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REVIEW

Hematological alterations in major burn patients: a bibliographic review

Alteraciones hematológicas en pacientes grandes quemados: una revisión bibliográfica

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ABSTRACT

Introduction: burns and their treatment have been studied constantly. Even with all the accumulated knowledge about this topic there are still subjects related to the pathophysiology that need further research.
Method: a bibliographical review to characterize the hematological alterations documented in major burn patients was conducted. The source of information for this matter was mainly internet (Google Schoolar, Scopus, PubMed, Dialnet and others).
Results: 16 texts in English and Spanish were read and referred on the paper. There were only contemplated articles, chapters of books, thesis and similar that were published within the last 5 years.
Conclusions: the most common hematological alterations documented on medical literature are either the pro coagulating initial status or the rapid thrombocytopenia due to the dilutional coagulopathy. The sudden rupture of balance between the pro-coagulating and anti-coagulating factor could lead to serious complications such as disseminated intravascular coagulation. Other disturbances mentioned are acute anemia, monocyte anisocytosis, delay of PT-PTT and VTE. Although further investigation is needed for a better understanding of this topic, an individualized and multidisciplinary approach will always be the best course of action.

Keywords: Burns; Hematologic Disease; Blood Coagulation Disorders.

RESUMEN

Introducción: las quemaduras y su tratamiento han sido ampliamente estudiadas. Incluso con todo el conocimiento acumulado sobre este tema existen aún lagunas en relación con la fisiopatología de las mismas que requieren futuras investigaciones.
Método: se realizó una revisión bibliográfica para caracterizar las alteraciones hematológicas documentadas en los pacientes grandes quemados. Se empleó como fuente de información principalmente internet (Google Schoolar, Scopus, PubMed, Dialnet y otros).
Resultados: fueron leídos y referenciados 16 textos en español e inglés. Se contempló únicamente artículos científicos, capítulos de libros, trabajos de tesis y similares que tuvieran un tiempo de publicación no mayor de 5 años.
Conclusiones: las alteraciones hematológicas más comúnmente documentadas en la literatura médica son el estado inicial procoagulante y la trombocitopenia dilucional. La ruptura súbita del equilibrio entre los

factores pro y anticoagulantes puede llevar a serias complicaciones como la coagulación intravascular diseminada. Otras alteraciones mencionadas son la anemia aguda, la anisocitosis monocitaria, el aumento de los TP-TTP y la TVP. Sin embargo, futuras investigaciones son necesarias para un mejor entendimiento del tema, un abordaje individualizado y multidisciplinario siempre será el mejor curso de acción.

Palabras clave: Quemaduras; Enfermedades Hematológicas; Trastornos de la Coagulación Sanguínea.

INTRODUCTION

Skin in the human body covers a surface area of 2 m^2 approximately and it´s a such important organ which develops functions as protection, detoxification, absorption, temperature adjustments and some more. That is why the loss of this major barrier generates very serious events that could lead to a quicker death. In this context, burns represent a threat not only for the skin itself, but also for the homeostasis of the entire organism. Even when the repair process of any burn initiates several hours after the tragic event, the shift of fluids to the third space is a physiological response that paradoxically affects the general hydric balance and could lead to some metabolic systemic problems in the short term.[1]

Burns and their treatment, as a very relevant medical issue, have been studied constantly. Even with all the accumulated knowledge about this topic there are still subjects related to the pathophysiology that need further research. One of these topics is associated with the hematological disturbances triggered by major burns, which is the central concern of the present review.

METHOD

A review of the medical literature was conducted. The main objective was to characterize the hematological alterations documented in major burn patients. The source of information for this matter was mainly internet (Google Schoolar, Scopus, PubMed, Dialnet and others). The general descriptors for the search were: “major burns”, “hematological alterations”, pathophysiology”, “treatment” and “laboratorial values”.

RESULTS

16 texts in English and Spanish were read and referred on the paper. Only were contemplated articles, chapters of books, thesis and similar that were published within the last 5 years. The table 1 shows in detail the texts used and their particularities.

