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Review Article

Infections in Burn Patients

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Abstract

Burn patients have a high susceptibility to infections due mainly to a disruption of the skin barrier and to a dysbiosis of the immune system. Infections are a main cause of morbidity and mortality among these patients. Among other damages, infections impair cicatrization, lead to graft loss, prolong treatment, and, consequently, prolong the length of stay and raise costs.

The most frequent sites of infection are burn wounds, respiratory tract, urinary tract and bloodstream. The epidemiology of infections in burn patients is different from that of non-burned. Hence, they require a specialized and multi-disciplinary approach.

In the present article, general aspects of the epidemiology and microbiology of infections in burn patients, as well as infection control practices, are discussed.

Keywords: *Infection; Colonization; Burn Patient; Multidrug Resistance; Quantitative Culture*

Abbreviations

TSBA: Total Body Surface Area; CENAQUE: Centro Nacional De Quemados; LOS: Length of Stay; MDR: Multidrug Resistant/Resistance; ICU: Intensive Care Unit; TTC: Time To Colonization; HCW: Healthcare Worker

Introduction

Burns are among the most frequent causes of accidental injuries worldwide. An estimated 265,000 deaths occur annually; the majority affects people in low- and middle-income countries [1].

Burn patients have a high susceptibility to infections due mainly to a disruption of the skin barrier and to a dysbiosis of the immune system [2-4]. The intact skin constitutes a physical barrier for infection. Also, the normal skin flora, the low pH and dryness along with desquamation, prevent local colonization with pathogenic organisms. Devitalized avascular tissue resulting from burn constitutes a favorable environment for microbial growth. At other anatomical sites, physical defenses altered in the burn patients are: the muco-ciliary lining of the respiratory tract because of smoke inhalation, frequent endotracheal and nosogastric intubation, adynamic ileus, gut permeability, urinary tract catheterization; the normal flora is often altered because of the use of antibiotics [5]. Thus, the most frequent sites of infection are burn wounds, respiratory tract, urinary tract and bloodstream, including catheter-associated bloodstream infections [6-8].

Infections are a main cause of morbidity and mortality among burn patients [6,9,10]. They impair cicatrization, lead to graft loss, prolong treatment, and, consequently, prolong length of stay and increase costs.

It is difficult to establish the diagnosis of infection in the burn patient because the clinical presentation is not as specific as in non-burn patients. It is also difficult to differentiate between burn wound colonization and infection. Quantitative cultures have been proposed as a tool to differentiate these two situations, but its utility is debated [11].

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In the present article, general aspects of the epidemiology and microbiology of infections in burn patients, as well as infection control practices, are discussed.

Epidemiology

The microorganisms that colonize or infect burn patients originate from the patient's own flora but also from the hospital environment [2,12].

The incidence of infections varies from center to center. Large series studied in India, Turkey and Bulgaria showed rates of 36.2, 23.1 and 10.6 infections per 1000 patient days respectively [7,10,13]. The incidence of bloodstream infections has been estimated in the USA at 1.82 cases per 1000 patient days over a 9 year period [8].

Factors that increase the risk of developing infections are: larger TSBA; late surgical treatment of the wound [14]; prolonged LOS at the hospital, which also increases the risk of acquisition of MDR microorganisms [8,10,15]. At CENAQUE, between July 1st 2013 and June 30 2014, we found that patients whose burn wounds were not colonized at all or that were colonized with only 1 group of microorganisms (fungi, *Enterobacteriaceae, Pseudomonas* spp., *Acinetobacter* spp., *Enterococcus* spp. and *Staphylococcus aureus*) had a significantly shorter LOS in ICU than those colonized with 2 or more groups. The mean time from admission to the first positive culture (TTC) with MDR microorganisms was longer than the mean TTC with non-MDR [16]. Inhalation injury is a risk factor for the development of pneumonia and increases mortality [17].

The sources of microorganisms that colonize and eventually cause infection are endogenous (patient's own flora) and exogenous (inanimate environmental items and HCW). The main mode of transmission is contact, either through hands of HCW or through contaminated equipment. At the same time, the colonized patient becomes a source of microorganisms for other patients [5].

Type of infections

Most common infections are those from: burn wound; respiratory tract, which have a high risk of mortality and are mostly associated to mechanical ventilation; urinary tract, most frequently catheter associated; bloodstream, which can be catheter-associated or can originate from another infectious focus. Bloodstream infections rates are higher in burn patients than in non-burn patients [5].

