ISSN: 2692-5370

Anaesthesia & Surgery Open Access Journal

DOI: 10.33552/ASOAJ.2024.05.000617

Iris Publishers

Review Article

An update on the role of antibiotic prophylaxis for preventing burn wound infections in burn patients

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Received Date: October 28, 2024

Published Date: November 04, 2024

Abstract

Background: Burns are a primary cause of morbidity and mortality in any health setting. They have a myriad of complications often resulting from the complex physiological changes they cause in the body. Burns provide an optimized medium for bacteria to grow, hence burn wound infection is a very common presentation in any Burns Unit. Infection may result in a longer stay in intensive care, longer length of hospital stays, higher need for debridement and grafting and higher mortality rates. For this reason, some units are using prophylactic antibiotics for all burn patients. However, other centers argue that routine prophylactic antibiotics increase adverse drug reactions and add lead to multi drug resistant organisms. This review will tackle these contradicting views and assess the rate of burn wound infection with or without prophylactic antibiotics.

Conclusion: The studies relating to prophylactic antibiotics in burns have inconclusive results. Different authors discuss the benefits and downsides of prophylactic antibiotics in burn patients. More studies with greater sample size are needed to be able to draw guidelines on the topic.

Keywords: Burns; Prophylactic antibiotics; Burn wound infection

Abbreviations: TBSA: Total body surface area; SAP: Systemic antibiotic prophylaxis

Introduction

Burns are a worldwide public health challenge with substantial number of infections and deaths annually [1]. They are a primary cause of mortality within any health institution along with significant physical and psychological morbidity in patients and their relatives [2]. Burn complications may be devastating and have lifelong sequelae like scarring and contractures [3]. Such injuries also have a substantial financial burden mostly associated with the complicated treatment they entail ranging from a long intensive care stay to specialized dressings, excision and grafting and extensive rehabilitation [3,4].

The local reaction to a burn comprises oedema, increased microvascular permeability namely due to the direct heat effect, vasodilation and increased extravascular osmotic activity. The change in interstitial fluid within the heat damaged tissue causes rise in hematocrit and fall in plasma volume with decreased cardiac output and hypoperfusion within the cells. If fluids are not adequately replaced, hypovolemic shock will develop [5]. A good understanding in burn pathophysiology is essential for effective fluid resuscitation however complications related to burn wound consequences still have a significant effect on morbidity and mortality rates to date [6].

Burns provide an optimized medium for bacteria to proliferate and enter the bloodstream. The epithelial barrier loss, hypermetabolic state and immunosuppression predispose to infection in burn patients [7]. The burn itself is a source of local and systemic complications as it leads to a dysfunction in the immune system, a higher bacterial load, the risk of bacterial translocation within the gastrointestinal tract, longer hospital length of stay and a variety of diagnostic and therapeutic interventions that may have devastating complications [6]. All these factors lead to a higher incidence of septic shock in burns patients [5]. Alternative sources of infection other than wound infection in burn patients include pneumonia, catheter associated infections and thrombophlebitis [8].

Improved outcomes for burn patients have been attributed to improved fluid resuscitation, better nutrition, optimum pulmonary and burn wound care and more efficient infection control guideline and practices [8]. The concept of early excision and grafting has made significant refinements in burn care. However, to this day and age, septicemia remains the major cause of death in burn patients [1,9].

The burden that infections in burn patients may create has led to some units to prescribe prophylactic antibiotics to their patients. However, prophylactic antibiotic therapy may increase adverse drug reactions and lead to multi drug resistance [7,8]. This controversy relating to prophylactic antibiotics has led to ongoing research to assess risks and benefits of such procedure. Drug resistance is an ever-increasing problem in any hospital setting [1].

In view of this, a literature review was carried out relating to available literature about antibiotic prophylaxis in burns. The aim of this review is to analyses rates of burn wound infection rates when using prophylactic antibiotics. Secondary outcomes include assessing the length of stay in intensive care and mortality rates in these patients. The aim was set according to PICO framework as illustrated in Table 1.

