

ROLE OF IMMUNONUTRIENTS IN POSTOPERATIVE OUTCOME IN PATIENTS UNDERGOING GASTROINTESTINAL ANASTOMOSIS

ABSTRACT

INTRODUCTION: Immunonutrition is the science of positive manipulation of immunity using macro or micronutrients to boost immunity. **AIMS AND OBJECTIVES:** To determine whether post-operative immunonutrition could improve the clinical outcomes in patient undergoing gastrointestinal anastomosis. **MATERIALS AND METHODS:** The study involved patients undergoing gastro-intestinal anastomosis from 1st June 2017- 31st May 2018 in Department of General Surgery, GMCH. **RESULTS AND OBSERVATIONS:** In 243 patients undergoing gastrointestinal anastomosis, rates of reduction in anastomotic leak, wound infection and mean hospital stay in study vs control group were 10% vs 32%, 12.5% vs 35% and 8 days vs 10 days respectively. The immunonutrition supplementation had a positive effect on increasing postoperative albumin level. The mean post-operative day-2 and day-6 serum albumin level in control vs study groups were 3.04mg/dl vs 3.47 mg/dl and 3.02mg/dl vs 3.64mg/dl respectively. **CONCLUSION:** The study showed substantial reduction in rates of anastomotic leak, postoperative infections and length of hospital stay following administration of immunonutrition formula with glutamine, arginine, omega-3 fatty acids and nucleotides in postoperative patients undergoing gastrointestinal anastomosis. **Keywords:** Immunonutrition, glutamine, arginine, omega-3 fatty acids, postoperative complications.

INTRODUCTION

Immunonutrition (IMN) or nutritional immunology is the science of positive manipulation of immunity using macro or micronutrients. It is well established that malnutrition impairs immunity and it is possible to reverse this effect by achieving nutritional balance. Immunonutrition goes one step further and uses specific nutrients in doses higher than normally found in food to augment immunity, its two broad goals being, enhancing host immune response or reducing the exaggerated inflammatory response. The recognized immunonutrients arginine, glutamine, omega-3 fatty acids and nucleotides have been shown to have immunomodulatory properties. The route of delivery may be enteral or parenteral, however enteral route is favored in most clinical studies.

Gastrointestinal anastomosis is a very important procedure in our day to day surgical practice for various causes like bowel obstruction, incarcerated hernias, benign and malignant tumors of small and large bowel etc. A major complication following bowel anastomosis is anastomotic leak leading to peritonitis, abscess, fistula, necrosis, stricture formation etc. and accounts for about 1.3 to 7.7%, that is often associated with increased morbidity and mortality and prolonged hospital stay. Other commonly seen complications include wound infection, intra-abdominal abscess, chest infection etc. Various factors are associated with these complications like the general condition of the patient, suturing technique, suture material used, presence of concurrent sepsis, vascular compromise and so on.

Arginine (protects against ischemia/reperfusion injury, promotes T cell maturation and activation and improves nitrogen balance.), **Glutamine** (serves as an important energy source for the gut mucosa, required in metabolic processes in immune cells and other rapidly dividing cells), **Omega-3-fatty acids** (have a role in modulating the production of both lipids viz. eicosanoids and proteins viz. cytokines mediators, reduce systemic inflammation, minimize hepatic ischemic injury and normalize vascular flow properties) and **Ribonucleic acid i.e. RNA** (improve protein synthesis, facilitate intestinal cell maturation and have a regulatory role in the T cell mediated immune response) are immunonutrients which can modulate the immune system and improve host defense mechanisms after major surgery.

This study was conducted to determine whether post-operative immune nutrition could improve the clinical outcomes in patient undergoing gastrointestinal anastomosis in our set up, too.

AIMS AND OBJECTIVES

To compare the effect of immunonutrient supplementation (both oral and parenteral) in postoperative period after gastro-intestinal anastomosis, in preventing postoperative complications as compared to the conventional approach.

