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Effect of Oral Glutamine on Clean and Clean Contaminated Wounds

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Abstract: ***L-glutamine is a nonessential and most prevalent amino acid. It was thought that glutamine was not a necessary component of the oral diet because of the relative amount of glutamine in the body compared with other amino acids and the fact that the body can independently produce glutamine but studies have suggested that the glutamine is indeed needed in surgical stress where the utilisation of Glutamine increases so does the requirement, thus can become conditionally essential in humans. Surgical patients with glutamine supplementation were found to have reduced incidence of wound complications such as infection, wound gaping and abscess formation compared to the patients without glutamine infusion. Clean wounds are that wound which consists of uninfected operative incisions in which there is no inflammation is found. Clean-contaminated wounds are those operative wounds in which the alimentary, respiratory, genito-urinary tracts are entered under controlled conditions and without unusual contamination. In our study, we supplemented oral glutamine at the dose of 15gm/day for 5 days in operated cases of clean (30) and clean contaminated (30) wounds and we compared the rate of wound infection in these cases with the patients who were not supplemented. The distribution of incidence of surgical site infection (SSI) among the cases studied is significantly higher in Group 2 compared to Group 1 (P-value>0.05). The distribution of incidence of surgical site infection (SSI) in hernia group among the cases studied did not differ significantly between two study groups (P-value>0.05). The distribution of incidence of surgical site infection (SSI) in appendicitis group among the cases studied did not differ significantly between two study groups (P-value>0.05).***

Keywords: glutamine, wound healing, wound infection, surgical wound

1. Introduction

Nutritional supplementation of micronutrients as well as macronutrients in Post-operative period has been known to improve the morbidity of patients, quality of life. Importance of oral nutrition in reduction of infections and complications associated with infections is well known after major abdominal surgeries.

Glutamine

It is a known fact that catabolic stressful condition such as surgeries, trauma or burns can lead to 50% glutamine loss from the body especially from the muscles. It is very important to deliver the glutamine for integrity of intestinal mucosa, to maintain glutamine levels in muscles and for better nitrogen balance during stressful conditions. Glutamine is a precursor of synthesis of protein and it is a very important immunonutrient. Along with all these, glutamine is takes part in many of metabolic pathways. It is also noted that severe reduction of glutamine from muscles may leads to muscle loss immunosuppression further raising the risk for post-op infection and sepsis. Many studies did in past have shown that glutamine supplementation in post-op patients especially with major abdominal surgeries helps in improving the recovery and their intestinal permeability. However, a conclusive data on this aspect have not been explored much in India.

Surgical patients with glutamine supplementation were found to have reduced incidence of wound complications such as infection, wound gaping and abscess formation compared to the patients without glutamine infusion.

Types of surgical wounds:

1) Clean wounds are that wound which consists of uninfected operative incisions in which there is no inflammation is found and the alimentary, respiratory, uninfected genito-urinary tracts are not entered. Along with this, clean wounds will be primarily closed and, closed drains are kept if required.
2) Clean-contaminated wounds are those operative wounds in which the alimentary, respiratory, genito-urinary tracts are entered under controlled conditions and without unusual contamination. In this we consider operations involving the appendix, biliary tract, vagina and oropharynx, provided no infection or major break in technique is noted.

Surgical Site Infections:

There are various definitions of Surgical Site Infection. Surgical site infection is also defined as an infection that occurs within 30 days after the operation and involves the skin and subcutaneous tissue of the incision (superficial incisional) and/or the deep soft tissue (for example, fascia, muscle) of the incision (deep incisional) and/or any part of the anatomy (for example, organs and spaces) other than the incision that was opened or manipulated during an operation (organ/space)

Evidences:

The following studies were conducted:-

This study was conducted with the objective to evaluate the wound healing potential of l-glutamine in laboratory rats using excision and incision wound models. In this study, they made wounds of size 500 mm2 and depth 2 mm on the

male Wistar rats (around 250 g) on dorsal aspect and were supplemented with oral l-glutamine (1 g/kg) to look for healing of wound and epithelisation. They were examined histologically as well. Also in this study, 6 cm two incisions on dorsal aspect in male Wistar rats (of around 250 g) were used. They used to study the effectiveness of oral l-glutamine (1 g/kg) on tensile strength of the wound, total protein and hydroxyproline content in the incision. The results showed that the use of Oral l-glutamine significantly decreased wound area, epithelisation period and wound index, whereas the rate of wound contraction significantly increased compared with control rats in the excision wound model. Tensile strength of wound, hydroxyproline content and protein level were significantly increased in rats supplemented with l-glutamine. It was proven Histologically as well, that wound tissue from the l-glutamine supplemented rats was completely epithelialized with neo-vascularization and high fibrous tissues. The above study shows that glutamine increases the healing of wounds, which is important for reducing surgical site infection.

