EFFECTS OF L-GLUTAMINE SUPPLEMENTATION ON REDUCING C-REACTIVE PROTEIN (CRP) LEVELS AND LENGTH OF STAY IN INTENSIVE CARE UNIT POST LAPAROTOMY

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ABSTRACT Backgrounds: Post-laparotomy ICU patients have an average length of stay in the ICU with an average of 7-14 days, depending on the procedure and postoperative complications. When the body is sick or injured, glutamine will become "conditionally-essential", which is a condition where a person needs additional food or supplements. Glutamine (Gln) has been shown to have an essential function for various organ systems, including the intestines, the immune system, and to maintain acid-base balance. C-reactive protein (CRP) is a sensitive inflammatory marker to assess non-specific inflammatory response, and there is an inverse relationship between Gln and CRP levels (r = -0.44, p < 0.05). Aims: L-Glutamin 20 gram intravenous per day for 3 days can reduce CRP levels and length of stay in ICU of the post-laparotomy patient. Method: This study used a double-blind, randomized clinical trial to compare a group with L-Gln supplementation and without L-Gln supplementation for laparotomy patients treated in the ICU from March to June 2021. Results: There were 40 patients divided into 2 groups. The statistical analysis results found the difference in CRP levels, p-value <0.001 and length of stay in ICU, p-value 0.011. Length of stay in the ICU of patients with high CRP was positively related with a significant correlation, r = 0.372 p = 0.018 Conclusion: L-Glutamin, 20 gram intravenous per day for 3 days, can reduce CRP levels and length of stay at ICU for post laparotomy patients.

KEYWORDS C-reactive protein, Glutamine, Intensive care unit, length of stay, laparotomy

Introduction

Laparotomy is a surgical procedure in the form of an incision of the abdominal wall or abdomen. [1] Characteristics of patients undergoing laparotomy surgery aged 15-75 years with a male to female ratio of 2:1. The most common aetiology is trauma with other concomitant conditions such as visceral and vascular damage. [2] Laparotomy can be performed in patients suffering from abdominal trauma with hemoperitoneum, gastrointestinal bleeding, acute abdominal pain, chronic abdominal pain, and if clinical conditions are found to be intra-abdominal requiring emergency surgery such as peritonitis, obstructive ileus and perforation. [3] Several main indications for laparotomy are intra-abdominal bleeding (39.0%) with a mortality rate of 75.6%, intestinal ischemia (24.4%) with a mortality rate of 80.5%, abdominal trauma (23.5%) with a mortality rate of 75.5%, intestinal obstruction 15.7% and diverticular disease 14.3%. [4]

The length of stay of patients in ICU undergoing laparotomy depends on postoperative complications. The treatment for postoperative patients varies, about 7-30 days, with an average length of stay in ICU of 7-14 days [4]. This is influenced by early mobilization after the postoperative wound healing process—research conducted in the ICU Prof. RSUP Dr RD Kandou
Glutamine (Gln) is a free amino acid, which is a precursor of protein synthesis, as well as a source of energy needed for immune and mucosal cells. [6] The chemical formula of glutamine is C5H10N2O2. L-glutamine is the most abundant amino acid in the bloodstream and constitutes 30-35 percent of the amino acid nitrogen in the blood. When the body is sick or injured, glutamine will become "conditionally-essential" which is a condition where a person needs additional food or supplements. [7] Glutamine is released in large amounts from skeletal muscle by acting as an important carrier and donor of nitrogen. Glutamine has been shown to have an important function in the function of various organ systems, including the intestines, the immune system, and to maintain acid-base balance. [8] The rationale for including glutamine in the diet regimen stems from the hypothesis that glutamine is an essential nutrient during illness. [9] Glutamine is synthesized by almost all tissues in the body, although only certain tissues (e.g. skeletal muscle, brain and lungs) are released into the circulation in significant amounts. Gln reduction was found in critically ill, postoperative, multi-traumatic, burns, sepsis, inflammatory bowel disease patients, prolonged fasting, and patients admitted to the intensive care unit (ICU). [9,10,11] although only certain tissues (e.g. skeletal muscle, brain and lungs) are released into the circulation in significant amounts. Gln reduction was found in critically ill, postoperative, multi-traumatic, burns, sepsis, inflammatory bowel disease patients, prolonged fasting, and patients admitted to the intensive care unit (ICU). [9,10,11]

C-reactive protein (CRP) is a sensitive inflammatory marker to assess the non-specific inflammatory response, which is mostly produced in the liver in response to increased levels of IL-1β, IL-6 and IL-8. Previous studies suggest an inverse relationship between Gln and CRP levels (r = -0.44, p < 0.05). [12] Administration of Gln is believed to reduce the length of stay in the hospital, duration of ICU observation, mortality, and other complications. Glutamine plays an important role in improving the systemic inflammatory response through mechanisms associated with accelerating the growth and proliferation of cells. [13,14,15]

Methods
This research is a double-blind, randomized clinical trial to compare obtained from post-laparotomy patients treated in the ICU Sanglah Hospital Denpasar from March-June 2021. In this case, L-Glutamin 20 gram intravenous per day was given for three days, and the control group did not give L-Gln supplementation.