General objective: Whether supplementation with immunonutrients in postoperative period is beneficial for the patients.

Specific objectives: Benefit of supplementation with immunonutrients after gastrointestinal anastomosis in reducing various complications like,

- i. Anastomotic leak
- ii. Wound infection
- iii. Intra-abdominal abscess formation
- iv. Chest infection
- v. Non-infectious complications
- vi. Mortality
- vii. Length of hospital stay

MATERIALS AND METHODS

It was a hospital based prospective interventional study involving the patients undergoing gastro-intestinal anastomosis during the study period of 1st June 2017 to 31st May 2018 under the Department of Surgery, Gauhati Medical College and Hospital, Guwahati.

METHOD OF DATA COLLECTION

All the elective and emergency patients undergoing gastrointestinal anastomosis during the study period were included in the study. A total No. of 243 patients had undergone gastro-intestinal anastomosis, out of which 41 patients were excluded by exclusion criteria (mentioned below) and due to refusal for giving consent to participate in the study. The remaining 202 patients were randomized by systematic random sampling. Every 4th and 5th patient were selected irrespective of age and sex. Written informed consent was taken. Every 4th patient was treated with conventional approach (**control**) while every 5th patient was given immunonutrition (**case**) in postoperative period. After randomization total 80 patients were selected into two groups i.e. case and control, each having 40 patients.

- **Case** (40 patients) were given parenteral formulations of immunonutrients (until orally allowed) and then immunonutrients enriched powder (containing Glutamine, Arginine & Omega 3 fatty acid) dissolved in water twice-a-day was started (when orally allowed). Immunonutrient supplementation was continued up to 7th post-operative day.

- **Control** (40 patients) of the control group were kept on maintenance intravenous fluids containing dextrose and saline (until orally allowed). The nasogastric tube was removed and feed was started orally depending on the clinical condition of the patient and appearance of bowel sounds as done conventionally.

Inclusion criteria:

Patients who have undergone gastro-intestinal anastomosis during the study period in the department of Surgery, GMCH.

Exclusion criteria:

- 1) Patient with ASA (American Society of Anaesthesiologist) grade IV to VI.
- 2) Re-laparotomies.
- 3) Immunosuppressed patients.
- 4) Patients with renal failure (both acute and chronic renal failure).
- 5) Age less than 12 years.
- 6) Pregnant females.

- The following parameters were studied in postoperative period –

- 1) **Anastomotic leak:**

They usually present between 5 - 7 days post-operatively. The definitive diagnosis of anastomotic leak is made by an urgent CT scan with contrast of the abdomen and pelvis, which shows the presence of extraluminal contents.

- 2) **Intra-abdominal abscess :**

Patients generally present with pain abdomen with fever, raised WBC counts. USG of the whole abdomen can detect the collection, but the CT scan with contrast can give the definitive diagnosis. It can also be confirmed by percutaneous drainage or after re-laparotomy.

- 3) **Wound infection:**

It is the presence of purulent exudate in the surgical wound with positive bacterial culture.

- 4) **Chest infection:**

Lung infection either in the larger airways (bronchitis) or in the smaller air sacs (pneumonia) diagnosed by abnormal chest radiograph.

- 5) **Noninfectious complications:**

These include a variety of conditions like Hemorrhage, Deep Vein Thrombosis, Pulmonary Embolism, Heart failure, Atelectasis, Paralytic ileus, Wound dehiscence etc.

- 6) **Length of hospital stay:**

The average length of stay (ALOS) is often used as an indicator of efficiency.

7) Mortality

8) Pre and post-operative immune-metabolic parameters (like Albumin and hemoglobin)

STATISTICAL ANALYSIS OF DATA

For statistical analysis, data were entered into a Microsoft excel spreadsheet and then analyzed by using software SPSS 20.0.1 and Graph Pad Prism version 5. Data were expressed in terms of mean and standard deviation for numerical variables and the count for categorical variables. Student's independent sample's t-test was applied to compare normally distributed numerical variables between groups; unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate for statistically significant, P- Value is considered to be ≤ 0.05 .