Due to the particular metabolic status of burn patients, who are chronically exposed to inflammatory mediators, clinical parameters and laboratory analysis used to detect infection cannot be applied in these patients. In 2007, the American Burn Association published a consensus for the use of specific criteria for the diagnosis of sepsis and wound infection in adult and children. The consensus establishes that the systemic inflammatory response syndrome (SIRS) is not clinically useful in burn patients, since these patients are in a state of chronic SIRS [18].

Microbiology

Wounds are sterile immediately after the occurrence of the burn. Later during the hospitalization, wounds are colonized with different microorganisms.

In the pre-antibiotic era, *Streptococcus pyogenes* was a main cause of infection in burn patients [19]. With the introduction of penicillin, the frequency of this microorganism decreased and *Staphylococcus aureus* began to predominate. Nowadays, the use of prophylactic penicillin is not justified [20]. Later on, *Pseudomonas aeruginosa* appeared as one of the leading etiological agents. At present, MDR microorganisms are particular threats: methicillin-resistant *S. aureus*, vancomycin-resistant *Enterococcus* spp., MDR *Enterobacteriaceae* including carbapenemase-resistant, MDR *Pseudomonas aeruginosa*, MDR and pandrug resistant *Acinetobacter baumanii* [5,21].

A non-exhaustive list of microorganisms that can colonize or infect burn wounds and other anatomical sites is shown in Table 1.

Bacteria	Gram positive	*Staphylococcus spp.*	*S.aureus* Coagulase negative staphylococci
		Enterococcus spp.	*E.faecalis* *E.faecium* Other *Enterococcus spp.*
		Streptococcus spp.	Viridans group streptococci Beta-hemolytic streptococci
	Gram negative	*Pseudomonas spp.*	*P.aeruginosa* Other *Pseudomonas spp.*
		Enterobacteriaceae	*Escherichia coli* *Klebsiella pneumoniae* *Proteus spp.* *Enterobacter spp.* *Serratia marcescens* Other Enterobacteria
		Acinetobacter spp.	*A.baumannii* Other *Acinetobacter spp.*
		Stenotrophomonas maltophilia	
		Burkholderia cepacia	
Fungi	Yeasts	*Candida spp.*	*C.albicans* *C.kruzei* *C.glabrata* Other *Candida spp.*
	Molds	*Aspergillus spp.*	*A.fumigatus* Other *Aspergillus spp.*
		Fusarium spp.	
		Rhizopus spp.	
		Mucor spp.	
Virus		Herpes virus	Herpes simplex
			Cytomegalovirus
			Varicella zoster

Table 1: *Microorganisms that colonize/infect burn patients.*

S. aureus and *P. aeruginosa* are among the most important colonizers and agents of infection [2,22]. *Candida* spp. are the most frequent fungi, originating from the patients' own flora, while molds are usually from exogenous origin [21].

The mean time from the occurrence of the burn to colonization of the wound is usually less than 7 days [2,12]. At CENAQUE, the mean TTC in 2015 was 6 days (range: 0 - 37 days) for any microorganism and of 13 days (range: 0 - 59) for MDR microorganisms (not published data).

At the same time, the microbial flora at other anatomical sites changes from normal to a flora predominantly composed of MDR nosocomial microorganisms. Bacteria and fungi that colonize the different body sites can eventually cause an infection.

It is described that Gram positive bacteria from the skin are the first colonizers of burn wounds, then Gram negative bacteria and later on yeasts and fungi [2,8,15]. Nevertheless, at CENAQUE in 2015, among 98 patients that were hospitalized for at least 15 days we found a similar mean TTC for Gram negative and Gram positive bacteria (17 days) and for fungi (18 days) (not published data).

Microbiological diagnosis

Wounds - The microbiological diagnosis of wound infection can be made by semi-quantitative or quantitative methods [2,23,24]. The histopathologic diagnosis is very accurate, but it is not practical to be applied routinely. A wound is considered to be colonized but not infected when bacteria are found in non-viable tissue, while it is considered infected when bacteria are found in significant number in the viable tissue [25].

Quantitative cultures are usually performed by culture of biopsies and determination of the colony forming units per gram of tissue. Alternatively, if a known surface area of the burn wound is swabbed, a quantitative result may be obtained per cm^3 of the burn surface.

The utility of quantitative methods has been debated. It has been observed that bacterial counts equal or higher than 10^5 cfu/gram of tissue are associated with infection rather than colonization [26,27]. Nevertheless, McManus., *et al*. showed that only 36% of patients with cultures with more than 5logs/g had histological evidence of invasive infection, concluding that the principal value of quantitative cultures is demonstration of predominant flora [28]. Also, Woolfrey et al found poor reproducibility and poor correlation between bacterial counts and development of burn wound sepsis [29]. On the other hand, some investigators showed a good correlation between semi-quantitative surface swab cultures and biopsy quantitative cultures [11]. For these reasons, semi-quantitative cultures are widely used, being the most cost-effective tools and also the best in terms of workload.

