Evaluation of Burn Wound Infection in a Referral Center in Colombia

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Abstract

Introduction Burn wound infection (BWI) is the second most important cause of death in burn patients. There is currently limited data about the incidence and clinical presentation of BWI using quantitative techniques as quantitative biopsy culture (QBC) to prevent progress to burn wound sepsis (BWS).

Methods This is a prospective cohort study of patients diagnosed with BWI, confirmed by QBC, from February 2018 to July 2019 at University Hospital of Santander (HUS). The primary outcome was to determine clinical, microbiological, and histopathological characteristics of patients diagnosed with BWI along with a positive QBC and their relationship with early diagnosis and progression to BWS.

Results 525 patients were admitted to HUS Burn Center. Of those, 44/525 (8.23%) presented a clinical diagnosis of BWI (median age, 20.5 years [1–67 years]; 25/44 [56.8%] male). QBC was positive in 26/44 (59%), *Staphylococcus aureus* 14/44 (31.8%), and *Pseudomonas aeruginosa* 7/44 (15.9%) were the mainly etiological agents isolated. Bacterial resistance to antibiotics was mostly to beta-lactams in 14/44 (31.8%), corresponding to methicillin-resistant *Staphylococcus aureus* (MRSA). Clinical signs more related to infection were erythema in 33/44 (61.3%). As many as 10/44 (22.7%) progressed to sepsis and 2/44 (6%) died.

Conclusion BWI increases hospitalization time and number of surgeries, increasing the risk of sepsis and death. The QBC allows an accurate diagnosis with lesser false-positive cases that impact antibiotic resistance and mortality. Protocols targeting this problem are needed to decrease the impact of this.

Keywords

- Burn Wound
- Burn Wound Infection
- Burn Wound Sepsis
- Quantitative Biopsy Culture

Introduction

Burn wound infection (BWI) is a significant cause of morbidity and mortality in burn patients. The implementation of an

early and aggressive debridement and silver sulfadiazine in the 90s pushed BWI from being the main cause of death to the second position, preceded only by pneumonia.^{1,2} However, this complication is associated with high mortality,

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especially in major burn patients (adults > 20% total body surface area [TBSA]; children > 10% TBSA), due to a rapid progression following immunosuppression induced by burn injuries.^{2,3}

BWI is usually caused by nosocomial microorganisms with high virulence in patients with major burns who are treated in a critical care facility. Initially, burn wound (BW) surface is sterile but rapidly colonized by bacteria of skin flora, creating a dynamic exchange with the external environment, denominated biofilms.⁴ The objective of surgical debridement is to remove biofilms and control their multiplication using topical derivatives of sulfadiazine.⁵ Thus, BW must be assessed during each wound dressing change by a trained surgeon to differentiate clinical signs of normal BW from signs of burn wound infection (BWI).⁵

Many clinical variables such as comorbidities, clinical presentation, and microbiological virulence have been associated with the progression of burn wound sepsis (BWS).⁶ For BWI assessment, qualitative techniques such as burn surface swab and culture by standard agar are used, but these have a higher rate of false positives, and overdiagnosis is common. There is not enough evidence to recommend one over the other, owing to the few studies in BWI confirmed by quantitative biopsy culture (QBC).^{6,7}

This study describes clinical characteristics, microbiological and histopathological outcomes, and sociodemographic variables of patients diagnosed with BWI in our burn unit, and BWS and their relationship with QBC positive and progression to BWS and death. The Burn Intensive Care Unit of University Hospital of Santander (HUS) in Bucaramanga, Colombia, includes a population of five million people, and over 300 patients with burns are admitted every year.

Materials and Methods

This study included all the patients admitted from February 2018 to July 2019 to the HUS's Burn Intensive Care Unit and who were diagnosed with BWI and BWS, according to the American's Burn Association (ABA) criteria.⁸ In all cases, the diagnosis was confirmed by QBC; two samples were taken in all cases, and mediums used for sample transfer were saline solution 0.9% for culture that was processed in blood agar and formaldehyde for histopathologic study.¹ The patients were monitored from clinical diagnosis until their discharge or mortality. Medical records and laboratory and pathology results were reviewed. Patients with a diagnosis of BWI prior to admission, those who had received antibiotic treatment before QBC test, and those with no clinical history data and/or incomplete histopathological and laboratory studies were excluded. All patients were taken to surgical debridement before admission to the burn unit. Data were tabulated with the help of Microsoft Excel and processed in 14th STATA version program. A univariate analysis was performed based on medians, means, proportions, and ranges. A bivariate analysis was used to find possible variables associated with outcomes, using Chi-square (or Fischer) and Mann-Whitney test.