Table 1. Texts consulted for the preparation of the bibliographic review

Title	Authors	Language	Country	Year
Complicaciones en los grandes quemados	Rodríguez Llamazares T.	Spanish	Spain	2021
Severe Altered Immune Status After Burn Injury Is Associated With Bacterial Infection and Septic Shock	Moins-Teisserenc H, Cordeiro DJ, Audigier V, Ressaire Q, Benyamina M, Lambert J, et al.	English	France-USA	2021
Hematologic Diseases	Sankar V, Villa A.	English	USA	2021
Major burns: Part 1. Epidemiology, pathophysiology and initial management	McCann C, Watson A, Barnes D.	English	UK	2022
Complicaciones en los pacientes quemados	Moya-Rosa EJ, Moya-Corrales Y, Moya-Rosa EJ, Moya-Corrales Y.	Spanish	Cuba	2022
Blood coagulation alterations over the first 10 days after severe burn injury.	Barbier JM, Viana MV, Pantet O, Alberio L, Berger MM.	English	Switzerland	2022
The Complexity of the Post-Burn Immune Response: An Overview of the Associated Local and Systemic Complications	Korkmaz HI, Flokstra G, Waasdorp M, Pijpe A, Papendorp SG, de Jong E, et al.	English	The Netherlands	2023
Burns: Classification, Pathophysiology, and Treatment: A Review	Żwierełło W, Piorun K, Skórka-Majewicz M, Maruszewska A, Antoniewski J, Gutowska I.	English	Poland	2023
Critical Care of the Burn Patient	Britton GW, Wiggins AR, Halgas BJ, Cancio LC, Chung KK.	English	USA	2023
Coagulation Alterations in Major Burn Patients: A Narrative Review	Guilabert P, Martin N, Usúa G, Vendrell M, Colomina MJ, Barret JP.	English	Spain	2023
Grandes Quemados	Santaolalla Fragoso MB, Martín García AI, San Juan E.	Spanish	Spain	2024

Venous Thromboembolism in Burn Patients: A 5-Year Retrospective Study	Bordeanu-Diaconescu EM, Grosu-Bularda A, Frunza A, Grama S, Andrei MC, Neagu TP, et al.	English	Romania	2024
Diagnostic and Prognostic Value of Thrombocytopenia in Severe Burn Injuries	Bordeanu-Diaconescu EM, Grosu-Bularda A, Frunza A, Grama S, Andrei MC, Neagu TP, et al.	English	Romania	2024
Afectación de la calidad de vida del paciente gran quemado. Una revisión bibliográfica	Pérez Casañas P.	Spanish	Spain	2025
Impact of red blood cell transfusion in massive burn: a multicenter cohort study	Du Y, Xia Y, You C, Wang Y, Duan D, Xu W, et al.	English	China	2025
Monocyte Anisocytosis Changes in Patients After Major Burn Injuries	Nazemidashtarjandi S, Muldur S, Supple MD, Ryan CM, Yonker LM, Karabacak MN, et al.	English	USA	2025

DISCUSSION

Major burns

A burn is the main result of skin contacting with a heat source. This definition includes factors like the high temperature, the friction and sometimes the presence of external factors like electricity, radiation and/or chemicals. The medical classification of burns is complex and includes topics like the percentage of the skin injured, the location, the specific temperature and the time of exposure. These variables have a synergistic effect that can certainly make a difference in the outcomes of the patient and its mortality risk.[1]

The injuries caused by fire, heat and hot substances was approximately 9 000 000 worldwide, from which about 120 000 ended in defunctions; all of this was registered in 2017. One thing that is very concerning is the fact that 90 % of these outcomes occurred in low our middle-income countries, reflecting the need to improve the early management of this patients and the resources available for this matter. According to literature, the most common cause of admissions in this context is scalds mostly accidents home or work – related.[1]

The first classification of burns is based on the depth of the injury. First-grade burns are those which compromise only the epidermis, the most superficial layer of the skin. These have the best prognosis and do not tend to form blisters. Second-grade burns, in the other hand, could be superficial when only the papillary dermis is affected so there is some redness, pain, exudate and finally blisters due to the filtration of blood capillaries. Second-grade burn becomes profound when reticular dermis is involved in the injured tissues, what changes the clinical picture to areas of redness and intense exudate with significant pain and whitish areas. Finally, third-grade burns are the most severe. They affect all the three layers of the skin and may also involve some adipose tissue, nerves, muscles or even bones in the worst scenarios. The typical injures are ulcers and necrosis and, if the nerves around them are damaged too, it could be a loss of pain.[1-3]

The denomination of a major burn includes a patient who suffers from injuries caused by thermal damage, also considered as a polytrauma patient. This definition also incorporates some severity criteria like the affectation of 25 % corporal area in adults or 20 % in the elderly, the presence of profound burns in more than 10 % of corporal surface, burns that affect the face or the neck, internal burns caused by inhalations, the associated trauma and the occurrence of burns in patients with some important comorbidities that lead to an ASA (American Society of Anesthesiologists) cataloguing of II or more.(2)

Continuing with this matter the American Burn Association has developed its own classification. According with them a major burn has to accomplish some of the next criteria:

- > 25 % of corporal surface with third grade burns in adults.
- > 20 % of corporal surface with second grade burns in children.
- Second or third grade burns that involve eyes, ears, face, hands, feet, major joints, perineum or genitals.
- All of the injures produced by inhalation.
- Electrical burns.
- Chemical burns that involve eyes, ears, face, hands, feet, major joints, perineum or genitals.
- Burns associated with trauma.
- Burns in patients with comorbidities like diabetes, malnutrition, pulmonary disease, cardiovascular disease, blood alterations, AIDS, immunosuppressors conditions and/or any type of cancer.