Table 1: Aim of literature review as per PICO Framework.

Patient	Burn patient
Intervention	Prophylactic antibiotics
Comparison	No prophylactic antibiotics
Outcome	Rate of burn wound infection, length of intensive care unit stays and mortality

Search Strategy: An online search was conducted on Ovid Medline and PubMed to answer the research question. Data from 2017 to 2022 in English language was considered. This five-year timeframe was chosen to obtain recent results about the topic. Studies retrieved included retrospective studies and systematic reviews. All studies were carried out after 2017 implying recent data from single or multi-center studies (Table 2).

Table 2: Search Results.

Keywords	Burns, Prophylactic Antibiotics, Burn Wound infection
Search terms	Antibiotic prophylaxis in burn patients and rate of burn wound infection Use of prophylactic antibiotics in burns for reducing burn wound infections
Inclusion Criteria	Burn wounds Accidental and non-accidental injuries All age groups Single or multi-centered studies Human studies Studies after 2017 in English language only
Exclusion Criteria	Non-burn wounds Animal studies Studies before 2017 in languages other than English
Database results	(see tables below)

	Keyword/s	Database	Number of hits
1	Antibiotic Prophylaxis	Ovid MEDLINE	15192
2	Burns	Ovid MEDLINE	35440
3	Wound Infection	Ovid MEDLINE	6241
4	1 AND 2 AND 3	Ovid MEDLINE	24
5	Articles in English language only	Ovid MEDLINE	3
6	Articles from 2012 - 2022	Ovid MEDLINE	3

	Keyword/s	Database	Number of hits
1	Burns	PubMed	13770
2	Prophylactic Antibiotics	PubMed	1625
3	Burn Wound Infection	PubMed	546
4	1 AND 2 AND 3	PubMed	79
5	Articles in English language only	PubMed	11
6	Articles from 2012 - 2022	PubMed	11

Screening Evidence	Titles and abstracts were screened to select the relevant articles. Inclusion and exclusion criteria were applied. Articles that do not fall in such categories were excluded. All relevant papers were reviewed and 3 were selected.
Final Number	3

Three articles will be considered for this literature review. Selection was based on satisfying as many criteria as possible of the inclusion and exclusion criteria. Literature will be evaluated using the Critical Appraisal Skill Programmed checklist [10] and graded by the Harbour & Miller [11] hierarchy of evidence.

Literature Review

The studies considered include:

1) Systemic antimicrobial prophylaxis in burn patients: systematic review by Ramos, et al. [7].

2) Role of systemic antibiotic prophylaxis in acute burns: A retrospective analysis from a tertiary care center by Muthukumar, et al. [1].

3) The Wound Microbiology and the Outcomes of the Systemic Antibiotic Prophylaxis in a Mass Burn Casualty Incident by, Yeong et al. [12].

Ramos et al. [7] analyze systemic antimicrobial prophylaxis in burn patients. The main objective of this systematic review was to review studies relating to systemic antibiotics in burn patients. A key finding was that antibiotic prophylaxis might be effective in prevention of graft loss however there is poor evidence relating to use of antibiotic in graft loss (Figure 1).

Table 3 summarizes the key points of Ramos et al [7].