Results

A total of 525 burned patients were admitted to the HUS Burn Unit from February 1, 2018, to July 31, 2019; out of these 44/525 (8.3%) developed BWI, based on clinical diagnosis, and 10/44 (22.7%) progressed to BWS.

Table 1 Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics	n	%	CI 95%
Sex			
Female	19	43.2	27.9–58.4
Male	25	56.8	41.6–72.1
Age			
Pediatric (under 18 years)	17	38.6	23.7–53.6
Adult (above 18 years)	27	61.4	46.4–76.3
Comorbidities			
No	30	68.2	53.9–82.5
Yes	14	31.8	17.5–46.1
Mechanism			
Scalds	24	54.6	39.2–69.9
Direct contact	18	40.9	25.8–56.0
Electric	2	4.5	0.0–10.9
Depth			
Second degree	32	72.7	59.0–86.4
Third degree	12	27.3	13.6–41.0
Extension			
Minor (less than 20% TBSA adults or 10% in children)	25	56.8	41.6–72.1
Major (above those percentages)	19	43.2	27.9–58.4
Location ^a			
Upper limb	32	72.7	59.0–86.4
Lower limb	28	63.6	48.8–78.4
Head and neck	27	61.4	46.4–76.3
Anterior torso	18	40.9	25.8–56.0
Posterior torso	12	27.3	13.6–41.0
Signs of infection ^a			
Erythema	33	75.0	61.7–88.3
Edema	27	61.4	46.4–76.3
Exudate	20	45.5	30.1–60.8
Eschar discoloration	15	34.1	19.5–48.7
Pain increasing	9	20.5	8.0–32.9
Separation of eschar	7	15.9	4.7–27.2
Loss of skin grafts	1	2.3	0.0–6.9
Lymphangitis	1	2.3	0.0–6.9

Abbreviations: CI, confidence interval; TBSA, total body surface area. HUS Bucaramanga 2017–2018.

^aChi-Square Test (or Fisher's Test)

The average age was 27 years, with a median of 20.5 years (range, 1–67 years), with a predominant adult population and male sex. Some comorbidities that caused immune disorders (diabetes, HIV, chronic corticosteroid disease, malnutrition) were recorded (►Table 1).

Scalds were the most frequent cause, followed by contact burns; second-degree burns predominated. The majority had less than 20% TBSA burns in adults and less than 10% TBSA burns in children. However, 19/44 (43.2%) had major burns. Of these, 10/44 (30.2%) were adults and 9/44 (13%) children. Most of them presented with more than one burned anatomical area, and the most frequent regions involved were the upper limbs, followed by the lower limbs. All patients with BWS had major burns (►Table 1).

Among the signs of infection, erythema was predominant (redness greater than 1 cm from the burn wound border), followed by edema, and exudate and eschar discoloration. In patients with BWS, erythema and edema were found in the same frequency 7/10 (70%) for each one (►Table 1). With regard to clinical presentation, latency period was defined as the time between burn wound and first signs of infection; early if clinical signs were evidenced into the first 72 hours since admission in Burn Unit and late if occurred after this time. Most cases developed signs in the first 72 hours after

arrival at Burn Unit (41; 93.2%), corresponding to early infection (►Table 2).

QBC was positive in 27/44 patients (61.4%); all of them presented quantitative culture with more than 10^3 colony-forming units (CFUs) per gram of tissue. However, in histopathological reports, the microbial invasion was not differentiated between IIB and IIC grades, according to Mitchell et al classification.⁹ There was a slight predominance of superficial invasion above the deep one (►Table 3).