With at least one of these criteria a patient could be cataloged as a major burn patient and its treatment should be very specific within the first 24 hours.[2,4]

Post-Burn immune response

Burn wound differ from any other types of traumas in their pathophysiology. Their most important mechanism is the inflammatory response, which is responsible not only for the acute compensatory phenomena's but also for the repairing process. Although the main focus on the management of major burns has always been the excision of necrotic tissue, the infection prevention and the adequate administration of fluids, burns caused both a local and systemic pathology in the acute and long term. The local and systemic post-burn disease is characterized by massive inflammatory response that can also influence complications at different levels of complexity, including hematological disturbances, sepsis and multiple organ failure.[5]

Some authors have demonstrated an upregulation of adaptative immunity and the persistent activation of biomarkers with a down regulation of native immunity and stress/inflammation biomarkers at the acute phase of major burns. High levels of interleukin-10 at the moment of admission were related to infections and septic shock within the first 48 hours. In this context, the absence of immune recovery configurations is strongly associated with a worst prognosis. Therefore, burn research requires further investigations to accomplish a better understanding of how immune factors are linked to the status of persistent inflammation and how to reverse it.[5,6]

Multiple organ dysfunction syndrome in major burn patients

Multiple organ disfunction syndrome (MODS) is a very serious complication in major burn patients. These lesions trigger a systemic inflammatory response syndrome, which turns into a general organ failure. The main mechanism here is the massive loss of liquids from burn wounds that lead into a hypovolemic shock with severe hypoperfusion of the main economy organs. This status could be aggravated with any opportunistic germ due to the high susceptibility of burn wounds to infections. MODS increases significantly the mortality in major burn patients.[1,7]

This dysregulated inflammatory response causes a significant increment in the capillary permeability, so the fluids start to leak into de interstitial space and the intravascular space turns out losing significant quantity of volume. In this unfortunate chain of events many plasmatic proteins and electrolytes kept trapped in the third space, so the osmotic pressure goes down as well. Finally, the molecular chemicals released by the inflammatory response led to a massive vasodilation which rapidly causes hypoperfusion on all tissues and contributes to the perpetuation and worsening of the states of shock and multiple organ failure. Some literatures propose the denomination of burn shock to this dysfunction due to its main characteristic which is a circulatory and microcirculatory impairment, generating edema in both burn and unaffected surfaces.[7,8,9]

Hematological alterations

Major burn patients present some alterations of the hematological system that are not fully described in medical literature. The majority of authors refer a burn-associated coagulopathy. The main mechanism of this phenomenon lays on the fact that injured tissue and its blood vessels release the well-known tissue factor that soon will start the chain of extrinsic coagulation pathway. The already existent state of hypoperfusion and metabolic acidosis also leads to a hyper consumption of coagulation factors, increased fibrinolytic activity and maybe am hemodilution coagulopathy caused by an inadequate fluid resuscitation.[10]

The prolonged state of consumption and requirement of coagulation resources will be followed by a disseminated intravascular coagulation (DIC), very common in this kind of patientsfluid replacement therapy, hypothermia, hypoperfusion, acidosis, and activation of the inflammatory cascade. However, the multiple coagulation alterations that occur are still poorly defined. The aim of this review is to combine the results of the different coagulation tests currently used to study coagulation changes in these patients. The PubMed database was searched for articles reporting factor levels or coagulation tests using the keywords "Burns" and "Blood Coagulation". Of the 720 articles retrieved from the search, 20 were finally included in the review. Coagulopathy in the MBP differs from that of the trauma patient, insofar as the former present with an increase in factors VIII, IX, and vW on admission accompanied by an increase in fibrin and thrombin production. This is followed by activation of fibrinolysis and prolonged prothrombin (PT. DIC is a clinical and laboratory syndrome distinguished by the uncontrolled activation of coagulation factors and the parallel increased risk of micro and macrovascular thromboses. Paradoxically this consumptive coagulopathy elevates the risk of bleeding, which can be lethal in major burn patients who are taking to surgery.[11,12]