STUDY TOOLS:

- 1) Patient informed consent form
 - 2) Patient record file
 - 3) Hematological and biochemical examination reports like complete haemogram, sugar, urea, creatinine, LFT especially albumin level, CRP, and electrolytes
 - 4) Radiological: Straight x-ray chest, x-ray abdomen.
 - 5) USG & CECT of abdomen as and when required.
- 6) Proforma for tabulation of data.

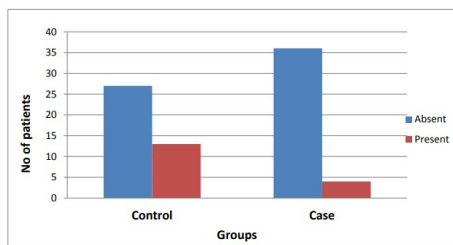
RESULTS AND OBSERVATIONS

After completion of the statistical analysis and discussion, the following observations were recorded.

- **Anastomotic leak** was found in 32 % of patient in control group as compared to 10% in the study group. This showed a positive effect of immunonutrition in reducing anastomotic leak.

Chi-square = 4.781 and P value = 0.0288

Group			
Anastomotic leak	Control	Case	Total
Absent	27	36	63
Present	13	4	17
Total	40	40	80

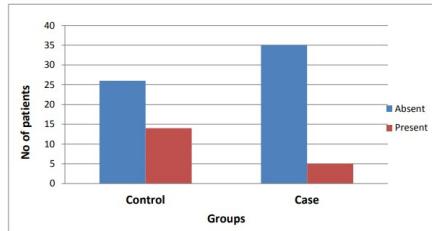


Bar diagram shows anastomotic leak in both case and control group.

- **Surgical wound infection** was also found to be reduced after giving immunonutrition postoperatively. Study showed 35 % of patient with wound infection in control group as compared to 12.5 % in the study group.

Chi-square= 4.418 and P value: 0.0356

Group			
Wound inf	Control	Case	Total
Absent	26	35	61
Present	14	5	19
Total	40	40	80

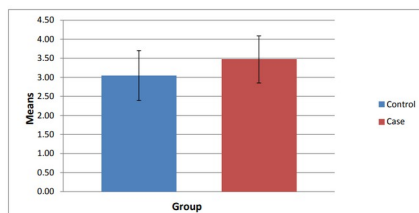


Bar diagram shows wound infection in both case and control group.

- No significant effect of immunonutrition was seen in reducing intra-abdominal abscess formation and reducing respiratory tract infection. RTI found in 22.5% patient in control group as compared to 7.5% in the study group.
- Immunonutrition supplementation seemed to have a **positive effect on increasing the post operative albumin level**. The mean post operative day-2 serum albumin level in control group was 3.04mg/dl as compared to 3.47 mg/dl in the study group. The mean post operative day-6 serum albumin level in control group was 3.02mg/dl as compared to 3.64mg/dl in the study group.

p=0.0039, statistically significant

Group	Number	Mean	Std. Dev	Minimum	Maximum	Median	p-value
Control	40.0000	3.0475	0.6540	2.0000	4.3000	3.0000	
Case	40.0000	3.4700	0.6174	2.6000	4.9000	3.3000	0.0039



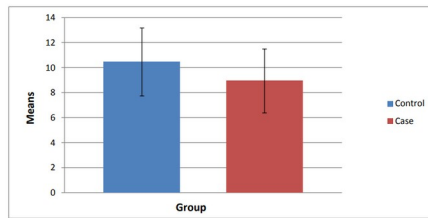
Bar diagram shows distribution of post-operative day-2 albumin level in both case and control group.

- No significant decrease in noninfectious complication was found. 25% of patient in control group was having noninfectious complications as compared to 17.5% in the study group.

- There was no effect of immunonutrition over the mortality rate. Mortality was found to be 2.5% in the control group as compared to 5% in study group.
- The mean length of stay in hospital was significantly lower in the study group. In control group, it was 10 days as compared to 8 days in the study group.

