

DYSLIPIDEMIA AFTER BURN INJURY: A POTENTIAL THERAPEUTIC TARGET

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ABSTRACT

Background: Thermal injury can cause many changes in the skin-local response- and in the body in general –systemic response- ; the metabolic changes represent an important one among systemic response. Dyslipidemia after burn injury is one of the important alterations that resulted from many factors like hypermetabolic state in burn, release of hormones and inflammatory mediators, the aim of this study is to evaluate the occurrence of dyslipidemia after burn injury, and the evaluation of possible targeting of these changes in burned patients aiming to improve burn management and outcomes

Patients and Methods: This study was carried out on 96 burned patients with different ages of both sexes and varying burn percentage group A, compared with group B which is 18 normal healthy subjects utilized for comparison. To each group, serum cholesterol, serum triglyceride and serum high density lipoprotein cholesterol levels, were measured depending on standard methods.

Results: Results of this study show the occurrence of changes in serum lipids of burned patients namely decrease in serum cholesterol level, increase in serum TG level and decrease in serum HDL level compared to normal subjects.

Conclusion: This study clearly showed the beneficial role of measuring serum cholesterol, TG and HDL in burned patients, also show the importance of targeting changes that occur in their levels along burn course which may have beneficial effect through protecting organ damage and lead to increase survival rates among burn subjects and improve burn outcome.

Key words: Burn, Dyslipidemia, serum lipids.

INTRODUCTION

An improved understanding of burn pathophysiology has contributed to improvement in fluid resuscitation, infection control, support of hypermetabolic response to trauma, nutritional support and early closure of the burn wound, and burn outcome in general ¹.

Thermal injury can cause many changes in the skin-local response- and in the body in general –systemic response- ; the metabolic changes represent an important one among systemic response ². The degree of metabolic changes experienced by burn patients is directly related to the extent of injury. In large burn injuries, cortisol, glucagon, and catecholamines are markedly elevated ³.

Cortisol is strongly catabolic and is associated with negative nitrogen and calcium balance, loss of tissue protein and bone mineral. It also stimulates gluconeogenesis, increase proteolysis and sensitizes adipocytes to the action of lipolytic hormones. Catecholamines increase the rate of glycogenolysis, hepatic gluconeogenesis, promote lipolysis and peripheral insulin resistance ⁴.

These changes lead to release of amino acids from muscles, and lipolysis of adipose triglycerides leading to the release of fatty acids into the plasma. The free fatty acids can be used directly by most peripheral tissues for their energy requirements ⁵. In burn patients, fat oxidation is increased to obtain endogenous energy substrates. In addition to that, there is increase recycling of fatty acids that lead to increase in triglyceride plasma level. Coombes *etal* documented an increase in triglyceride level and a fall of serum cholesterol level following severe burn injury ⁶. Brike *etal* demonstrated that the cholesterol level fell gradually after thermal injury and that these changes were proportional to the extent of burn trauma ⁷.

The present study was performed in order to evaluate the occurrence of dyslipidemia after burn injury, and the evaluation of possible targeting of these changes in burned patients to be considering one of the steps in improving burn management and outcomes.

Patients and Methods:

This study was carried out on 96 burned patients of both sexes, with age range of 18-45 years, table (1), and varying burn percentage 25-

70% of total body surface area (TBSA), estimated according to the rule of nine; consent was taken from each patient when admitted to department of surgery, burn unit in Baquba Teaching Hospital, and the study done according ethical guidelines which are approved by ministry of health.

Subjects involved in this study allocated into 2 groups:

- 1- Group A (96) burned patients treated according hospital policy.
- 2- Group B (18) healthy subjects, of both sexes and with the same age range as that of patients were selected as control for comparison.

Blood samples were collected from all subjects by venepuncture on admission to burn unit within the first 24 hours post burn and this value designed to be of the first week; in addition to that blood samples were taken at the second and third weeks which is the time of discharge from burn unit; to check the changes in the serum cholesterol (Chol), serum triglyceride (TG) and serum high density lipoprotein cholesterol (HDL-C) levels; which were measured according to the method of Fossati and Prencipe 1982 ⁸, Richmond 1974 ⁹, and Burstein *etal* 1970 ¹⁰ respectively.