Table 3 Histopathological findings

Histopathological findings	n	%	CI 95%
Invasion			
Superficial	6	13.6	3.1–24.2
Deep	5	11.4	1.6–21.1
Not determined	33	75.0	61.7–88.3
Infiltration			
I	2	4.6	0.0–10.9
I A	0	0.0	–
I B	2	4.6	0.0–10.9
II	6	13.6	3.1–24.2
II A	5	11.4	1.6–21.1
II B	7	15.9	4.7–27.2
II C	9	20.5	8.0–32.9
Not observed	13	29.6	15.5–43.6
Etiological agents*			
<i>S. aureus</i>	14	31.8	17.5–46.1
<i>P. aeruginosa</i>	7	15.9	4.7–27.2
<i>K. pneumoniae</i>	3	6.8	0.0–14.6
<i>S. marcescens</i>	2	4.6	0.0–10.9
<i>A. baumannii</i>	2	4.6	0.0–10.9
<i>S. saprophyticus</i>	1	2.3	0.0–6.9
<i>A. veronii</i>	1	2.3	0.0–6.9
<i>P. mirabilis</i>	1	2.3	0.0–6.9
<i>P. penneri</i>	1	2.3	0.0–6.9
<i>E. faecalis</i>	1	2.3	0.0–6.9
<i>E. aerogenes</i>	1	2.3	0.0–6.9
Fungi	1	2.3	0.0–6.9
Other	1	2.3	0.0–6.9
Bacterial resistance			
Beta-lactams	14	31.8	17.5–46.1
Carbapenems	2	4.6	0.0–10.9
Aminoglycosides	1	2.3	0.0–6.9
Lincosamides	2	4.6	0.0–10.9
Quinolones	3	6.8	0.0–14.6
Sulfonamides	7	15.9	4.7–27.2
Ureidopenicillins	1	2.3	0.0–6.9

HUS Bucaramanga 2017–2018.

Table 2 Clinical evolution

Clinical evolution	n	%	CI 95%
Latency period			
Early-onset (before 72 hours)	41	93.2	85.4–100.0
Late-onset (after 72 hours)	3	6.8	0.0–14.6
Infection			
No	17	38.6	23.7–53.6
Yes	27	61.4	46.4–76.3
Initial treatment			
No	3	6.8	0.0–14.6
Yes	38	86.4	75.8–96.9
Not reported	3	6.8	0.0–14.6
Debridement			
No	6	13.6	3.1–24.2
Yes	38	86.4	75.8–96.9
Skin graft			
No	13	29.6	15.5–43.6
Yes	31	70.4	56.4–84.5
Health care-associated infection			
No	32	72.7	59.0–86.4
Yes	12	27.3	13.6–41.0
Mortality			
No	41	95.4	88.8–100.0
Yes	2	4.6	0.0–11.2

Abbreviations: CI, confidence interval; n, number.

HUS Bucaramanga 2017–2018

*Chi-Square Test (or Fisher's Test)

Table 4 Bivariate analysis of sociodemographic and clinical characteristics and signs of infection

Sociodemographic and clinical variables	n	No infection	Infection	OR	CI	p-value ^a
Sex						
Female	19	42.1	57.9			
Male	25	36.0	64.0	1.29	0.31–5.18	0.680
Age						
Pediatric	17	41.2	58.8			
Adult	27	37.0	63.0	1.19	0.28–4.85	0.784
Comorbidities						
No	30	36.7	63.3			
Yes	14	42.9	57.1	0.77	0.17–3.49	0.694
Mechanism						
Scalds	24	37.5	62.5			
Direct contact	18	44.4	55.6			
Electrical	2	0.0	100.0	0.9	0.22–3.61	0.865
Depth						
Second degree	32	46.9	53.1			
Third degree	12	16.7	83.3	4.41	0.73–46.3	0.066
Extension						
Minor	25	44.0	56.0			
Major	19	31.6	68.4	1.70	0.41–7.28	0.402
Location^a						
A single affected anatomical area	15	40.0	60.0			
More than one affected anatomical area	29	37.9	62.1	1.09	0.24–4.62	0.894
Signs of infection^a						
Erythema	33	33.3	66.7	2.4	0.47–12.2	0.210
Edema	27	33.3	66.7	1.77	0.42–7.32	0.363
Exudate	20	35.0	65.0	1.32	0.33–5.43	0.651
Eschar discoloration	15	40.0	60.0	0.91	0.21–4.06	0.894
Pain increasing	9	44.4	55.6	0.73	0.13–4.46	0.688
Separation of eschar	7	40.0	60.0	4.57	0.46–223.1	0.894
Loss of skin grafts	1	100.0	0.0	–	–	–
Lymphangitis	1	100.0	0.0	–	–	–

Abbreviations: CI, confidence interval; OR, odds ratio.