P value is 0.0116.

Group	Number	Mean	Std. Dev	Minimum	Maximum	Median	p-value
Control	40.0000	10.4500	2.7170	7.0000	19.0000	10.0000	0.0116
Case	40.0000	8.9250	2.5560	6.0000	16.0000	8.0000	



Bar diagram shows length of hospital stay in both case and control group

The study showed that administration of immunonutrition formula supplemented with glutamine, arginine, omega-3 fatty acids, and nucleotides in the postoperative period to patients undergoing gastrointestinal anastomosis significantly improves clinical outcomes, as evidenced by a substantial reduction in anastomotic leak and postoperative infections by improving immunity and hence decreasing the length of hospital stay.

DISCUSSION

A number of facts have been enumerated, some of which are in accordance with the literature, while a few differ. This study performs a survey on the effect of immunonutrient supplementation after gastrointestinal anastomosis in the prevention of postoperative complications and the results are compared with that of the conventional approach.

The present study finds an **anastomotic leak** in 13 Patients of the control group against 4 patients of the case group. A statistically significant P Value (0.0288) has been obtained indicating that feeding patients with immunonutrients in postoperative period is beneficial and the finding of this study is very similar with the earlier studies.

Series	No.of cases	% of anstomic leak in study group	P value	Remark
Marano et al ⁸⁵ . (2013)	109	3.7%	0.045	Significant
Yildiz et al ⁸⁸ (2016)	41	4%	0.018	Significant
Present study	80	10%	0.0288	Significant

In this study, it is found that patients treated with immunonutrients in the postoperative period (cases) have less wound infections (5 patients) as compared to those treated conventionally (control) (14 patients). P value is 0.0356, which is statistically significant and was comparable with the earlier studies.

Series	No of cases	wound infection in study group	P value	Remarks
Heyand et al. (2001) ⁷⁹	2419	RR, 0.66; 95% CI	P=<.001	significant
Gianotti et al ¹³ . (2002)	200	10%	P=<.04	significant
Zheng et al. (2007) ⁸²	1269	Odd ratio=0.41	P=<0.0001	significant
Klek et al. (2011) ⁸⁶	305	28.3%	P=0.04	significant
Marano et al ⁸⁵ . (2013)	109	7.4%	P=<0.05	significant
Present study	80	12.5%	P =0.0356	significant

The mean length of stay in conventional group was 10.45 days as compared to 8.9 days of immunonutrient group. A decrease was noted in mean length of stay in hospital days if immunonutrients are given in postoperative period. The P value is 0.0116 which is very significant. Thus supplementation with immunonutrient decreases length of stay in hospital and hence cost of treatment. This study was at par with the previous studies.

Series	No of cases	Length of hospital stay in study group(WMD)	P value	Remrks
Yan Zhaang et al	2311	2.62 days	<0.01	significant
Wong et al ⁸⁹	2016	2.92 days	<0.00001	significant
Present study ⁹²	80	1.55 days	0.0116	significant

The mean serum albumin level is again measured on postoperative day 6. In conventional group it is 3.02mg/dl as compared to 3.64mg/dl in immunonutrient group. The P value is 0.0001(statistically significant). **Selim Yigit Yildiz88** in his study found that Serum prealbumin levels increased significantly in the ENIN group (P = 0.033) which supports my result.

CONCLUSION

The potential to modulate the activity of the immune system by interventions with specific nutrients is the true concept of immunonutrition. Currently, arginine, glutamine, omega-3 fatty acids and nucleotides are the nutrients that are most commonly used in clinical studies. After comparing the data of this study, some important facts were noted regarding the effect of immunonutrients. We saw an obvious benefit of giving diet enriched with immunonutrients to the patients in postoperative period who underwent gastrointestinal anastomosis. The rates of some complications were less, especially anastomotic leak, wound infection and the mean length of stay in hospital.