The inclusion criteria in this study were: (1) All respondents in both groups were patients who were admitted to the ICU after laparotomy and fasting postoperatively for 3-5 days; (2) CRP levels were measured on day 4 for all respondents; (3) agreed to the informed consent. While the exclusion criteria in this study were: (1) respondents with liver disease, malignancy, and post-radiotherapy, (2) responses with anti-inflammatory drug therapies such as dexamethasone, prednisone, prednisolone or methylprednisolone. Data were analyzed using SPSS version 23 for windows.

Results
In this study, from 40 respondents to post-laparotomy ICU patients, samples of subjects met the eligibility criteria, 20 patients were included in the case group given L-Gln supplementation 20 g IV / day for 3 days, and 20 patients were not given L-Gln.

The sample characteristics in this study include gender, age, Body Mass Index, CRP level, and length of stay in ICU at table 1.

In this study, a person correlation test was conducted between CRP and length of stay in ICU. It was found that there was a positive relationship with a significant correlation with r = 0.372 with p = 0.018.

Discussion
In this study, a total of 40 samples of female patients resulted in 23 (57.5%) and 17 males (42.5%); this result is the same as emergency laparotomy audits, which were mostly in the case of women 20,990 (52%) and men 18,740 (48), %. The causes of emergency laparotomy include cases of torsion of an ovarian cyst (24.5%), acute peritonitis (14.5%), bowel obstruction (7.9%), cholecystitis (7.2%), ectopic pregnancy (0.7%), intestinal obstruction (7.2%), abdominal wall abscess (0.7%). [16] There was no significant difference between the two groups (p-value < 0.05). In the age results, it was found that the age in the group with L-Gln administration Mean Age±SD (48.30±6.14) and in the group without L-Gln administration was 47.30±6.76, with p = 0.627, which means that the two groups are not different. These results are the same as plasma glutamine studies in intensive care obtained at age 47.4 ± 16.6 [12] and in the South African
Table 1 Characteristics of Research Subjects

| Demographic Profile | Patients post laparotomy with L-Gln 20 g IV / day for 3 days (20 Subjects) n (%) | Patients post laparotomy (20 Subjects) n (%) | p* |
|---------------------|--------------------------------------------------------------------------------|-------------------------------------------|----|
| Gender              |                                                                                   |                                           |    |
| • Male              | 9 (45)                                                                              | 8 (40)                                   | 0.757 |
| • women             | 11 (55)                                                                             | 12 (60)                                  |    |
| Mean Age ± SD (years) | 47.30 ± 6.14                                                                       | 48.30 ± 6.76                             | 0.627 |
| Body Mass Index (kg/m²) | 22.57 ± 2.25                                                                        | 22.62 ± 2.42                             | 0.952 |
| CRP (mg/L)         | 7.55 ± 4.87                                                                         | 16.95 ± 6.94                             | < 0.001† |
| Length of stay in ICU (days) | 6.64 ± 1.31                                                                         | 9.45 ± 2.72                              | 0.011† |

*Independent sample t-test significant

The duration in the ICU for patients with high CRP was positively related with a significant correlation, r = 0.372, p = 0.018, which means that length of stay in ICU will be longer when the CRP value is higher. It can be concluded from the results of this study that the administration of L-Glutamin 20 gram intravenous per day for 3 days can reduce the duration of patients by 2.81 ± 1.41 days. This is following the study by Gülcher in 2016 that showed the duration of stay in ICU was 9 (6-16) days for the patients with high CRP value (≥ 10 mg/L). CRP can be used as a marker of adverse risk factors 1.69 (95% CI 1.14-2.50; P 0.009). [20]

The weakness of this study is the short duration of the study. In addition, this study used subjects in certain populations in certain places; hence, this study’s results cannot describe the same conditions in different populations and places. Further research is needed to improve this study’s results using a larger sample size involving various types of cancer and using cohort research methods.

Conclusion

Giving L-Gln 20 g IV / day for 3 days can reduce CRP levels by p < 0.001 and reduce the length of stay in the ICU with p = 0.011, thereby increasing the recovery rate of post-laparotomy patients who require fasting conditions. Further research is needed to analyze the association of CRP, another infection/inflammatory marker, with L-Gln supplementation in patients with a statistically critical condition. However, the results can be used for the well-being of patients in the future.

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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