Even with all the mechanisms involved in the coagulation alterations of major burn patients, the results in laboratorial test differ from other patients with diagnosis of shock and trauma. According to medical texts, there is a notable increase of factors VII, IX and von Willebrand which companies the production of serum fibrin and thrombin. A significant delay of prothrombin (PT) and thromboplastin (PTT) times within the first 24 hours is mainly documented. After 48 hours, there is a remarkable increase of fibrinogen and in the next two to three weeks there is still a status of thrombocytosis. Regarding the viscosity tests, they show a pattern characterized by either a normal viscosity or a hypercoagulable state with no signs of hyperfibrinolysis. Some authors defend

the theory that the disturbance on PT and PTT combined with the elevation of factor VIII have been associated with higher risk of mortality. In the other hand, a rapid normalization of antithrombin and protein C levels is related with a better prognosis.[10]

In this context, the thinking of thrombotic events is only logical. However, even when major burn patients present all components of Virchow´s triad (endothelial injury, blood viscosity and hypercoagulability), the existence of venous thromboembolism (VTE) has not been documented so frequently and the administration of routine thrombosis prophylaxis still remains on debate. Nevertheless, many medical articles have shown that the occurrence of VTE depends of each patient´s and burn lesion features, which leads to the importance of an individualized management. The use of Caprini Risk Assessment Model is highly recommended as well as the indication of thromboprophylaxis and careful monitoring in those patients with Caprini score above 8 points.[13]

Other studies divide the coagulations alterations in fractions of time. They delimited the first 72 hours as a period in which a significant delay of PT is the most common finding. This prolonging of PT is inverse associated with infused fluid volumes. Although further research is needed, it seems that those patients with over resuscitation protocols. Some isolated complications are mentioned as well, such as heparin-associated thrombocytopenia, DIC, cardiorespiratory arrest. Medical literature also specifies that those conditions are mostly related to preexistent comorbidities such as hepatitis, deficiency of factor VIII, cancer or even prolonged treatment with anticoagulants. After the acute phase of 72 hours, the most important hematological alteration is thrombocytopenia which seems to be statistically related to the percentage of burn surface.[11]

Some authors call this hematological environment a burn-induced coagulopathy due to the complex cascade of events triggered by the burn itself. Despite the advances already made, it is still very difficult to manage both the injuries related to the burn and the systemic complications. At this point, thrombocytopenia seems to be the most reliable and early indicator of severe complications in major burn patients. Its appearance is related to negative prognosis and also with the occurrence of sepsis on short and long term. Thrombocytopenia is related to a higher mortality risk as well, being the main causes of it burn shock, inhalation injuries and general sepsis.[9,14]

Another hematological alteration present in major burn patients is acute anemia due to massive tissue loss and associated surgical procedures. Medical articles refer that red blood cells transfusion is a standard measure on these cases. However, blood transfusions may lead to complications and worst clinical outcomes according to some studies. Multicentric investigations have shown that the correlation of blood cells transfusion and the outcome of these patients is not linear, meaning that the indication of up to 6 red blood cells units has been proved to reduce both complications and mortality. When the transfusion volume is higher than 6 units, it is not as effective and sometimes seems to be related with a major risk of negative outcomes including death. Also, massive blood transfusions in severe burns are associated with longer hospital stay and mechanical ventilation time. A few studies talk about a transfusion related lung injury characterized by lobar pneumonia.[9,15]

There are some hematological markers that recently have shown a prognostic value in major burn patients. Although the analysis of blood cells from burn patients demonstrates an important and sustained innate immune activation in those who had poor clinical outcomes, the measurement of monocyte anisocytosis throughout the recovery until the end of the hospitalization has captured some interest. Studies have proved that increases monocyte anisocytosis during the first week after major burns are related to worst prognosis. Among survivors, the levels of monocyte anisocytosis had decreased within the second week of recovery and reached normal values by the end of the hospital stay. This indicator also seems to lowers after excision and debridement of necrotic tissue, but not after the graft's surgeries. Finally, monocyte anisocytosis has been correlated to positive blood culture samples and respiratory infections, showing the relevance of monitoring it in this type of patients.[16]

CONCLUSIONS

The management of major burn patients is a matter that still presents knowledge gaps. The most common hematological alterations documented in medical literature are either the pro coagulating initial status or the rapid thrombocytopenia due to the dilutional coagulopathy. The sudden rupture of balance between the pro-coagulant and anti-coagulant factors could lead to serious complications such as DIC. Other disturbances mentioned are acute anemia, monocyte anisocytosis, delay of PT-PTT and VTE. Although further investigation is essential to improve clinal outcomes, and in the meantime needed for a better understanding of this topic, an individualized and multidisciplinary approach, remains the best strategy for managing these patients.

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