

Role of L-Glutamine, L-Alanine in Post Operative Recovery and Wound Healing

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Abstract: Wound-healing complications are a clinical problem with a considerable socioeconomic burden. Since several nutrients play a physiological role in wound healing, supplementation of these nutrients may improve wound healing. Under surgical stress, the metabolic demand for nutrients increases, which if not met may slow down or stop the wound from healing thus becoming chronic wound. This article directed to acknowledge the effect of L-ALANINE L-GLUTAMINE and other nutrient supplementation in post operative wound healing. This is a case study of 300 patients operated in Noble Hospital, Pune, Maharashtra, India. Cases were selected after taken well informed consents from patients. Patients were aware of the cost and period of treatment before starting the study.

Keywords: Glutamine, alanine, arginine, collagen deposition, growth factor, gut permeability, interleukin, re epithelisation, wound healing

Core Tip:

This Article highlights the role of amino acid supplementation like L-glutamine L-alanine arginine and hydroxymethyl butyrate for healthy wound healing. After reviewing related literature this article recommends use of micro supplements amino acid during post operative wound healing.

1. Introduction

Wound healing is a complex process that is planned over time by soluble mediators, blood cells, and parenchymal cells. ¹ Wound healing requires energy, protein, a variety of vitamins and trace elements, and certain amino acids. Normal wound healing consists of four phases: haemostasis, inflammation, proliferative and remodelling. During the proliferative phase, tissue granulation, epithelisation and collagen production occur. An increase in fibroblasts occurs during the proliferative phase in normal wound healing (the fibrotic index increases). Collagen production and release begin the third day and continue for 3 weeks. Collagens release from fibroblasts and their cross-linkage increases wound tensile strength. The amount and quality of collagen synthesis determine the wound tension strength, which is the mechanical integrity of the wound. The final phase of wound healing is the remodelling phase, which is characterised by the reorganisation of collagen fibrils and gradually increasing wound tension strength. There are many studies available that report the need for replacing amino acids such as glutamine (Gln), alanine, hydroxymethyl butyrate (HMB) and arginine (Arg) to increase wound healing.

Gln is a free, non-essential amino acid, which is found in substantial amount in the human body. Gln deposits decrease more than 50% and plasma levels decrease more than 25% and continue to be low for a long time, following catabolic events such as trauma, wound and sepsis.

The Arg is a semi-essential amino acid received with diet or which emerge as a result of endogenous catabolic reaction of citrulline. However, it becomes essential in critical patients and serious trauma.

HMB appears in the body as leucine metabolite 7.

Increase in the collagen amount in the wound area affects wound healing positively if there is no factor preventing the regular sequence of collagen fibres. Hydroxyproline (OHP) is an amino acid found in significant amounts in collagen structure and is used for determining the collagen of the tissue.

The primary objective of this article is to present the effects of Gln in wound healing.

For a normal wound healing, sufficient protein intake is essential because collagen synthesis is inhibited when insufficient protein is taken. Amino acids such as Gln, Ala and Arg are required for collagen synthesis. Biochemically, three principal amino acids in the structure of collagen are glycine, proline and OHP. A total of 99.8% of the total body OHP is found in the collagen molecule. These molecules are either received as a diet or synthesised in the body. They also have an essential role in sepsis and critical intensive care patients. Thus, for individuals who eat healthy food, deficiency of these molecules is not expected, with the exception of the serious factor like sepsis that can prevent the synthesis and intake of molecules with diet. However, daily protein intake at old ages should be higher because of the decrease in the ability of body for protein synthesis. Wound healing can be effected negatively in the presence of factors that increase collagen synthesis such as chronic malnutrition, diabetes mellitus, uraemia and advanced age or any other immune deficient state. Therefore, in such cases, to increase wound healing, the requirement for the replacement of molecules like Gln, Arg and HMB that increase collagen synthesis cannot be denied. The essential question to be answered is whether additional molecules containing Gln, Arg and HMB are necessary to increase wound healing in young patients, eating properly and without any additional disease, because these molecules required for collagen synthesis shall be sufficient in the

body. Because using preparations containing these molecules in patients eating healthy food to increase wound healing would bring additional treatment cost in clinical practice.

Sample Size

The study was performed in 300 patients in Noble Hospital, Pune.

Inclusion Criteria:

Age group of 20 to 70 years
Giving consent
IPD and OPD patient
Hb1c between 5.5 to 9.5

Exclusion Criteria:

Patient not willing for supplements
More than 70 years and children
Chronically bedridden patient
Chronic kidney disease and chronic liver disease

2. Method

This study was conducted over a period of 10 months from March 2022 to December 2022 on 300 patients attending OPD and IPD in Noble Hospital, Pune.

