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General Surgery

ROLE OF GLUTAMINE SUPPLEMENTATION IN WOUND HEALING POST CORN EXCISION SURGERY

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ABSTRACT

Introduction: Wound healing is a complex phenomena and is affected by numerous factors, nutritional deficiencies being on of them. Glutamine is required at every stage of wound healing. We aimed to study the role of glutamine supplementation in wound healing in patients who presented to our hospital for corn excision surgery.

Methodology: 80 patients who visited our hospital for corn excision surgery were randomly assigned to either the group receiving glutamine supplementation (Group G) or the control group receiving normal diet (Group C). Pre- and post-treatment comparisons were made between the two groups using the Bates Jensen wound assessment tool.

Results: Baseline characteristics and mean wound appearance and depth scores of the patients in the two groups were similar. However, after the treatment, mean wound appearance score was significantly higher in the glutamine group (4.39 ± 0.18) as compared to the control treatment (3.61 ± 0.34). Similarly, there was a significantly higher wound depth score in the glutamine group as compared to control group (p value <0.05). Post-treatment, wound constriction was 1.75 ± 0.01 cm2 and 1.63 ± 0.03 cm2 in the glutamine and control group respectively (p value <0.05). Fibrinolysis time was significantly lower in patients in the glutamine group (298.20 ± 112.20 minutes) as compared to the control group patients (332.72 ± 82.31 minutes).

Conclusions: The results of this study demonstrate that glutamine supports and accelerates the wound healing and decrease chances of infections. Further studies are required to identify the optimal dose and duration which will benefit patients in wound healing.

KEYWORDS : glutamine, nutritional deficiency, wound

INTRODUCTION

Wound healing consists of a coordinated sequence of cellular and biochemical events that include coagulation, inflammation, formation of the extracellular matrix, fibrous tissue, epithelialization, wound contraction, and tissue remodeling.[1] There are various factors which influence wound healing. Local factors like blood supply, infection, foreign bodies and surgical technique influence wound healing. Systemic factors like age and gender, nutritional status, vitamins and trace element deficiencies, pharmacotherapy like steroids, chemotherapy, immunosuppressants, diseases like diabetes, jaundice, malignancy, hypoxia, also influences wound healing. Wound healing is closely related to nutritional status.[2] Normal processes of wound healing may be impeded due to nutritional deficiencies. Nutritional deficiencies may prolong the inflammatory phase, decrease proliferation of fibroblasts, and altering the synthesis of collagen fibres.[3] This will translate into decreased tensile strength of the wound upon repair and increased chance of infection.[4]

Glutamine provides two thirds of the free intracellular amino acid supply and one fifth of the total circulating free amino acid pool, making it the most abundant amino acid in the plasma.[5]Animal studies have demonstrated the potential of glutamine in wound healing.[6] Most of the studies about the role of glutamine in promoting wound healing has been from burn patients.[7] We aimed to study the role of glutamine supplementation in wound healing in patients who presented to our hospital for corn excision surgery.

METHODOLOGY

Trial Design

An interventional, prospective, open label randomized clinical trial.

Participants

Patients aged more than 18 years undergoing corn excision at the Department of Surgery, Bharti Hospital, Dhankawadi, Pune were included in the study. Patients were taken from inpatient wards or outpatient clinic from November 2015 till November 2017. Patients who are known to have pre existing congenital abnormalities leading to deranged healing process, who were known cases of medical renal diseases with deranged renal functions, with contraindications to glutamine due to their pre existing co-morbidities, or with bleeding disorders were excluded from the study. Approval from Institutional Ethical Committee was obtained and informed written consent was taken from all the patients enrolled after explaining study procedure, its potential benefits and side effects.

Intervention

All patients were randomly assigned to either the group receiving glutamaine supplementation (Group G) and the control group receiving routine nutrition (Group C). Group G received glutamine supplementation in the form of glutamine powder 500 mg eight hourly till they had complete the process of wound healing. Equal number of patients were assigned to the two groups i.e. 40 each.