Aim:
The aim is to evaluate effect of oral glutamine on occurrence of surgical site infections in clean (Hernia) and clean contaminated (non-perforated appendicitis) wounds.

Objectives
1) To study the role of glutamine in clean wounds on occurrence of surgical site infections (groin hernias)
2) To study the role of glutamine in clean contaminated wounds on occurrence of surgical site infections (appendicitis)
3) To compare the effects glutamine in each group

2. Materials and Methods

The study was conducted on 60 post-operative Patients of clean and clean contaminated wounds admitted at Bharati Hospital and research center, Pune from august 2018 to July 2020 after giving informed consent and ethical clearance.
It's a randomized controlled trial with a period of study of 24 months.

Inclusion Criteria
All post operative patients of age group 18 years -55 years who have undergone open abdominal surgeries for clean (groin hernia) or clean contaminated (appendix).

Exclusion Criteria
Patients with comorbidities such as- Diabetes mellitus, Renal diseases (creatinine concentration >2.5 mg/dl), Cardiac disorders (Class III or IV), Hepatic disease (total bilirubin concentration >3 mg/dl), Autoimmune diseases, Chronic use of steroids (30 mg or more for more than a month), Chronic obstructive pulmonary disease (partial pressure of carbon dioxide>375 kPa or 50 mmHg) or Pregnant women, Perforated appendicitis or Strangulated hernia.

3. Methodology

After ethics committee clearance and written informed consent, patients undergoing open abdominal surgeries fitting in inclusion criteria- 60 patients are selected of age group 20-55 years and divided into 2 Experimental group (veg diet + supplement) and 2 control group (veg diet only). 1st Group will be containing patients of groin hernia and 2nd group will be containing patients of non perforated appendicitis which further will be divided into experimental group and control group.

All patients will be scrubbed with betadine scrub thrice prior to surgery.

All patients will undergo shaving of body hair prior to surgery.

Tests will be supplemented with glutamine 0.5gm three times a day for 5 days.

The study protocol was divided into 4 sections:

The primary study period of 5 post-operative enteral feeding of glutamine. Follow-up and tracking the incidence of infection till the patient was discharged and also during post operative follow-up.

4. Results

The present study was a prospective comparative study on effect of oral glutamine on clean incised wounds and clean contaminated wounds- a randomised control trial.

The study included 60 post operative patients of clean and clean contaminated wounds admitted at Bharati Hospital and research center, Pune from August 2018 to July 2020.

The cases were divided in 2 groups randomly of 30 size each using simple random sampling (SRS) procedure. Group 1 cases were allocated to glutamine. Group 2 cases were allocated to non- glutamine.

Following section shows the detailed statistical analysis of the available data.

Table 1: Inter-group comparison of mean age

Age (years)	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	Mean	SD	Mean	SD	
Age (years)	35.90	11.62	35.37	14.63	0.876^{NS}
Values are mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.					

Inter-group comparison of mean age
The mean ± SD of age of cases studied in Group 1 and Group 2 was 35.90 ± 11.62 years and 35.37 ± 14.63 years respectively. The minimum – maximum age range in Group 1 and Group 2 was 19 – 55 years and 18 – 55 years respectively.

Distribution of mean age of cases studied did not differ significantly between two study groups (P-value>0.05).

Table 2: Inter-group sex distribution of cases studied.

Sex	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	n	%	n	%	
Male	27	90.0	23	76.7	0.299^{NS}
Female	3	10.0	7	23.3	
Total	30	100.0	30	100.0	

Values are n (% of cases), P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.