Patients were divided into two groups of 150 having equal number of male and female to eliminate gender bias and having similar age group to eliminate age bias on wound healing. 150 patients were given supplementation of glutamine and alanine with wound care during healing phase while another group of 150 patient were given equal quality of wound care without supplementation of glutamine alanine. Patients were followed up on OPD base. Results were obtained after 2 months.

3. Result

After follow up of 2 months for each patient it was found that from the study group 20/150 patient had secondary wound infection, 10/150 patient missed follow up. 9/150 patient underwent re-debridement.

From the control group 40 patients had secondary wound infection, 5 patient missed follow up. 32 patient underwent re-debridement.

From the study it was obtained that patients given glutamine alanine supplements had shorter wound healing period and lesser chance of wound related complications and patients of control group needed longer wound care and more chances of conversion into non healing wound and other wound related complications.

4. Review of Literature

From studies performed *in vitro* and with animals, it is well known that several nutrients are essential for wound healing. For example, retinol stimulates the proliferation and differentiation of epithelial cells and collagen synthesis. Ascorbic acid stabilizes collagen. Zinc is a cofactor of several

enzymes and a transcription factor of several genes that are involved in proliferation. Arginine provides metabolites that are indispensable for collagen formation, cell proliferation, and angiogenesis. Glutamine provides energy and DNA bases in rapidly proliferating cells. Hence, an increased intake of these nutrients by supplements may improve wound healing, thus being of interest in wound care.

Besides the presence of studies reporting that Gln replacement increases tissue OHP levels in the literature there are also studies reporting that it does not provide any contribution.

In the study performed by

Ozturk *et al.*

It was reported that preoperative enteral Gln replacement increased the tissue collagen amount in anastomosis line in rats to which colon anastomosis was performed. When it is considered that tissue OHP level decreased by 40% in the first 3 days in anastomosis line and anastomosis strength increased with the trophic effect on mucosa of Gln as the primary energy source of enterocytes in the study performed by Ozturk *et al.* the result showing that Gln replacement in addition to normal diet increased tissue OHP level was an expected result.

da Costa *et al*

it was reported that oral Gln replacement in preoperative and postoperative periods in rats to which colon anastomosis was performed increased collagen level in anastomosis line.

Gokpinar *et al.*

It was shown that tissue OHP level increased significantly in colon anastomosis applied rats in groups where early enteral feeding was performed. However, in the same study, it was shown that the addition of Gln to enteral nutrition did not have a significant contribution to tissue OHP level. This result showed that there is no need for additional Gln support to increase wound healing when sufficient nutritional support is provided.

It is seen that the studies found in literature, on the effects of Gln on tissue OHP levels, are performed mostly on colon anastomosis. While there are many studies available in the literature regarding the effects of Gln on tissue OHP level in colon anastomosis, studies regarding its effects on secondary dermal wounds caused by burns and tissue loss are considerably limited.

Jalilimanesh *et al.*

Gln replacement in the second-degree burns has a positive effect on wound healing. Considering that the model used in this study was burn and the degree of burn was serious, requirement for additional Gln support was inevitable. In this study, while approximately 1.75 cm² burns are created in mice, in our study secondary wounds are created in order to develop 2 cm² cutaneous and subcutaneous tissue loss in rats.

Seifter *et al*

Decrease in tissue OHP levels in rats fed with low Arg diet in perioperative period shows the requirement for sufficient amounts of Arg for wound healing. It is also reported that

HMB regulates protein turnover, decreases muscle breakdown and when combined with exercise increases muscle mass.

Williams *et al.*

Daily Gln, Arg and HMB administration to patients with deltoid implants increases collagen level. The study conducted by Williams *et al.* is performed on patients with ages 70 and above. It is a well-known fact that protein level to be taken with the diet should be higher in older patients because the ability of the body to synthesise protein and collagen decreases with increased age.

5. Conclusion

In conclusion, there should be sufficient amounts of Gln, Arg, Ala and HMB in the body for healthy wound healing. All these molecules are taken as part of a diet or are synthesised in the body. While wound healing is affected negatively in the absence of these molecules, there is no sufficient evidence to show that presence of excessive amounts of these molecules accelerates wound healing. In accordance with the data obtained from certain study, we consider that there is supplementation of Gln, Ala, Arg and HMB may accelerate the wound healing and decrease other wound related complications.

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