Outcomes

Patients in both the groups received treatment for one month. Baseline data of the patients enrolled in the study was obtained from the patients themselves or their medical records. Information about age, gender, comorbidities and relevant laboratory investigations were obtained at the time of enrolment in the study. Bates-Jensen wound assessment tool was used to assess the patients before and after supplementation of glutamine (Table 1).[8] This tool assesses the patients on wound depth and appearance. Safety evaluations were done on every visit by asking patients about any adverse event related to medication.

Statistical methods

Using SPSS version 23 qualitative variables were compared using the chi square or Fisher's exact test and quantitative variables were compared using the student's t test. P value less than 0.05 was considered statistically significant.

RESULTS

Table 2 describes the baseline characteristics of patients included in the study. Approximately two thirds of all patients were in the age group 31 to 50 years in both the groups. There were 23 males in the glutamine

group and 22 in the control group. Diabetes mellitus was the most common comorbidity in the patients, followed by hypertension and smoking. All patients underwent biochemical investigations. The two study groups were not different significantly when the means levels of various biochemical investigations were compared. Using the Bates Jensen wound assessment tool, the two groups were compared pre- and post-treatment (Table 3). At baseline, the mean score of wound appearance was similar in the glutamine and control group (1.37 ± 0.03 and 1.41 ± 0.04 respectively, p value >0.05). However, after the treatment, mean wound appearance score was significantly higher in the glutamine group (4.39 ± 0.18) as compared to the control treatment (3.61 ± 0.34). Similarly, mean wound depth score was similar in both the patient groups at baseline (1.32 ± 0.03 and 1.39 ± 0.04 in glutamine and control group respectively, p value >0.05). After treatment, there was a significantly higher wound depth score in the glutamine group as compared to control group (p value <0.05). Post-treatment, wound constriction was 1.75 ± 0.01 cm^2 and 1.63 ± 0.03 cm^2 in the glutamine and control group respectively (p value <0.05). Fibrinolysis time was significantly lower in patients in the glutamine group (298.20 ± 112.20 minutes) as compared to the control group patients (332.72 ± 82.31 minutes). There were a total of 3 surgical site infections in the glutamate group; two were superficial and one was deep infection. In the control group patients a total of 9 surgical site infections were observed in the post-treatment group; five were superficial and four were deep infections.

DISCUSSION

Glutamine is the most abundant amino acid in the plasma and is a nitrogen donor for the amino acids synthesis. It is critical for the synthesis of nucleotides, required for gluconeogenesis which provides fuel during wound healing. Glutamine is also required for lymphocyte proliferation, thus playing a role in stimulating the inflammatory response during the inflammatory phase of wound healing. By improving nitrogen balance and enhancing immune function after trauma, and sepsis, supplementation with glutamine has been associated with good clinical outcomes in such patients.[9] Although, there are no standard guidelines based on clinical evidence which specifies safe dose of glutamine to promote healing of chronic wounds, some authors have suggested an adult dose of is 0.57 gm/kg/day of supplemental glutamine for wound healing.[10]

Sipahi et al examined the effect of four week treatment of beta-hydroxy-beta-methylbutyrate, arginine and glutamine supplementation on the wound healing using the Bates-Jensen scoring.[11] The authors observed significantly improved wound appearance and depth scores with treatment. Glutamine supplementation was tolerated well by the patients in their study and no side effect was observed. A double blinded randomized controlled study in which eternally administered glutamine dipeptide was administered to patients with severe burn injury was associated with faster wound healing at the end of 30 days.[12] Peng X et al observed that oral or tube fed glutamine granules to burn patients abated glutamine depletion, promoted protein synthesis, inhibited protein decomposition, improved wound healing and reduced hospital stay.[13] A systematic review of clinical trials studying the role of glutamine supplementation in critically ill patients observed reduced mortality and length of hospital stay.[14] A meta-analysis found that there was a significant reduction in infection among participants who received enteral glutamine in critical illness.[15]

Other amino acids has been shown to influence wound healing. Methionine is a cysteine precursor which stimulates fibroblast proliferation and synthesis of collagen which are necessary for wound healing. Another amino acid cysteine is a cofactor for enzyme which is required for formation of collagen. Lysine and proline are precursors of collagen and contribute to wound healing as well. However, no randomized clinical trials have been conducted which have evaluated the impact of these amino acids on wound healing.

