Research Article

Effect of N-acetylcysteine on wound healing in burned patients

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Abstract

Background: The magnitude of free radical generation and their disposal mechanisms are known to be altered in burn; and there is some kind of correlation exists between altered free radical cascades and delay wound healing. **Aims:** Exploration of the variable effect of N-acetylcysteine on Wound Healing in Burned Patients. **Methods:** 60 burned patients with different ages of both sexes and varying burn percentage were involved in this study. Patients allocated into 2 groups: A, B each group include 30 patients. Groups: B treated with antioxidant N-acetylcysteine, compared with group A which is treated according to hospital policy without antioxidant; also 30 healthy subjects (group C) were involved in the study as control group for comparison.To each group, serum malondialdehyde and serum glutathione levels, microbiological examination, healing time and mortality rate were measured depending on standard methods. **Results:** Administration of N-acetylcysteine to burned patients produce significant reduction in the wound healing time and improvement in mortality rate, compared to group A, where no antioxidant was given. **Conclusions:** This study clearly showed the beneficial effect of N-acetylcysteine in the treatment of burned patients represented by shortening of healing time, in addition to reduction in hospitalization period; it is recommended to add antioxidant to the treatment list of burned patients.

Key Words: Burn, Antioxidants, N-acetylcysteine, Oxidative stress, wound healing.

INTRODUCTION

Burn is a common traumatic injury that results in both local tissue damage and a systemic mediator induced response; there is evidence of both local and systemic oxidant changes manifested by increased oxygen free radical activity and lipid peroxidation in animal burn models and also in burned humans. It has been reported that both oxygen free radicals and lipid peroxidation play a major role in the injuries caused by skin burns.[1]

While a major source of ROS in burn trauma is XO, adherent and activated neutrophils produce a burst of free radicals. In addition to that, while burn trauma up regulates free radical production, this type of traumatic injury also impairs antioxidant defense mechanisms, rendering the burn subject more susceptible to ROS mediated injury. Furthermore, it has been reported that ROS contribute in part to burn mediated immune suppression; and use of antioxidants have a positive effect on immune function, that may reduce incidence of wound infection and related complications.[2]

In addition to that, free radicals and their scavenging systems are known to play a very important role in healing of normal and delayed healing types of wounds.

[3] The magnitude of free radical generation and their disposal mechanisms are known to be altered in burn; and there is some kind of correlation exists between altered free radical cascades and delay wound healing. It has been shown that low levels of antioxidants accompanied by raised levels of markers of free radical damage play a significant role in delaying wound healing.[4]

Further, ROS produced in response to cutaneous injury, impede the healing process by causing damage to cellular membranes, DNA, proteins, and lipids, and that antioxidants have been shown to promote wound healing. [5] Moreover, Dissemond et al. showed that when ROS are overproduced, oxidative stress results with detrimental cytotoxic effects causing delayed wound healing, therefore, elimination of ROS could be an important strategy to improve healing of wounds.[6] Many trial conducted utilizing administration of antioxidants both systemically and locally have been used to improve wound healing in burned patients; in this study the choice occur on using N – acetylcysteine (NAC), aiming to accelerate healing process of the burn wound that may improve burn outcome in general.

N – acetylcysteine (NAC) is a drug historically used as a mucolytic agent, also indicated in paracetamol overdose to prevent hepatotoxicity.[7] NAC is rapidly absorbed following an oral dose. After absorption, NAC is rapidly metabolized to cysteine, which is a direct precursor in the synthesis of intracellular GSH. In this way it acts as an antioxidant by restoring the pool of intracellular reduced glutathione, which is often depleted as a consequence of increased status of oxidative stress.[8] NAC also has reducing and antioxidant properties by acting as a direct scavenger of free radicals such as OH •, H2O2, and $O2^{\bullet -}$. [9] As a direct consequence of its antioxidant and SH donating properties, NAC restores cellular redox status and can in this way modulate the activity of redox-sensitive cell signaling and transcription pathways such as the nuclear factor – κB which regulates a variety of pro inflammatory genes.[10]

MATERIALS AND METHODS

This study was carried out on (60) burned patients of both sexes, with age range 20 – 45 years, and varying burn percentage 15- 40% total body surface area TBSA, estimated according to the rule of nine.

Burned patients were allocated into 6 groups and treated as follow: 1-Group A (30) Patients, this group already present in the burn unit and treated according to the hospital policy, where no antioxidant was given.

2-Group B (30) Patients, treated with 500 mg /day N-acetylcysteine capsule.

3-Group C (30) healthy subjects, with the same age range as that of patients were selected to serve as control for comparison.

All the treated groups take their drugs prescribed according to hospital drug policy including topical antimicrobial agent, where Silver sulfadiazine 1% cream was used in this study.

Blood samples were collected from all subjects by venepuncture. Ten milliliters were taken on admission to the burn unit within the first 24 hrs post burn, and before starting drug treatment, which considered (zero time), and then at days 3,7,14, and at discharge day, to check the changes in the studied parameters.

Serum malondialdehyde MDA levels were measured according to the standard method of Stocks and Dormandy[11], which is modified by Gilbert et al.[12]. Serum glutathione level measured according to the method of Godin et al.[13]

Statistical analysis

Student t-test and ANOVA test were used to examine the degree of significance, P value less than 0.05 considered significant; the results were expressed as mean ± standard deviation SD.