Other infections – General rules used for the diagnosis of respiratory tract infections, urinary tract infections, bloodstream infections in other patients apply in burn patients [30].

Besides diagnostic purposes, microbiological cultures are useful for surveillance of the microbial ecology so that policies on empiric use of antibiotics can be more rationale, and also for early detection and tracing of cross-colonization. It is a common practice to regularly perform surface swab cultures (e.g. weekly or twice a week) of burn wounds, respiratory secretions, urine and other sites that could be of interest (e.g. catheter insertion site). In these situations, it is valuable to study microorganisms that grow below the limit of significance. These results can be reported in the patient's report, clarifying that it probably corresponds to colonization. Alternatively, the laboratory may report the overall results periodically to the infection committee; this later strategy may help avoid unnecessary antibiotic treatments. In any case, it is important that microbiologists maintain good communication with clinicians in order to establish the value that each result can have for each particular patient.

Infection control and prevention

Because of the lack of the skin barrier, the first barrier against the infection, the application of infection control and prevention measures is of paramount importance in burn patients [5].

Ideally, the burn patient should be placed in an individual room with contact precautions at any time. The use of personal protective equipment consisting of gloves, gown, mask, head cover and, eventually, shoe cover, should be respected whenever a HCW takes contact with the patient. However, some authors propose that, because patients become colonized predominantly with endogenous flora, strict isolation is not necessary except during outbreaks [31].

Each centre has to establish clear protocols according to their situation: epidemiology, infrastructure and economic condition and cultural habits.

It has no sense to write strict and complicated infection control protocols if HCW are not willing to get involved and to adhere to the practices. That is why it is more truthful to adapt "textbook" protocols to real life, but always keeping the essential: hand hygiene with a

correct technique is absolutely required in all cases to prevent cross contamination. Contact precautions are also of outstanding importance to prevent infections in these patients. However, when HCW do not cooperate, the exigence of contact precautions becomes dangerous because measures are applied incorrectly; for instance, gowns are not changed between patients, inanimate items within the room (such as monitors and computers) are touched with the same gloves that touched the patient's skin, shoe covers are not discarded when leaving the patient's area, and so on. This way, the possibilities of cross transmission are amplified instead of being reduced.

Of course, during outbreak strict precautions for each specific microorganism and mode of transmission are mandatory. HCW are more willing to comply with measures during these situations, which should be exploited for education.

Several topical antimicrobials are used to reduce the colonization of burn wounds and have proven to decrease morbidity and mortality [2].

Selective decontamination of the digestive tract with different non-absorbable antimicrobials has been studied in different groups of patients, including burnt, to decrease the colonization and subsequent infection with Gram-negative enteric microorganisms. It has proved to be effective in most cases in terms of reduction of infection and mortality [32]. Nevertheless, there is the problem of the selective pressure for the emergence of resistant bacteria and it alters the normal flora of the gut [33]. It is possible that decolonization is temporary and that colonization with MDR bacteria is restored once the antimicrobials are withdrawn; this has not been thoroughly studied.

S. aureus nasal decolonization has also been studied in burn patients [34]. Eradication of the carriage state has been achieved in different degrees in the different studies. The duration of the eradication has also been different, but in general no longer than 12 months. However, one study showed that, after decolonization with mupirocin, the overall rate of *S. aureus* burn wound colonization was reduced during the study period [35]. Because nasal decolonization is done with mupirocin, a topical antibiotic active against Gram-positive bacteria, the effect on the normal flora is more restricted than the effect of decontamination of the digestive tract. Though, mupirocin resistance in *S. aureus* is not uncommon [36].

Environmental hygiene is important to control inanimate reservoirs of microorganisms. After a patient is discharged, an exhaustive cleaning should be performed, and then, the cleaning efficiency should be controlled, for instance, with the ATP-bioluminescence assay. Environmental microbiological cultures are taken in cases of outbreak, but not routinely.

Outbreaks in burn centers have been described quite often [5,37-40]. Hand carriage, hydrotherapy equipment, aspirator probe, mattress and disinfectant solutions are some of the sources identified in these outbreaks.

Conclusion

Infections are a main cause of morbidity and mortality in burn patients. Particular considerations regarding the clinical and microbiological diagnosis of infections are required. A specialized and multi-disciplinary approach is essential for an optimal management of these patients.

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