Inter-group sex distribution

Of 30 cases studied in Group 1, 27 (90.0%) were male and 3 (10.0%) were female. Of 30 cases studied in Group 2, 23 (76.7%) were male and 7 (23.3%) were female. The distribution of sex of cases studied did not differ significantly between two study groups (P-value>0.05).

Table 3: Inter-group distribution of type of diagnosis

Diagnosis	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	n	%	n	%	
Hernia	15	50.0	15	50.0	0.999^{NS}
Appendicitis	15	50.0	15	50.0	
Total	**30**	**100.0**	**30**	**100.0**	

Values are n (% of cases), P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.

Inter-group distribution of type of diagnosis

Of 30 cases studied in Group 1, 15 (50.0%) had hernia and 15 (50.0%) had appendicitis. Of 30 cases studied in Group 2, 15 (50.0%) had hernia and 15 (50.0%) had appendicitis. The distribution of type of diagnosis among the cases studied did not differ significantly between two study groups (P-value>0.05).

Table 4: Inter-group comparison of mean weight, height and body mass index (BMI) of cases studied.

Parameter	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	Mean	SD	Mean	SD	
Weight (kg)	74.47	5.71	71.83	6.13	0.090^{NS}
Height (m)	1.71	0.03	1.72	0.06	0.671^{NS}
BMI (kg/m^2)	25.40	1.74	24.36	1.70	0.023*

Values are mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant. *P-value<0.05, NS-Statistically non-significant.

Inter-group comparison of mean weight, height and body mass index (BMI)

The mean ± SD of weight of cases studied in Group 1 and Group 2 was 74.47 ± 5.71 kg and 71.83 ± 6.13 kg respectively. Distribution of mean weight of cases studied did not differ significantly between two study groups (P-value>0.05).

The mean ± SD of height of cases studied in Group 1 and Group 2 was 1.71 ± 0.03 m and 1.72 ± 0.06 m respectively. Distribution of mean height of cases studied did not differ significantly between two study groups (P-value>0.05).

The mean ± SD of BMI of cases studied in Group 1 and Group 2 was 25.40 ± 1.74 kg/m^2 and 24.36 ± 1.70 kg/m^2 respectively. Distribution of mean BMI of cases studied is significantly higher in Group 1 compared to Group 2 (P-value<0.05).

Table 5: Inter-group distribution of co-morbidity

Co-morbidity	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	n	**%**	**n**	**%**	
No	30	100.0	30	100.0	0.999^{NS}
Yes	0	0.0	0	0.0	
Total	**30**	**100.0**	**30**	**100.0**	

Values are n (% of cases), P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.

Inter-group distribution of co-morbidity

Of 30 cases studied in Group 1, none had co-morbidity. Of 30 cases studied in Group 2, none had co-morbidity. The distribution of co-morbidity among the cases studied did not differ significantly between two study groups (P-value>0.05).

Table 6: Inter-group distribution of incidence of surgical site infection (SSI)

SSI	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	n	**%**	**n**	**%**	
No	29	96.7	25	76.7	0.050*
Yes	1	3.3	7	23.3	
Total	**30**	**100.0**	**30**	**100.0**	

Values are n (% of cases), P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. *P-value<0.05.

Inter-group distribution of incidence of surgical site infection (SSI)

Of 30 cases studied in Group 1, 29 (96.7%) had surgical site infection and 1 (3.3%) had surgical site infection. Of 30 cases studied in Group 2, 25 (76.7%) had surgical site infection and 7 (23.3%) had surgical site infection. The distribution of incidence of surgical site infection (SSI) among the cases studied is significantly higher in Group 2 () compared to Group 1 () (P-value<0.05).

Table 7: Inter-group distribution of incidence of surgical site infection (SSI) according to type of diagnosis

		Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
Diagnosis	SSI	n	%	n	%	
Hernia	No	14	93.3	12	80.0	0.598^{NS}
	Yes	1	6.7	3	20.0	
Appendicitis	No	15	100.0	11	73.3	0.100^{NS}
	Yes	0	0.0	4	26.7	

Values are n (% of cases), P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

Inter-group distribution of incidence of surgical site infection (SSI) according to type of diagnosis

Of 15 hernia cases studied in Group 1, 14 (93.3%) did not have surgical site infection (SSI) and 1 (6.7%) had surgical site infection (SSI). Of 15 hernia cases studied in Group 2, 12 (80.0%) did not have surgical site infection (SSI) and 3 (20.0%) had surgical site infection (SSI).

