Assessment of Major Burn Patients with Biochemical Markers

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Abstract

Burn injury causes serious mortality and morbidity. Especially all pathophysiologic responses are seen in burn patients who are affected in more than 20% of total body surface.

In the literature, biochemical studies on burns are usually studies investigating the effects of inflammation, sepsis and inhalation. However, studies that evaluated the wound healing and clinical course with biochemical parameters are limited. In particular, there were no studies investigating the effects of early physiotherapy on burn patients.

Using biochemical parameters to evaluate these physiological changes seen in major burns can give more objective data. Therefore, the aim of this review is to discuss the recent advances in research into the utility of biomarkers in burn injury and to examine the effect of physiotherapy on these parameters.

Keywords: Major burns; Prealbumin; Fibronectin; Transferrin; Physiotherapy

Introduction

In skin and organic tissues; injuries caused by many factors such as chemical, electrical, friction, flame, and radioactivity are called burns [1]. Burn injury causes serious mortality and morbidity. In addition, hospitalization period and rehabilitation period is one of the longest traumas [2].

Lipolysis, proteolysis, glycolysis and high fever and hyperdynamic and hypermetabolic responses are seen in burn patients who are affected in more than 20% of total body surface area. These hypermetabolic responses in patients lead to a decrease in lean muscle mass, delay in wound healing, weakening of the immune system and serious mortality [3]. In the first 24 hours after the major burns, fluid accumulation is seen in the interstitial space due to increased vascular permeability. The reduced intravascular volume affects tissue perfusion if not interfered. Cardiac output decreases, all systems including the gastrointestinal system and renal system are affected. Depending on the burn, the electrolytes in the body are also affected and as a result of this effect cell death may occur [4].

For an optimal treatment after burn, all pathophysiological changes that may occur locally and systemically after injury should be known well. A good evaluation of burn injury is also required for a good treatment. The area affected by the burn should be evaluated in depth and the clinical process should be shaped accordingly [5].

The role of physiotherapy in the treatment of burns with surgery and medical treatment is becoming increasingly important. In particular, major burn patients need a long period of physiotherapy and rehabilitation, including the acute phase and the post-discharge period [6].

There are several studies in the literature evaluating the effects of inflammation and inhalation burns in burn patients with biochemical parameters. However, studies that evaluated the wound healing and clinical course with biochemical parameters are limited. In particular, there were no studies investigating the effects of early physiotherapy on burn patients.

Using biochemical parameters to evaluate these physiological changes seen in major burns can give more objective data. Therefore, the aim of this review is to discuss the recent advances in research into the utility of biomarkers in burn injury and to examine the effect of physiotherapy on these parameters.

Which Biochemical Markers can be Evaluated in the follow-up of Burn Injury?

Biochemical parameters; It can be defined as markers that can be measured and evaluated as an objective indicator of normal biological processes, pathogenic processes, or responses to a treatment. The World Health Organization (WHO) has defined each measure as a biochemical parameter, which allows for the comparison of a potential biological system with any potential hazard [7].

An ideal biomarker should be obtained easily and quickly. It must be precise, specific and repeatable. These markers should help us to understand the pathophysiology of diseases, identifying early and accurate diagnoses of certain complications and determine the severity of the disease [7].

There is no sharp definition of biochemical markers used in burn injury. The markers are determined according to the ascertained prognostic purpose and evaluated pathophysiological changes, according to the patient [7].

Historical Development of Biochemical Markers related to Burn Injury

Inevaluated the biochemical marker of interleukin-1 receptor antagonist (IL-1RA) in burn patients [8]. They observed that this parameter increased especially in inhalation burns. In another study by Vindenes in 1998, plasma cytokine levels were evaluated in burn patients. In particular, patients with more than a percentage of burns were reported to be more elevated [9]. Biochemical markers related to burn injury continued in 2000. Procalcitonin parameter could be used for the evaluation of sepsis in burn patients [10]. Biochemistry studies of burn patients have been continuing until today as shown in Table 1.

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but the most common cause of inflammation is acute inflammation. Decreases in dialysis, hyperthyroidism and marked hyperglycemia, the use of corticosteroids, non-steroidal anti-inflammatory agents and factors, including new dietary intake. In cases of severe renal failure, synthesis is controlled by sex steroid hormones [36]. In women may be slightly lower than in men because prealbumin and gender can be important to interpret a test. The prealbumin levels sensitive marker [36]. The reference range is 0.20 to 0.40 g/L, but age prealbumin, procalcitonin, transferrin, CRP, glucose, insulin to evaluate effects of physiotherapy.