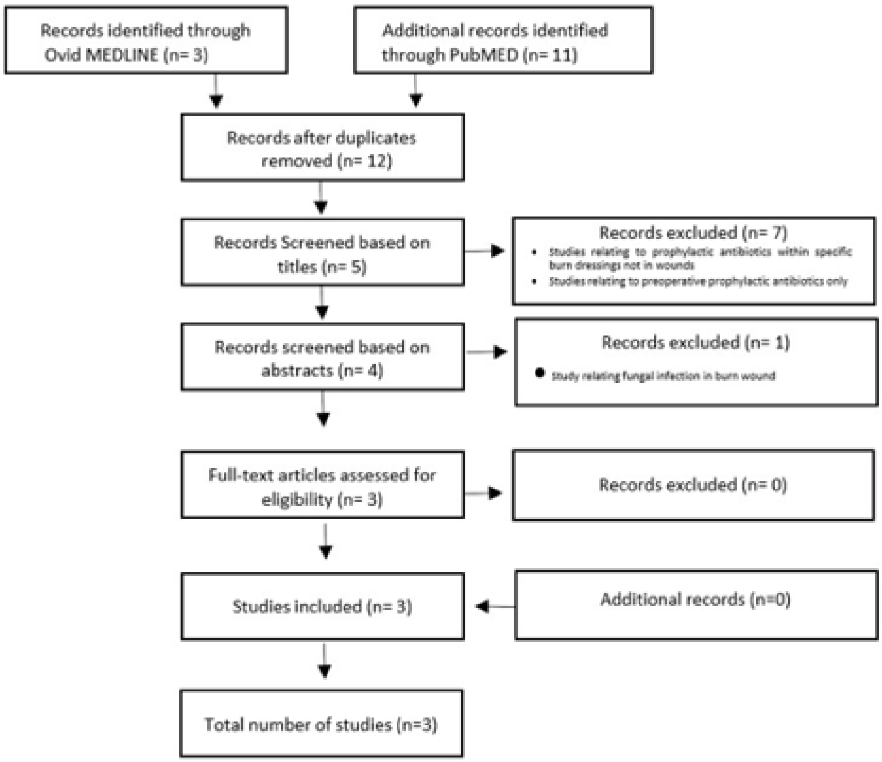

Figure 1: PRISMA flowchart.

Table 3: Aims, method and results for Ramos et al. [7].

Aim	To analyze studies regarding antibiotic prophylaxis in burn patients.
Methodology	A database search was carried out between 1966 and 2016 with no restrictions on sex, age or language. All titles and abstracts were screened by two reviewers and appropriate trials were chosen based on full text with the aid of a standardized data extraction form. Data from studies was extracted using standardized forms. The quality of evidence and strength of recommendation of these guidelines were based on the GRADE system with classification as high (Grade A), moderate (Grade B), low (Grade C) or very low (Grade D). Analysis was done by stratifying results into subgroups. The endpoints were mortality, wound infection rates, evidence of toxic shock syndrome, pneumonia and bacteremia.
Keywords	'Antibiotic prophylaxis', 'bacteremia', 'infection', sepsis' and 'toxic shock syndrome'

Inclusion Criteria	Randomized and non-randomized clinical trials; Humans with burn injuries; Burns of any TBSA or burn degree, with or without inhalational injury; Antibiotic systemic prophylaxis without clinical or documented infection through any route (intravenous, intramuscular of gastrointestinal routes)
Exclusion Criteria	Non-human trials; No systemic antibiotic use
Results	Initial search produced fifty-three results but only nineteen publications, published between 1982 and 2016 met the inclusion criteria and were considered. These include 12 randomized prospective trials, 3 before and after trials comparing consecutive periods with or without intervention and 4 retrospective studies. The main finding inferred is that prophylaxis may be effective for prevention of graft loss due to risk of infection, however its clinical relevance in acute burns is not clearly exhibited. A weak recommendation is proposed to consider prophylactic antibiotics for skin grafting.
Limitations	Variable antibiotics in different studies, different doses and duration of treatments.

The objective of the study is clearly identified at the beginning and clear inclusion and exclusion are set out as indicated. A clear indication of inclusion and exclusion criteria limits confounding as much as possible. However, the authors fail to include primary and secondary outcomes that were sought from each trial and may introduce room for bias. Additionally, selection methods are not indicated at any point and this promotes selection bias.

Ramos, et al. [7] declare no conflict of interest and no funding sources in this literature review. However, individual studies do not all contain this declaration. Some also lack ethical approval. Research studies involving human studies are bound to obtain the necessary informed consent and ethical approval to achieve good research governance. Hence lack of mention of these two points implies poor research governance.