The distribution of incidence of surgical site infection (SSI) in hernia group among the cases studied did not differ significantly between two study groups (P-value>0.05).

Of 15 Appendicitis cases studied in Group 1, none had surgical site infection (SSI). Of 15 Appendicitis cases studied in Group 2, 11 (73.3%) did not have surgical site infection (SSI) and 4 (26.7%) had surgical site infection (SSI).

The distribution of incidence of surgical site infection (SSI) in appendicitis group among the cases studied did not differ significantly between two study groups (P-value>0.05).

Table 8: Inter-group distribution of length of hospital stay

Length of hospital stay	Group 1 [With Glutamine] (n=30)		Group 2 [Without Glutamine] (n=30)		P-value
	n	%	n	%	
≤7 days	26	86.7	21	70.0	0.209^{NS}
7 – 14 days	4	13.3	9	30.0	
Total	30	100.0	30	100.0	
Values are n (% of cases), P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.					

Inter-group distribution of length of hospital stay.
Of 30 cases studied in Group 1, 26 (86.7%) had length of hospital stay less than 7 days and 4 (13.3%) had length of hospital stay between 7 – 14 days.

Of 30 cases studied in Group 2, 21 (70.0%) had length of hospital stay less than 7 days and 9 (30.0%) had length of hospital stay between 7 – 14 days.

The distribution of length of hospital stay among the cases studied did not differ significantly between two study groups (P-value>0.05).

5. Discussion

The oral L- glutamine and wound healing has been studies on various conditions such as in gastrointestinal surgeries, major wounds and all complicated cases where it was found to be effective and essential to supplement for major post-operative cases. Though its effect on clean and clean contaminated wounds has not been studied fully and its importance of supplementation still remains a question. The use of L-glutamine for routine surgical cases may not seem essential and its utilization for the wound healing in completely healthy individual with no co-morbidities but the previous literature suggests its utilization increases as the Surgical Stress sets in. In our study, 30 patients of operated groin hernias and 30 patients of operated appendectomy with no co-morbidities were considered and 15 random patients of each group were taken as case and control for glutamine supplementation in post-operative period.

Studies have shown that, the incidence of inguinal hernias is 91% in men and 3% in women. [1] In our study, the incidence was similar with 96% of male and 3% of female inguinal hernia within the age group of 18 years to 55 years. As per the literature, The incidence of the same increases after the age of 45 years which is truly suggested by our study with 46% of the cases i.e. 14 out of 30 inguinal hernia cases were of the age more than 45 years.

In case of appendicitis, patients are more of younger age with age less than 30 years and it was noted that the incidence was around 30% in females (9 in 30 cases) as compared to 70% in males.

In a large community-based sample of middle-aged men overweight and obesity were associated with a lower risk for groin hernia during an extended follow-up. Obesity, in comparison with normal weight, reduced the risk of groin hernia by 43%. [2] In our study, we found that, only 8 patients out of 30 patients of inguinal hernia were overweight with BMI of 25 kg/m2- 30 kg/m2 . Also, we found that, there were no patients with BMI > 30 kg/m2.

In our study, it was found that the mean BMI of patients with glutamine and without glutamine was 25.40 ± 1.74 kg/m2 and 24.36 ± 1.70 kg/m2 respectively. Though, the Distribution of mean BMI of cases studied is significantly higher in Group 1 compared to Group 2 (P-value<0.05), none of our patients were underweight or malnourished.

14 out of 60 patients' LFTs were done which were completely normal suggesting normal metabolism and amino acid content. All patients were on vegetarian diet till the oral glutamine was given.

The effects of L-glutamine on wound healing has been studied by many scientists before but the studies on wound healing in clean and clean contaminated cases are very less.

None of my patients were co-morbid as co-morbidities can cause the changes in levels of amino acids in body. In a study done in 2011 in children with autism, The levels of glutamine was low. [3] proving any co-morbid condition can be a factor for change in levels of glutamine and other amino-acids.