**Prealbumin (Transthyretin)**

Prealbumin first described as Transthyretin (TTR) in 1942, was increasingly popular as a new infection marker in the ICU. It has been emphasized in several studies that it is a valuable marker that identifies increasing popularity as a new infection marker in the ICU. It has been emphasized in several studies that it is a valuable marker that identifies prealbumin, procalcitonin, transferrin, CRP, glucose, insulin to evaluate the effectiveness of physiotherapy.

**Fibronectin**

Fibronectin is a kind of glycoprotein found in all kinds of tissues and has an important role in the interaction of many different cell matrices. Fibronectin is one of the building blocks of extracellular matrix formation [37]. All fibronectin molecules consist of the same basic functional areas. Although encoded by single genes, it is subdivided into approximately 50 exons in sequence in an RNA sequence. The fibronectin gene consists of three general types of homologous repeating units or modules called Type I, II and III. In this gene, each repeating module of type I or II homology unit is encoded by a separate exon. However, the type-II gene is formed by the contribution of the other gene. Type I modules are used to connect fibrin, heparin or collagen. Type II modules are only found in the collagen binding domain and type III modules are used in the domain that binds to cells. Due to specific functional areas and binding sites, fibronectin interacts with different cell types, cytokines, and extracellular matrix (ECM) [37].

Fibronectin is required for both tissue formation and wound repair and connective tissue repair. Fibronectin interacts with other cells to form an ECM at each stage of wound healing, but at the same time, the role of fibronectin in the early stage of wound healing is more important, where it is bound to thrombocytes and fibrin. The fibronectin marker is also used to monitor wound healing in the clinic. A low-progression indicates a delay in wound healing, whereas a higher than normal gives clues about an adhesion or scar formation [37,38].

**The transferrin receptor (TfR)**

Transferrin receptor

Transferrin receptor is the iron source of various organ cellular components [39]. The level of serum ferritin is a useful indicator for the condition of the iron reservoir. When iron stores are depleted, serum ferritin is below 12-15 µg/L, but this is not an indicator of inflammation alone. In view of these mutations of TfR and ferritin, the ratio of TfR/ferritin is a valuable measure of the degree of iron deficiency. In a phlebotomy study in which iron status and iron deficiency were calculated, the rate of serum TfR/ferritin reflected body iron status and iron deficiency. In other words, positive values indicate that iron is stored and negative values indicate iron deficiency [39].

**CRP (C-Reactive protein)**

CRP is often used as a biomarker for an acute inflammatory condition. CRP values indicate the presence and severity of inflammation [40].

**Procalcitonin (PCT)**

Procalcitonin is a biochemical parameter that positively correlates with sepsis and mortality rates. In the last decade, PCT has become increasingly popular as a new infection marker in the ICU. It has been emphasized in several studies that it is a valuable marker that identifies the seriousness of the guiding treatment of the underlying disease [41].

**Table 1: Historical development of biochemical markers related to burn injury.**

| Year | Biochemical marker | Reference |
|------|--------------------|-----------|
| 1995 | IL1Ra              | Mandrup-Polsen et al. [8] |
| 1996 | IL1Ra              | Endo et al. [11] |
| 1997 | TNFa               | Yeh et al. [12] |
| 1998 | IL1Ra, IL1b        | Vindenes et al [9] |
| 1999 | IL6                | Yeh et al. [13] |
| 2000 | IL10               | Yeh et al. [14] |
| 2002 | TGFb1              | Yeh et al. [15] |
| 2008 | G-CSF, MCP-1, IL6, IL8 | Jeschke et al. [16] |
| 2010 | IL6, IL8, IL-10, IL6, Leukocyte surface markers | Csanos et al. [17] \ Voldt et al. [18] |
| 2011 | IL10               | Inatsu et al. [19] \ Mann et al. [20] |
| 2012 | IL8                | Albright et al. [21] \ Davis et al. [22] \ Salgado et al. [23] \ Lavrentieva et al. [24] |
| 2013 | IL1Ra, IL1b, IL6, IL10, IL12p70, C5a, IL1b, Receptor of TNF a Procalcitonin | Davis et al. [25] \ Jones et al. [26] \ Simonetti et al. [27] \ Yin et al. [28] |
| 2014 | IL6, IL8, TGFb1, MCP-1, CRP IL6, IL8, G-CSF, MCP-1, MIP-1b, CRP Leucocyte surface markers, N-terminal pro-B-type natriuretic peptide Cystatin C, NGAL | Kraft et al. [29] \ Jeschke et al. [30] \ Szigel et al. [31] \ Paratz et al. [32] \ Yang et al. [33] |
| 2015 | IL8, IL6, IL8, TNFa | Yeh et al. [34] \ Reper et al. [35] |
Early stage burn physiotherapy protocol (ESBPP)