CONCLUSION

Wound healing is a complex chain of biochemical events during which nutritional needs are significantly increased. The results of this study demonstrate that glutamine supports and accelerates the wound healing and decrease chances of infections. This study also highlights the importance of assessing patients with major trauma nutritionally and involving a trained nutritionist in the plan of management. Further studies are required to identify the optimal dose and duration which will benefit patients in wound healing.

Table 1. Bates Jensen wound assessment tool[8]

Wound depth score		Wound appearance score	
Necrotic	1	Necrotic	1
Deep	2	Scabbed	2
Moderate	3	Granulated	3
Easy	4	Epithelial	4
Minimal	5	Closed	5

Table 2. Baseline characteristics of patients with corn surgery included in the study

	Glutamine group (n=40)	Control group (n=40)
Age distribution [n(%)]		
15-30	2 (5%)	1 (2%)
31-50	26 (65%)	25 (63%)
51-75	12 (30%)	14 (35%)
Gender distribution [n(%)]		
Males	23 (57.5%)	22 (55%)
Females	17 (42.5%)	18 (45%)
Comorbidities/addiction [n(%)]		
Hypertension	05 (12.5%)	06 (15%)
Diabetes mellitus	09 (22.5%)	08 (20%)
Ischemic heart disease	02 (5%)	01 (2.5%)
Asthma	02 (5%)	02 (5%)
Smoking	06 (15%)	05 (12.5%)
Alcohol	03 (7.5%)	04 (10%)
Biochemical investigations (mean ± standard deviation)		
Fasting blood sugar (mg/dl)	89.82 ±12.12	91.02 ±13.16
Hemoglobin A1C (%)	6.10 ±1.09	6.12 ±1.13
C-reactive protein (mg/L)	8.90 ± 5.81	9.70 ± 7.8
Serum albumin (gm/dL)	4.0 ±0.3	4.1 ±0.2
Hemoglobin (gm%)	11.7± 2.0	11.5± 2.0
Total cholesterol (mg/dL)	154.51± 32.43	163.35 ± 34.66
Triglycerides (mg/dL)	190.65± 41.13	198.71 ± 45.91
Blood ammonia (µmol/L)	19.21± 8.14	20.23 ± 9.21

Table 3. Pre- and post- treatment comparison of patients in the two groups

	Pre-treatment		Post-treatment	
	Glutamine group	Control group	Glutamine group	Control group
Wound appearance [n(%)]				
Necrotic	23 (58%)	24 (60%)	2 (5%)	4 (10%)
Scabbed	12 (30%)	10 (25%)	4 (10%)	6 (15%)
Granulated	2 (5%)	3 (7.5%)	3 (7.5%)	16 (40%)
Epithelial	2 (5%)	1 (2%)	6 (15%)	10 (25%)
Closed	1 (2%)	2 (5%)	25 (63%)	14 35%)
Mean score	1.37 ± 0.03	1.41 ± 0.04	4.39 ± 0.18	3.61 ± 0.34
Wound depth [n(%)]				
Necrotic	24 (60%)	21 (53%)	0	3 (7.5%)
Deep	10 (25%)	9 (23%)	1 (2%)	5 (12.5%)
Moderate	3 (7.5%)	4 (10%)	2 (5%)	17 (43%)
Easy	3 (7.5%)	5 (12.5%)	9 (23%)	10 (25%)
Minimal	0	1 (2%)	28 (70%)	5 (12.5%)
Mean score	1.32 ± 0.03	1.39 ± 0.04	4.12 ± 0.12	3.29 ± 0.32
Wound constriction in cm2 (mean ± standard deviation)				
	--	--	1.75 ± 0.01	1.63 ± 0.03
Fibrinolysis time in minutes (mean ± standard deviation)				
	--	--	298.20 ± 112.20	332.72 ± 82.31
Surgical site infection [n(%)]				
Superficial	--	--	2 (5%)	5 (12.5%)
Deep	--	--	1 (2%)	4 (10%)

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