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The effect of ascorbic acid on leukocyte reduction in burns injury patient: A short communication

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ABSTRACT

Introduction: Challenges in managing burn injury include a high risk of sepsis and mortality. The study aimed to determine the effect of ascorbic acid on leukocyte reduction in burns injury patients.
Methods: The design of this study was a case series reported using retrospectives. Data collection was carried out from January to December 2020. All participants were diagnosed with burn injuries. Participants received burn wound care with and without ascorbic acid or Vitamin C (Vit. C). Participants measured leukocyte levels on the first and fifth days.
Result: The mean age of the participants was 32.08 ± 17.78 years, of which most of the participants were men (59.38%) with an average age of 35.21 ± 13.45 years, while the average age in women was 27.51 ± 22.52 years old. The mean TBSA of participants was 34.20 ± 21.21%, of which the mean TBSA for males was 39.45 ± 20.01% and for females 26.54 ± 21.32%. The mean participant leukocyte value on the first day was 21.49 ± 9.55 × 103/µL and on the fifth day, it was 11.26 ± 3.86 × 103/µL (z = -4.507; p <0.001). There was a significant difference in the leukocyte participant values on days 1 and 5 of -10.23 ± 9.77 × 103/µL (t = -2.504; p = 0.018).
Conclusion: Use of Vit. C in the management of burn injury has been shown to significantly reduce the number of leukocytes on the fifth day and reduce the risk of sepsis and mortality.

Keywords: Ascorbic acid, burns injury, leukocyte level, vitamin C, wound care.
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INTRODUCTION

Burns are a significant cause of morbidity and mortality worldwide. Burns can cause lifelong injuries and have severe psychological and economic impacts.[1] Burns can occur from various sources. Hot objects, electricity, and chemicals are the most common sources that cause individual burns. The severity of injuries associated with burns varies greatly, which can be demonstrated by a trend of increasing morbidity and mortality with increasing burn surface area. It is crucial to classify burns accurately, as it can help determine the outcome, as well as guide initial treatment. The skin area, degree of temperature, and duration are factors that cause the severity of the burn.[2]

Severe burns cause a local inflammatory response and a systemic inflammatory response.[3] Several systemic reactions from burns include increased capillary permeability, bronchospasm, decreased heart muscle contractility, contraction of peripheral and visceral vessels, and increased metabolism up to three times the original level. Non-specific down regulating immune response mechanisms can affect cellular and humoral pathways. The immune response initiates pro-inflammatory and anti-inflammatory phases, simultaneously or sequentially, to maintain homeostasis and normal physiology. Thermal damage causes 80% of the leukocyte transcriptome to change, stimulating innate genes (pro-inflammatory and anti-inflammatory) and suppressing the adaptive immune response. Neutrophil dysfunction, shedding of immature granulocytes, and reduced numbers and impaired expression of CD14+/HLA-DR+ monocytes have also been observed. In contrast, up to 3 years after burn injury, there may be a simultaneous increase in the levels of granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin 10 (IL-10) and other cytokines.[4]

The management of burn wounds is often faced with many challenges, including acute and critical management, long-term management, and rehabilitation.[5,6] The management of burns must affect the intensity of the pro-inflammatory and anti-inflammatory responses. However, the main goal of management is to reduce inflammation and improve the patient's prognosis. Therapies that focus on blocking specific cytokines such as IL-1, TNF or IL-6 have been considered ineffective. For this reason, the focus is on other strategies to reduce inflammation and hypermetabolism associated with burns. One option to improve clinical outcomes is supplementation with antioxidants (e.g., ascorbic acid, glutathione, acetylcysteine, or vitamins A, E, and D).[4,7]

Ascorbic acid or vitamin C (Vit. C) is important in treating critically ill patients.[8] Vit. C is vital for tissue regeneration due to its role in collagen formation and antioxidant properties.[9] Vitamin C is a well-documented antioxidant that reduces oxidative stress and high doses of fluid infusion.[10] Burn patients are at high risk of developing sepsis, the leading cause of death for burn patients. In burn injury patients, the circulation of ascorbic acid is deficient, so the administration of Vit. C helps minimize the effects of injury due

to free radicals.[11] Based on the description above, this study aimed to report 32 cases of burns injuries with and without Vit. C administered.

METHODS

The design of this study is a retrospective study reported, and data collection was carried out from January to December 2020 at the hospital. Participants in this study were burn injury patients which collecting data was based on preferred reporting of case series in surgery (PROCESS) 2020 guidelines.[12] Calculating the area of burns to injury participants uses the total body surface area (TBSA) based on the Lund and Browder diagram.[5] Inclusion criteria include all participants with burn injury diagnosis and exclusion criteria include death and treatment decline. Participants received a wound care procedure with and without ascorbic acid (Vit. C), which Vit. C dose of 500 mg/day. Participants were examined for leukocyte levels on the first and fifth days. Based on wound clinical, participants get burns wound care in the surgery room.[13,14] This research has been ethically approved by health research ethics committee in the Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (ethic number of 1265/LOE/301.4.2/III/2023).