Statistical analysis of data was done utilizing student t-test and P value lower than 0.05 were considered significant.

Table 1: Burned patient's data.

1	Patient total no.	96
2	Sex (male/female)	45/51
3	Age (year)	18-45
4	Burn %	25-70
5	Degree of burns	1 and 2 (50%) 2 and 3 (50%)
6	Cause of Burn	Hot water (60%) Flame (20%) Oil (20%)

RESULTS

Results in table (2) showed the normal values of serum levels of Chol, TG and HDL-C for normal healthy subjects (Group B); in addition to that, values for burned patients (Group A) at different time periods. Table (2) and figure (1) showed that serum Chol level significantly $P \leq 0.05$ lower in burned patients by 35.42% at the first week compared to healthy subjects.

In burned patients; serum Chol level non significantly increase at the second and third weeks compared to the first week by 12.86% and 15.57% respectively, figure (1). Results in table (2) showed that there is no significant change in serum TG level of burned patients compared to normal subjects in spite of small increase by 19% in serum TG level of burned patients at third week compared to first week results, figure(2).

Concerning serum HDL-C level, results in table (2) clearly showed the significant $P \leq 0.05$ decrease at the first week in burned patients compared to normal subjects. Figure (3) showed that serum HDL-C level decreased by 108.6% in burned patients at the first week and this low level maintained at second and third weeks.

DISCUSSION

Dyslipidemia after burn injury is one of the important alterations that resulted from many factors like hypermetabolic state in burn, release of hormones and inflammatory mediators and organ dysfunction; in spite of this, few authors have reported on the changes in lipid profile in patients with burn ^{6,7}; especially there is trace publication that describe the targeting of these changes in burned patients or the importance of correcting such dysregulation in serum lipids of burned patients and the effect of such targeting on burn outcomes in general.

Coombes *et al* describe changes in cholesterol and triglyceride levels in 16 patients with mild to moderate burns ⁶. According to their finding, there is initial decrease in serum level of cholesterol, and an increase in TG level. In different study, Coombes *et al* showed that changes in the levels of cholesterol, phospholipids, and triglyceride have been measured in the serum of 20 patients who had sustained burn injury; in the group of patients with severe burns, serum TG rose, reaching a peak on day 4-6 post burn, whilst cholesterol and phospholipids fell drastically; they suggest that the changes observed are reflection of block in the conversion of very low density lipoprotein to low density lipoprotein ¹¹.

On the other hand, studies in this regard, documented that severe burn injuries led to liver cell damage and changes in lipid metabolism ¹²; in addition to that, it has been shown that low cholesterol level in burned patients is due to in part to increased catabolism of cholesterol rich lipoprotein ¹³. Furthermore, data obtained by others, showed that the plasma TG level increase in burned patients due to mainly increased availability of free fatty acids released by stimulated lipolysis in adipose stores due to catecholamines, cytokines, tumor necrosis factor alpha, interleukin-1, interferon-alpha,beta and gamma; and recently interleukin-6, growth factors such as platelet derived growth factor, transforming and colony-stimulating factors; all modulate the lipid metabolism and may be the cause of these changes ¹⁴.

Data obtained by this study are compatible with all the above mentioned findings, and can be explained on such basis, except for changes concerning HDL-C level which was found to be significantly low in burned patients compared to normal subjects, figure (3). Targeting of the changes in serum cholesterol, TG and HDL-C that occur in burned patients may represent a new subject in burn therapy, where interfering with these changes by therapeutic means

may be new strategy through correcting such changes that may lead to improve burn outcome in general. Review of literature concerning this subject revealed very rare reports that addressed such problem. Akcay *et al* documented that administration of 20mg/day atorvastatin to severely burned group composed of 10 patients effectively prevent the release of E-selectin in those patients compared to control; which results in decreasing organ damage in treated group since E-selectin is one of the cellular adhesion molecules which are expressed by activated endothelial cells in severe burn and lead to organ damage ¹⁵.