The methodology of each clinical trial is briefly indicated. Details about search strategy, sample size and power calculation, correspondence to authors and details about unpublished or incomplete data are unheard of in the literature review. These create publication bias. Moreover, lack of power calculation introduces risk of Type II error and may hinder validity of some of the studies. A good number of the studies are multicentered to encounter this problem and get a big sample size as much as possible, yet still there is no reference to any power calculation of the publications.

Ramos et al. [7] had two reviewers to select the publications that match inclusion criteria. However, there is no mention of blinding of each study to aid selection. The GRADE system was used to assess evidence with no clue of the grades of each study and the grading difference between the two reviewers. This potentially means reduced power and suggests a potential source of selection bias.

Results are very well displayed in Table 4.

Table 4: Clinical trials comparing antibiotic prophylaxis in burns vs placebo or no intervention adapted from Ramos et al. [7]). ATB=antibiotic, MV=mechanical ventilation, TBSA=total body surface area.

Study	Prophylaxis period	Age of participants	Burn severity	Study design	Objective	Intervention	Participants	Outcomes	Adverse effects	Major limitations
Durtschi et al. [13]	Early postburn	Adults	Non-severe	Prospective, randomized, double-blind, placebo-controlled trial, single-center	Early wound infections	Penicillin (5 days)	ATB: 25 Control: 26	Cellulitis 44 vs 27% Burn wound sepsis 8 vs 11%	Yeast colonization 1/11 vs 0/17	Unpowered trial, Heterogenous population. Patients excluded after randomization: 46 (47%) Retrospective
Timmons [14]	Early postburn	Pediatrics	Non-severe	Retrospective three cohorts of consecutive periods, single- center	Betahaemolytic streptococcal wound infections	Erythromycin (5 days)	ATB: 102 Control: 167	Burn wound infections 2 vs 4%	Not assessed	Retrospective
Alexander et al. [15]	Perioperative	Pediatrics	Severe	Prospective, stratified, randomized, single-center	Bacteremia, skin graft loss	Targeted antibiotics (during surgery)	ATB: 35 Control: 24	Bacteremia 8 (8%) vs 16 (18%) Graft takes 79.5 vs 83.1% Mortality 14.3 vs 8.8%	Not assessed	No information about allocation concealment
Piel et al. [16]	Perioperative	Adults and pediatrics	Severe	Prospective, randomized, placebo-controlled trial, single-center	Bacteremia	Cephalosporin (12h)	ATB: 25 Control: 26	Bacteremia TBSA <30% = %, 30-60% = 8.3 vs 7.7%, >60% = 40 vs 75%	Not assessed	Incomplete data
Griswold et al. [17]	Perioperative	Adults	Non-severe	Retrospective, single-center	Donor- and graft-site infections	Cephalothin	ATB: 190 Control 23	Less donor-site infection (7 vs 30%)	Not assessed	Non-random assignment

Munster et al. [18]	Early postburn and postoperative	Adults	Severe	Prospective, randomized, single- center	Endotoxemia complications	Early postburn polymyxin B (7 days) and perioperative polymyxin B (5 days with excision in procedure in day 3)	ATB early postburn: 22 Control early postburn: 23 ATB perioperative: 6 Control perioperative: 11	Endotoxemia level >10pg/mL (81 vs 44.5%) Postoperative endotoxemia increase (15 vs 62%)	Not assessed	Unpowered trial to significant clinical impact
Deutsch et al. [19]	Early postburn	Adults	Severe	Prospective, randomized, single-center	Burn wound infection	Systemic and non-absorbable oral/nasogastric tube, Erythromycin, neomycin, nystatin (10 days)	ATB: 15 Control: 12	No differences in overall outcomes	Diarrhea, Earlier infection by *Pseudomonas* spp.	Unpowered trial for more relevant outcome variables
Steer et al. [20]	Perioperative	Adults	Non-severe	Prospective, randomized, double-blind, placebo-	Bacteremia, burn wound infections	Teicoplanin (single dose)	ATB: 110 Control: 110	Bacteremia 8 (7%) vs 51 (46%)	Adverse events 24 (22%) vs 15 (14%), abnormal liver	N/A

The results are self-explanatory yet they lack details on the calculations used and whether univariate and/or multivariate analysis were performed for each study, increasing risk of covariance. As previously mentioned, the power of the studies is indeterminable from the information presented hence one cannot assess significance of results fully.