ESBPP patients who were previously exposed to burn trauma were taken to a physiotherapy program after an immobilization period of 7 to 10 days. But in the last 10 years, this understanding has been replaced by the idea that it is necessary to start the physiotherapy program in the early period. In particular, if the hypermetabolic response begins within the first 48 hours, the patient should start the physiotherapy program as early as possible from the time of admission. For this reason, we applied Early Stage Burn Physiotherapy Protocol (ESBPP) to our patients as shown in Table 2 [42].

In patients with major burns; delayed wound healing, impaired protein metabolism, and the emergence of the inflammatory process adversely affect the clinical course of the disease. Parameters such as fibronectin, prealbumin, and transferrin also provide important information in the follow-up of these processes. Çınar stated in their study that decreasing fibronectin values in the acute period have increased to the normal reference range in patients with major burns physiotherapy [42].

In another study he reported that physiotherapy reduced the level of increased glucose and triglycerides due to hypermetabolic response in burn patients [43].

In the study, Çınar investigated the effect of physiotherapy on biochemical parameters in patients with major burns and concluded that early physiotherapy (ESBPP) positively affects parameters such as fibronectin, prealbumin, and transferrin [44]. They also stated that the positive effect of fibronectin and the prealbumin values that inform the patient about the muscle metabolism and clinical course of the wound healing process in the acute phase will bring a different perspective to the literature and add power to it [44].

Çınar stated that physiotherapy is effective on glucose, insulin, prealbumin, and procalcitonin levels in both types of burns. In the study that named “The Effect of Physiotherapy on Glucose, Insulin, Prealbumin and Procalcitonin in two Different Burn injuries: Pilot Study” [45].

Conclusion

The occurrence of inflammation is inevitable after burn injuries. In particular, it has been reported in the literature that major post-burn inflammatory mediators have increased. In addition, the effects of inhalation burns and sepsis were evaluated in burn patients. Consequently, some biomarkers have been described as potential therapeutic targets [7]. However, these markers may not be sufficient for the follow-up of burn patients. In particular, the use of fibronectin biomarker to monitor wound healing may guide the evaluation of professionals working in this area [42].

In recent years, prealbumin has been used to monitor the clinical course of the patient rather than the nutritional marker in patients who have undergone major trauma. Especially in burn patients, prealbumin levels are thought to be directly effective on the clinical course of the disease and patient mortality [46]. Therefore, we believe that the use of prealbumin biomarker may be important in the evaluation of burn injury.

Iron deposition is reduced due to inflammation and impaired liver function in major burn patients and therefore the transferrin value is adversely affected. We believe that in addition to other parameters, transferrin should be evaluated especially in the follow-up of elderly patients.

Treatment of burn patients requires a very serious multidisciplinary approach. The treatment program of the patient does not include a single understanding; many parameters such as medical treatment, surgical treatment, nutrition, and physiotherapy should be included in the treatment program. Surgical treatment has a great place among these parameters. The patient undergoes multiple surgical procedures until he is discharged from hospital admission and these operations prolong the immobilization period of the patient. The prolonged immobilization time affects the clinical course of the patient negatively.

Physiotherapy of burn patients has many parameters. It is not considered that any parameter gives direct superiority to another parameter. However, we concluded that the mobilization of patients in the earliest possible period is a very important parameter. Especially, considering that surgical treatments affect patient mobilization, mobilization training should be given priority in the physiotherapy program.

ESBPP must be presented in the treatment programs of major burn patients. In order to follow the clinical course of the patients; parameters such as fibronectin, prealbumin, transferrin, procalcitonin should also be taken into consideration.

Therefore, searches that related to burn injuries, especially major burns, should focus on preventing complications, wound healing and designing new therapeutic targets such as physiotherapy and validating new experimental findings.

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