Zheng *et al* investigate the protective effect of HDL on the cardiac function in rats with severe burns, they found that injection of HDL 80mg/kg to rats with severe burns significantly lower CK, ICAM-1, and TNF-alpha levels compared to control group; in addition to that, compared with burn group, degeneration, inflammatory infiltration and mitochondria swelling were found to be less marked in the experimental group, and there is no focal lysis and necrosis were found, which were observed in burn group; they concluded that HDL can be beneficial to the protection of cardiac tissue in protecting from secondary injury in rats with severe burns ¹⁶. Another study by Zheng *et al* showed that HDL exhibits protective effect on the lung function of rats with severe burns via reducing the expression of ICAM-1 and TNF-alpha ¹⁷.

Taken together, the above mentioned evidences clearly documented the beneficial role of measuring serum cholesterol, TG and HDL in burned patients, also show the importance of targeting changes that occur in their levels along burn course which may have beneficial effect through protecting organ damage and lead to increase survival rates among burn subjects and improve burn outcome. It has been proposed that many therapeutic agents may be used for such purpose to correct alteration in serum lipids of burned patients among which HMG-CoA reductase inhibitors where according to their action decrease in TG level and increase in HDL level is of great therapeutic value, other strong candidates for such purpose are antioxidant agents that have organ protective effect like melatonin ¹⁸, and silymarin ¹⁹, in addition to many other agents that possess such therapeutic activity.

In conclusion, this study show the occurrence of changes in serum lipids of burned patients namely decrease in serum cholesterol level, increase in serum TG level and decrease in serum HDL level compared to normal subjects; and that targeting of these changes is important contributor for improving burn outcome.

Table 2: Serum cholesterol, Triglyceride and High density lipoprotein levels of burned patients compared to normal subjects.

Groups	Time period (week)	Serum Chol mmol/L	Serum TG mmol/L	Serum HDL-C mmol/L
Group A	1	2.71±0.3*	1.74±0.15	0.7±0.12*
	2	3.11±0.38	1.75±0.13	0.74±0.18
	3	3.21±0.52	2.15±0.25	0.54±0.18
Group B	-	3.67±0.12	1.82±0.08	1.46±0.07

Results represent Mean ±SE; Group A: burned patients; Group B: normal healthy subjects; *: represents significant change $P \leq 0.05$.

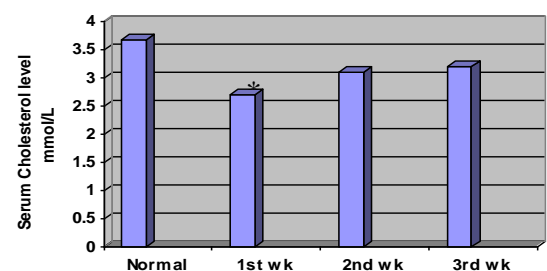


Figure (1): Serum Cholesterol level in burned patients compared to normal subjects

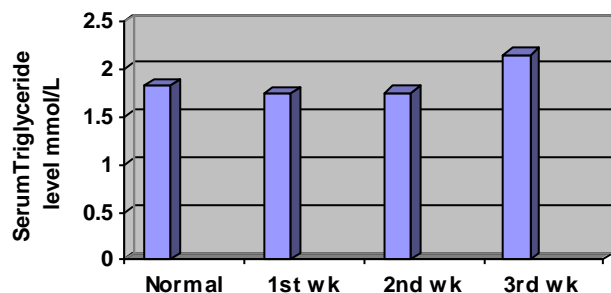


Figure (2): Serum Triglyceride level in burned patients compared to normal subjects

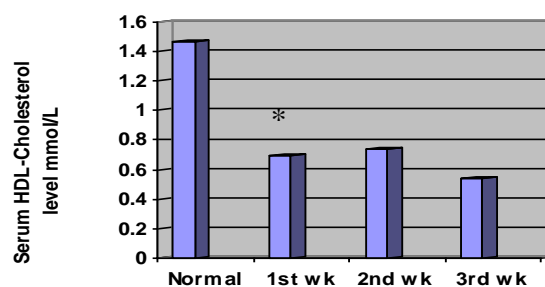


Figure (3): Serum High Density Lipoprotein Cholesterol level in burned patients compared to normal subjects

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