In conclusion, data from most of the clinical trials reviewed implies that there is not enough evidence to support the role of systemic antibiotic prophylaxis in the management of burn patients. Prophylaxis may be considered in those needing mechanical ventilation and in skin grafting surgery as it may reduce rate of infection. The systematic review may be graded 1- according to Harbour & Miller [11] classification given the high risk of bias.

The retrospective study by Muthukumar et al. [1] relates to the role of systemic antibiotic prophylaxis in acute burns. The study analyzed data of one hundred fifty-seven patients divided in two study arms-with and without antibiotic prophylaxis. It was a single-centered study carried out at a tertiary burn care center in India over six months. The aim of the study was to assess the role of antibiotic prophylaxis with regards to infection and mortality rates.

The main conclusion of this analysis was that routine use of prophylactic antibiotics in burn patients does not affect the rate of infection and mortality. Antibiotic prophylaxis is useful in some subgroups such as in patients with inhalational burns and burn patients suffering from pneumonia.

The aim, methods, results and limitations of the study are summarized in Table 5. The objective of the study is well defined with primary and secondary outcomes indicated so the study is well designed to answer the research questions. Data collection methods were also chosen to meet these outcomes. The authors define inclusion and exclusion criteria of the study so that it is easily reproducible and it has increased reliability. The selection method of patients is not indicated creating risk of selection bias. Additionally, the study lacks a power calculation increasing risk of Type II error. Patients included are from a single-center in a developing country and may not be completely relevant to the local population or to most European countries. This reduces external validity.

Table 5: Aims, method, results and limitations for Muthukumar et al. [1].

Aim	To determine the role of routine prophylactic antibiotics in burn patients with respect to infection and survival rates. Secondary outcomes include assessing rate of infection in inhalational burns and pneumonia subgroups.
Methodology	One hundred and fifty-seven patients treated at a tertiary burns centre in Delhi, India were included in this retrospective, single-centred study. The patients were subdivided in two groups with seventy-seven patients in the prophylaxis group and eighty patients in the non-prophylaxis group. All had a standard one month follow up. Sepsis was considered in cases of clinical suspicion or documented infection and fulfilling a set of criteria as determined by the authors. Microbiological cultures were taken by surface swabs after cleaning the wound. Tissue biopsies or sputum cultures were taken depending on the particular case. Diagnosis of inhalational burns and pneumonia was standardized according to defined criteria within the history and examination. Prophylactic antibiotics prescribed included intramuscular penicillin with beta lactam or third generation cephalosporin. These were initiated on admission or within the first twenty-four hours of the hospital stay. Statistical analysis was carried out using t test for continuous variables and Tukey's multiple comparison test for individual or multiple variables.
Inclusion Criteria	Patients aged eighteen to fifty years; Treated at Department of Burns, Plastic & Maxillofacial Surgery, Vardhman Mahavir Medical College & Safdarjung hospital, Delhi, India; Thermal burns and scalds with TBSA of 30-60%
Exclusion Criteria	Documented pre burn infection; Patients with history of diabetes mellitus; Organ failure at time of presentation; Patients with comorbidities relating to the respiratory tract
Results	The mean age of each cohort was 31.36 years with most patients falling in the 2029 years category. The majority of patients were males. Seventy-six percent of burns were accidental injuries with a mean TBSA of 47.26%. Inhalational burns occurred in sixty-eight patients while sepsis occurred in a total of seventy patients. Sepsis developed in 42.86% of the prophylaxis group with mean detection day being the sixth day from injury. The first febrile episode was on the fifth day on average with a mean length of hospital stay of twenty -two days. In comparison, out of the eighty patients in the no prophylaxis group, 46.25% developed sepsis. The average day for detection was day seven post injury with a mean first febrile episode on day six. Antimicrobial treatment was started on the sixth day on average. Pseudomonas aeruginosa was a common causative organism in both groups. Subgroup analysis was done for patients with inhalational injury and pneumonia for both groups. Multivariate analysis for no prophylaxis group was carried out and pneumonia was identified as an independent risk factor for mortality.
Limitations	Study design (single-centred retrospective study), small sample size, no power calculation, variable antibiotic dosages