HUS Bucaramanga 2017–2018.

^aTest chi cuadrado (o Fisher).

The most etiological agents were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Others presented with more than one bacteria growth. The bacterial resistance to antibiotics was mostly to beta-lactams, corresponding to methicillin-resistant *S. aureus* (MRSA) in all these cases. The same etiological agents were found in patients who developed BWS, with five cases each (►Table 3).

Statistical Analysis

The bivariate analysis to identify clinical variables associated with a positive histopathological result evidenced that the compromise of more than one anatomical segment has the higher relationship, followed by adult age and comorbidities.

However, none of these were statistically significant (►Table 4).

On clinical variables, rapid eschar separation was the most common sign in the cases of positive, followed by eschar discoloration, disproportionate pain, and exudate (►Table 4). The median of hospitalization days was 34 days (range, 7–146 days), and an average of 3.2 surgical procedures were performed per patient.

Discussion

BWI remains a leading cause of morbidity and mortality, despite advances in the use of topical and parenteral

antimicrobial therapy and the practice of early tangential excision.^{10,11} BWI is a clinical diagnosis, based on the evaluation of burn wound surface. In noninfected BW, overdiagnosis results in unnecessary antibiotic therapy, which has seen increased antibiotic resistance in the last decade.^{12–15} Discoloration and separation of the eschar are the signs with the highest correlation with positive QBC and BWI, in others studies skin graft loss has been reported too, although these were not evident in these cohort of patients.

For confirmation of BWI, many centers globally, including the UK, use qualitative techniques in contrast to 47% in the USA that uses QBC, despite correlation between a negative culture and negative histopathologic biopsy having a specificity of 96% to discard BWI⁹; the reason is that there are few studies using QBC according to Mitchell et al. Techniques (taking two samples with at least 0.5 grams of tissue) that evaluated their impact in early detection of BWI diagnosis were early specific antibiotic treatment, lower nosocomial infections, lesser surgical procedures and lesser time of hospitalization, as reported by Halstead et al.⁷ in their systematic review; however the evidence based on the utility and reliability of quantitative microbiology for diagnosing or predicting clinical outcomes in burned patients is limited and poorly reported.^{7–16}

Our results confirm the results of previous studies in burn intensive care units (Lilly et al¹⁷, Clark et al¹⁸) where antibiotic resistance to beta-lactams is the most frequent, followed by sulphonamide resistance. Also describing infection by multidrug resistant microorganism was associated with an increased progression to sepsis and death.^{14,17–20}

Probably, the major utility of QBC is in the diagnosis of BWI in microbial barrier property (MBP), where signs of infection are inconsistent, due to immunosuppression induced by the burn.^{6,9} Once white blood cells (WBCs) are colonized, qualitative techniques has a higher rate of false positives; 43% of our patients corresponded to MBP, of these 23% progressed to BWS with positive QBC in all cases, and an early and specific antibiotic therapy was started, compared with Ramirez et al study in the same unit burn care, where there was a reduction of 6% reduction of mortality after implementation of QBC in a longer follow-up time.^{1,2,9,16,21}

Histopathological changes did not correlate with BWS progression, and the level of invasion did not determine BWS progression; however, in this study, many samples were not were differentiated like Wolfrey et al study.²¹

Prevention of BWI requires an early clinical diagnosis and a specific antibiotic treatment to prevent progression to BWS. QBC allows an accurate diagnosis with lesser false-positive cases that impact the long-term reduction in antibiotic resistance and mortality.¹⁶ More studies are necessary for a unified approach.

Conclusion

BWI is a frequent complication in BW patients, and overdiagnosis is also common, as signs of infection are often confused with signs of burn wound healing. Confirmation

of the diagnosis is the main goal, and quantitative techniques are an accurate way to select a specific antibiotic therapy and prevent progression to sepsis.

Declaration

None.

Financial Disclosure and Products

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Author's Role/Participation in the Authorship of the Manuscript

All the authors have made substantial contributions to the realization of this manuscript, including study design, collection of data, data analysis/interpretation, and writing of the manuscript.

Conflict of Interest

None.

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