid colectomy:

Sigmoid colectomy is the resection of the sigmoid part of the colon for benign or malignant diseases. Benign diseases that need sigmoidectomy include diverticulitis, sigmoid volvulus, trauma, and rectal prolapse when combined with rectopexy, and the malignant disease as in sigmoid resection for colon cancer **(Figure 1)** *(Fischer and Heise, 2016)*.

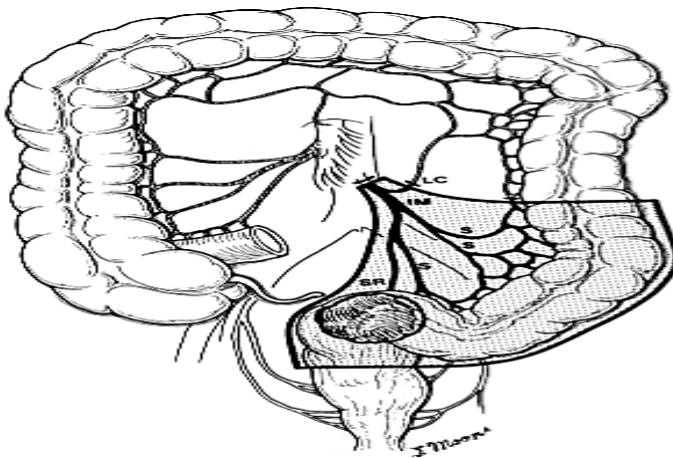


Figure (1): Sigmoid colectomy *(Simmang and Huber, 2005)*

B-Colostomy:

Colostomy is the surgical procedure in which the large bowel is exteriorized to the anterior abdominal wall. It may be temporary or permanent. It will be temporary, when its aim is to convert the fecal stream away from an area of concern as before radiation treatment, and after colon repair, but permanent colostomy is created after resection for rectal cancer *(Sohn and Steele, 2010)*.