The study has a number of standardized factors namely criteria for sepsis, technique for microbiological samples, examination findings for inhalational burn diagnosis and type of antibiotics used. However, there is no mention of the level of expertise of the surgeon/nurse taking swabs for culture or the experience of the surgeon carrying out initial diagnosis of inhalational injury. Additionally, there is no indication as to whether the same surgeon follows the patient throughout the whole month. All these factors introduce risk of information bias and create a high degree of variability. These might lead to decreased sensitivity of the study.

Statistical analysis was adequately designed. The authors had particular tests for categorical and noncategorical data such as the t test being used for continuous variables. A significance level of $p<0.05$ was set. A combination of univariate and multivariate analysis decreases risk of covariance and increases statistical rigor. Muthukumar et al. [1] declare no conflicts of interest however fail to mention ethical approvals which reflects poor research governance as there is a higher risk of breach of Declaration of Helsinki [13].

Results are well explained with graphic representation that help the reader even more. A number of characteristics in the prophylaxis vs no prophylaxis group are identified and compared as per Figure 2 [14-21].

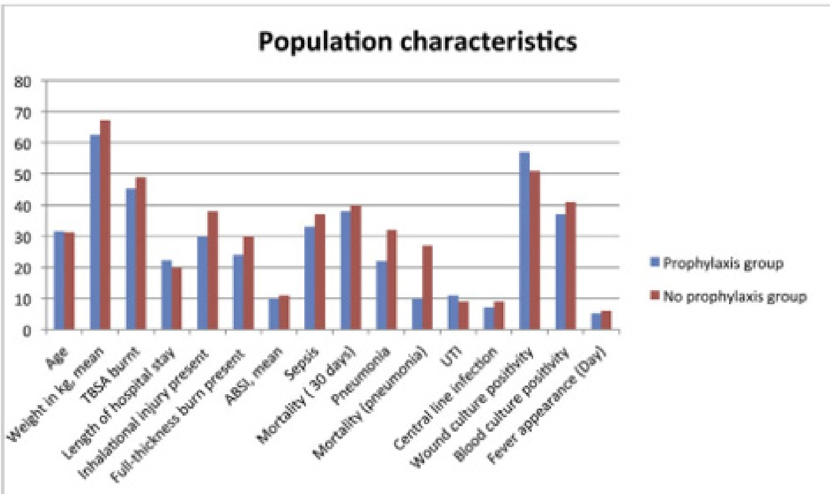

Figure 2: Population characteristics (prophylaxis vs no prophylaxis group) [1].

Results show no difference between both groups with regards to rate of sepsis and length of stay. Very minimal difference is noted in the inhalational/pneumonia prophylaxis group with marginally improved outcomes– lower rate of sepsis, decreased length of stay and decreased mortality. These results provide an answer to the research question however they are very limited with high degree of bias.

In summary the study concludes that there is no significant difference in infection rates in burns patients with or without prophylactic antimicrobial therapy. The study has high degree of bias and confounding and would be graded as 2- according to Harbour & Miller classification [11]. Larger studies from multiple centers are required to improve external validity and have solid conclusions for any recommendations or change in practice.