Data analysis used paired t-test, Wilcoxon, and Independence t-test to determine the effect of ascorbic acid (Vit. C) on leukocyte reduction in burns injuries patients. Before carrying out statistical tests, the data was subjected to the Shapiro-Wilk test for data distribution. Analysis used the statistical package for the social sciences (SPSS) 25.0 version (IBM Corp., Armonk, NY, USA) software which was declared significant if the p-value <0.05.

RESULTS

The mean age of participants was 32.08 ± 17.78 years, with a median of 30.5 (19.75 – 47.00) years. The youngest participant is 8 months old and the oldest participant is 63 years old. Most participants were male (59.38%) with an average age of 35.21 ± 13.45 years, while the average age in females was 27.51 ± 22.52 years old. Most

Table 1. Characteristic of burn injuries

Participant	Age	Sex	TBSA	Caused	Vit. C	Leukocyte	
						First day	Fifth day
1	3	F	5.00	Scald	No	13.20	5.33
2	35	M	55.00	Fire	No	17.00	14.00
3	25	F	30.00	Fire	No	31.40	13.58
4	53	M	39.50	Fire	No	20.26	15.67
5	18	F	8.00	Fire	No	13.00	14.70
6	30	M	49.50	Fire	No	12.91	13.20
7	27	M	3.00	EIHV	No	16.70	19.30
8	25	M	49.50	Fire	Yes	23.07	8.20
9	19	M	58.50	Fire	No	15.50	11.10
10	31	M	25.00	Fire	No	12.52	8.04
11	27	F	27.00	Fire	No	21.97	6.50
12	6.67	F	7.00	Scald	No	14.60	10.48
13	17	M	56.50	Fire	No	17.20	10.00
14	31	M	62.00	Fire	No	30.51	10.56
15	20	F	65.00	Fire	No	33.95	16.25
16	51	M	65.50	Fire	No	24.00	11.55
17	56	M	63.50	Fire	Yes	13.20	9.55
18	59	M	56.50	Fire	Yes	18.90	6.53
19	63	F	70.00	Fire	Yes	21.70	6.41
20	4	F	15.50	Scald	Yes	25.00	12:03
21	2	F	17.50	Scald	Yes	22.26	7.06
22	47	M	37.50	Scald	Yes	23.60	13.40
23	50	F	7.00	Hot metal	No	8.80	14.40
24	36	F	20.00	Hot liquid	Yes	13.40	8.45
25	47	F	31.00	Hot liquid	Yes	44.95	12.15
26	45	M	39.00	Scald	Yes	39.00	6.20
27	62	F	42.00	Scald	Yes	47.63	15.32
28	17	M	27.00	Fire	Yes	14.37	5.04
29	28	M	10.00	Fire	Yes	15.59	10.09
30	44	M	16.00	EIHV	Yes	27.22	13.90
31	23	M	17.00	Fire	Yes	13.69	11.93
32	31	M	20.00	EIHV	No	20.60	19.32

EIHV: Injury high voltage; F: Female; M: Male; TBS: Total body surface area; Vit.C : Vitamin C.

participants experienced burns injuries caused by fire (56.25%). The mean TBSA participants was 34.20 ± 21.21% with a median of 30.50 (16.75 – 55.38) %, while the mean TBSA in males was 39.45 ± 20.01% and in women was 26.54 ± 21.32%. As many as 46.88% of the participants received ascorbic acid (Vit. C), 47.37% for men and 46.15% for women (Table 1). Some descriptions of burns can be seen in Figure 1.

The mean participant leukocyte value on the first day was 21.49 ± 9.55 × 103/µL and on the fifth day it was 11.26 ± 3.86 × 103/µL (z = -4.507; p <0.001). In women, the leukocyte participant value on the first day was 23.99 ± 12.36 × 103/µL and on the fifth day, it was 10.97 ± 3.83 × 103/µL (t = -4.118; p = 0.001). Whereas in men, the leukocyte participant value on the first day was 19.78 ± 6.89 × 103/µL and on the fifth day, it was 11.45 ± 3.98 × 103/µL (z = -3.622; p <0.001). There was a significant difference in the leukocyte participant values on days 1 and 5 of -10.23 ± 9.77 × 103/µL (t = -2.504; p = 0.018; Figure 1). In women, there was no significant difference between leukocyte values on days 1 and 5 of -13.02 ± 11.40 (t = -1.911; p = 0.082). Meanwhile, in men there was also no significant difference between leukocyte values on days 1 and 5 of -8.33 ± 8.27 (t = -1.682; p = 0.111).