RESULTS

Results in table (1) showed that serum MDA levels were significantly P> 0.05 increased at zero time in burned patients when compared with control; in group A where no antioxidant used, serum MDA level non- significantly decreased at day 3, 7 and 14 compared with zero time, but at discharge day serum MDA level significantly decreased by 61.37% compared to zero time but this result still significantly higher than control (group C). Results in group B show significant reduction in serum MDA level at day 3 compared to zero time; in addition to that serum MDA level significantly reduced at discharge day compared to zero time and group A (no antioxidant).

In case of serum glutathione, table (1) showed that serum GSH levels significantly reduced in burned patients at zero time compared to healthy subjects; in group A serum GSH level remained significantly lower than control till discharge day , while in group B serum GSH level significantly increase at discharge day compared to zero time. Table (2) showed that mortality rate reduced from 20% in group A to 0% in group B and. Table (2) showed also that in group A, healing time represented as mean ± SD was 20 ± 2.4 days, which reduced in group B to only 9 ± 1.6 days.

Table 1. Effects of N-acetylcysteine on serum malondialdehyde (MDA) and serum glutathione (GSH) in burned patients.

Parameters	Timing	Groups		
		A	B	C
Serum MDA nmol/ml	Zero time	5.54± 0.34 [b]	6.2± 1.12 [b]	0.81± 0.16 [a]
	Day 3	4.6± 0.21 [b]	1.8± 0.8 [c]	0.82± 0.15 [a]
	Day 7	3.75± 0.31 [c]	1.1± 0.7 [c]	0.77± 0.2 [a]
	Day 14	3.33± 0.42 [b]	*	0.8± 0.19 [a]
	Discharge day	2.12± 0.25 [c]	0.8± 0.2 [d]	0.82± 0.17 [a]
Serum GSH µmol/l	Zero time	0.07± 0.01 [b]	0.06± 0.01 [b]	0.24± 0.04 [a]
	Day 3	0.085±0.02 [b]	0.21± 0.04 [c]	0.21± 0.09 [a]
	Day 7	0.08± 0.01 [b]	0.29± 0.01 [c]	0.23± 0.1 [a]
	Day 14	0.09± 0.02 [b]	*	0.26± 0.11 [a]
	Discharge day	0.11± 0.02 [b]	0.32±0.03 [d]	0.22±0.05 [a]

•A: no antioxidant, B: N-acetylcysteine, C: healthy subjects.
•Results represent mean ± SD.
•Results with non-identical superscripts (a, b, c, and d) were considered significantly different (P<0.05).
*Discharge day for group A is more than 3 weeks, and for group B is less than 2 weeks.

Table 2. Effects of N-acetylcysteine on mortality rate and healing time in burned patients.

Groups	No.	Mortality rate*	Healing time** (days)
A	30	6 (20%)	20±2.4
B	30	0 (0%)	9±1.6
C	30	-	-

A: *no antioxidant*, B: *N-acetylcysteine*, C: *healthy subjects*.
*Results represent percentage of total.
**Results represent mean ± Standard deviation.

DISCUSSION

Thermal injury of the skin is an oxidation process, associated with biological and metabolic alterations; thermal injury generates free radicals from various cellular populations through many pathways; and the modulation of generated free radical activity with antioxidants seems to be an important part in pharmacological treatment of burn.[14] In burned patients alterations in antioxidant micronutrients status and endogenous antioxidants defenses against deleterious effects of free radicals seems crucial as pointed out by recent studies[1,2]. Data reported by Cetinkale[15] et al., demonstrated that in addition to loss of plasma antioxidants like vitamin E and sulfhydryl groups in patients with burns, vitamin C diminished early post-burn.

Concerning the antioxidant effect of N-acetylcysteine, it has been shown that NAC act as a source of sulfhydryl groups and facilitate GSH synthesis, also it is a direct scavenger for ROS. [16]

It is clear that data obtained in this study regarding reduction of MDA serum level and elevation of serum GSH level – the natural antioxidant – in burned patients are compatible with the results obtained by others as mentioned above.

It has been reported that infection is one of the most important causes of systemic inflammatory response syndrome (SIRS) developed in burned patients[17]; in addition to that, the etiology of multiple organ dysfunction syndrome (MODS), was thought to be due to uncontrolled infection, and source of infection control was considered the major therapeutic aim,[18] since it

may develop further into progressive organ failure and death[19].

Moreover, it has been found that oxidative stress plays an important role both in the activation of the inflammatory response and in tissue damage that result in systemic inflammatory response syndrome SIRS the leading cause of multiple organ dysfunction syndrome MODS, several antioxidant substances have been proposed as treatment in SIRS; It has been shown that, antioxidants, given postburn restored antioxidant defenses, and prevents mortality[20]; where results obtained in this study were compatible.

In conclusion, results obtained in this study showed the beneficial effect of N-acetylcysteine in the treatment of burned patients as represented by reduction in healing time and improvement in mortality rate compared with other patients treated classically according to hospital policy without the addition of antioxidant to treatment list.

Conflict of interest: none

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