In 2007, a study was conducted to look for association between obesity and incidence of appendicitis in children and it was found that Childhood obesity is associated with longer surgery and hospital stays and increased risk of postoperative infections. in our study, 10 out 30 cases i.e. 33% of cases with appendicitis were obese and rest of the cases were overweight showing no statistical significance with appendicitis and obesity in the given age group.

The effects of L-glutamine on wound healing has been studied by many scientists before but the studies on wound healing in clean and clean contaminated cases are very less.

In 1993, T. R. ZIEGLER*, R. J. SMITH*, T. A. BYRNEt and D. W. WILMORE, found out that the oral and parenteral glutamine was absorbed from the gut and was converted to other amino acids in normal individuals without any of the side effects on the systems. In our study, oral glutamine was given to 60 healthy individuals with no co-morbidities and none of the patients had any sort of reaction to glutamine.

Douglas Wilmore [4] did a meta-analysis and proved that the Patients receiving GLN were discharged an average of 4 days sooner than the control group. In our study, The distribution of length of hospital stay among the cases studied did not differ significantly between two study groups (P-value>0.05).

In 2011, Mohammad Jalilimanesh, Hassan Mozaffari-Khosravi, Maryam Azhdari, [5] et al studied the effect of oral glutamine on 2nd degree burns in 30 male mice, and the results were statistically significant for use of glutamine in wound healing. our study shows a statistically significant results with use of oral glutamine.

Sandra C. Blass et al [6] studied the time required to close the wound in patients with disorders of wound healing with supplementation of micronutrients and oralglutamine. They found that the time was significantly reduced in study group (who were supplemented by micronutrients and oral glutamine) than in control group. In our study, out of 30 cases studied in Group 1, 26 (86.7%) and of 30 cases studied in Group 2, 21 (70.0%) had length of hospital stay less than 7 days which was significantly less than the control group but not statastically significant.

6. Conclusion

The distribution of incidence of surgical site infection (SSI) among the cases studied is significantly higher in Group without glutamine compared to Group with glutamine. But The distribution of SSI in hernia group and in appendix group among the cases studied did not differ significantly in with each diagnosis. Also, the distribution of length of hospital stay among the cases studied did not differ significantly between two study groups as patients were discharged early in most cases and were followed up on OPD basis.

Thus, in our study, it is seen that the incidence of SSI in clean and clean contaminated cases is significantly less in the group with glutamine than without glutamine but it's significance in each group is less.

Hence, the oral glutamine in routine clean and clean contaminated cases can be used but it needs further evaluation in relation to diet and co-morbidities.

References

[1] Kingsnorth A, LeBlanc K. Hernias: inguinal and incisional. Lancet2003;362:1561-71.
[2] Rosemar, Anders MD*; Angerås, Ulf MD, PhD*; Rosengren, Annika MD, PhD† Body Mass Index and Groin Hernia:A 34-Year Follow-up Study in Swedish Men, Annals of Surgery: June 2008 - Volume 247 - Issue 6 - p 1064-1068doi: 10.1097/SLA.0b013e31816b4399
[3] C. Shimmura, S. Suda, K. J. Tsuchiya et al., "Alteration of plasma glutamate and glutamine levels in children with high-functioning autism," PLoS ONE, vol. 6, no. 10, Article ID e25340, 2011.
[4] Zhou YP, Jiang ZM, Sun YH, Wang XR, Ma EL, Wilmore D. The effect of supplemental enteral glutamine on plasma levels, gut function, and outcome in severe burns: a randomized, double-blind, controlled clinical trial. Journal of Parenteral and Enteral Nutrition. 2003 Jul;27 (4):241-5.
[5] Jalilimanesh M, Mozaffari-Khosravi H, Azhdari M. The effect of oral L-glutamine on thehealing of second-degree burns in mice. Wounds. 2011 Mar 1;23 (3):53.
[6] Blass SC, Goost H, Tolba RH, Stoffel-Wagner B, Kabir K, Burger C, Stehle P, EllingerS. Time to wound closure in trauma patients with disorders in wound healing isshortened by supplements containing antioxidant micronutrients and glutamine: aPRCT. Clinical nutrition. 2012 Aug 1;31 (4):469-75.