Figure 1. Burns caused by (A) fire, (B) hot liquid, and (C) electricity

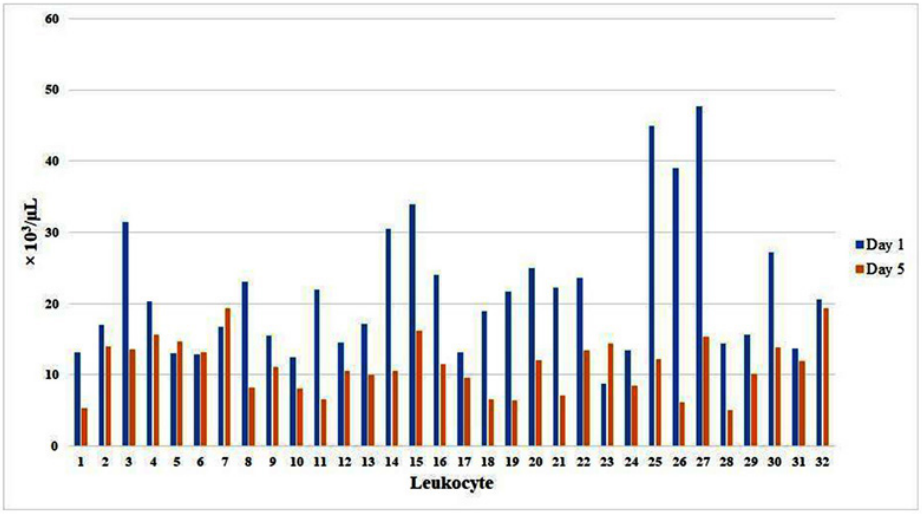

Figure 2. Comparison of participant leukocyte values on the first and fifth days (t = -2.504; p = 0.018)

DISCUSSION

Men experience most patients with burns. This can be caused because men more often do most jobs or hobbies involving exposure to heat or fire and it can increase the risk of burns in men. Such work is like work in an industry or factory that involves the use of tools and machines that generate heat or fire, such as workers in steel factories or petrochemical factories, firefighters who carry out rescue and fire fighting tasks, and workers in the construction or civil engineering involved in the use of heavy equipment, such as welding or metal cutting.[15,16]

They were giving Vit. C can enhance the immune response through several pathways. First, Vit. C enhances chemotaxis, stimulates interferon production, increases motility, neutrophil phagocytic capacity and oxidative killing, and supports lymphocyte proliferation. On the other hand, Vit. C. deficiency is associated with impaired cellular immunity. For example, cytotoxic T responses, natural killer activity, and bacterial clearance are suppressed. Vit. C as an antioxidant, is better than other antioxidants in burn wounds.[11] Vit. C affects all phases of wound healing, such as the inflammatory phase, proliferative phase, and collagen maturation, synthesis, and degradation. Synthesis, maturation and stabilization of collagen are also the roles of Vit. C. In addition, Vit. C is also responsible for the migration of neutrophils to the injury site and plays a role in clotting when the skin is exposed.[17] Vit. C (66 mg/kg/hour) administered to burn patients (>20% TBSA) can reduce overall resuscitation fluid requirements in the first 24 hours by approximately 25%. In addition, urinary production of ascorbic acid groups increased, causing decreased fluid balance and side effects such as increased risk of renal failure was not found.[18]

Vit. C can stimulate the production and support the optimal function of leukocytes (white blood cells), especially neutrophils, lymphocytes and phagocytes. Function of Vit. C is specific to leukocytes such as cellular motility, chemotaxis and phagocytosis. The capabilities of Vit. C mediates these functions, in which to increase neutrophil movement in response to chemoattractant (chemotaxis), increase microbial phagocytosis and stimulate the production of reactive oxygen species (ROS) for microbial destruction. Vit. C is also thought to be involved in the proliferation and differentiation of B and

T lymphocytes. Protective antioxidant properties of Vit. C mainly support leukocytes. Accumulated concentration of Vit. Large amounts of C into neutrophils, especially after an oxidative burst, are thought to protect neutrophils. Based on previous studies, Vit. C can reduce the generation of oxidants and activation of the pro-inflammatory transcription factor nuclear factor κB (NFkB) in neutrophils. Vit. C also demonstrated the ability to attenuate IL-4 secretion and increase IFN-γ secretion. In addition, Vit. C can attenuate microglial activation, consequently reducing the synthesis of pro-inflammatory cytokines.[19]

The limitation of this study is the small number of participants due to the rare incidence of burn injuries. Future study is expected to relate nutritional intake to the wound-healing process in burn injury patients.

CONCLUSION

Burn injury patients are experienced by many adult men, and this condition is influenced by work and hobbies. Burn injuries are also at risk for infection, characterized by an increase in leukocytes, which can progress to sepsis and increase the risk of mortality. Administration of ascorbic acid (Vit. C) has been shown to significantly reduce the number of leukocytes in burn injury patients on the fifth day.

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CONFLICT OF INTEREST

All authors declare that they have no conflict of interest.

ETHICAL STATEMENT

Ethical approval for this study (1265/LOE/301.4.2/III/2023) was provided by the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia on March 24 2023.

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AUTHOR CONTRIBUTION

MIW responsible for data collection, data analysis, study design, writing, and revising; IDS responsible for supervision, visualization, methodology, and review; ASB responsible for conceptualization, supervision, and review.

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