Yeong et al [12] describe the wound microbiology and the outcomes of the systemic antibiotic prophylaxis in a mass burn casualty incident. Thirty-one patients treated at a tertiary hospital in Taiwan in 2015, following a cornstarch explosion, were considered in this retrospective study. The authors analyzed the wound microbiology and effect of SAP of patients involved in this incident. They looked at wound infection rate, type of wound pathogens and rate of blood stream infections [22-30].

The main finding from the study was that the use of SAP for two to fourteen days following admission resulted in a reduction of wound infection rate from 45% at week 1 to 10% at week 4. Polymicrobial and rare pathogen wound infections were common among this cohort, namely due to sterility breech. No blood stream infections were evident at week 1 following burn injury [31].

Table 6 highlights the aims, method, results and limitations of this study [12]. The aim of this retrospective study is similar to the study's title. Although self-explanatory, there are no primary or secondary outcomes defined and the objective is subject to the reader's interpretation. Data is collected from a single-center for one mass burn casualty incident over one month. A power calculation was not done when choosing the sample size. Additionally, there are no inclusion or exclusion criteria and the selection criteria are not identified. These limited parameters reduce external validity and increase chance of bias with a higher potential for Type II error.

Table 6: Aims, method, results and limitations for Yeong et al. [12].

Aim	To assess burn wound microbiology and effects of using SAP in mass burn casualties to prevent development and progression of wound infections.
Methodology	The study was carried out at a tertiary center, the National Taiwan University Hospital. The Centre has fourteen beds within the burn unit including four intensive care beds. Thirty-three patients who sustained burns following a cornstarch explosion in Taiwan in June 2015 were considered. The cohort included patients admitted between 27th June and 1st July 2015 only. Patient data was collected in a database from electronic data and case notes. Ethics approval was obtained from the local Ethics Committee. Wound infection was diagnosed through a swab culture following clinical signs of infection. Silver sulfadiazine was the initial topical antibiotic used. Wound cultures were performed on the day of admission and weekly thereafter or on suspicion of wound infection. Burn excisions were initiated on day 3 to day 5 post injury and tissue specimens were submitted upon excision. Central lines were routinely changed every seven days on normal skin and every three days on burnt skin. Pulse-field gel electrophoresis was used to determine the genotypes of multi-drug-resistant organisms. The isolates showing pulse-field gel electrophoresis profile with more than 80% similarity were defined as being of the same pulso type. SAP was started for all patients on admission and continued as an empirical treatment for 2-14 days together with central and peripheral line insertions and ventilatory support. Antibiotics were switched to therapeutic types depending on culture results. Demographics and culture data were analyzed using descriptive analysis. Continuous variables were expressed as mean and standard deviation. Unpaired student's t-test was used for comparison analysis and p<0.05 indicated a significant difference.
Results	Out of the 31 casualties, there were 10 men and 21 women. The average age of the patients was 21 years. The mean surface area of burns was 41.9% total body surface area TBSA. The most common injuries were deep dermal to full thickness burns, mostly in the lower extremities. Fourteen patients needed mechanical ventilation. Ten patients had minor inhalation injuries based on bronchoscopy results. Fifty-three positive cultures were obtained as follows: -Burn wound, n=37 -Bloodstream, n=9 -Lung, n=5 -Urinary tract, n=2 Over the first week, 55% of wound pathogens were gram negative and the rest were gram positive organisms. Fourteen days later, organisms changed to 46%-gram negative organisms, 22% gram positive and 22% Candida species. Within 72 hours from time of injury, 83% of bacterial cultures were polymicrobial. The overall wound infection rate was 95% in burns with 40% or more TBSA and 42% in burns with TBSA <40%. The incidence of multiple drug-resistant organism infection rate was 39%. On the day of admission, SAP was started in 29 patients. Two patients were referred from another hospital at one week post burn injury and were started on therapeutic antibiotics based on existent cultures. No mortality occurred in the cohort sample.
Limitations	Study design (small single-centered study), limited study period, no standard guidelines with regards to SAP use, lack of quantitative differential diagnosis for infection

Standard techniques were used to obtain diagnosis through swab cultures upon signs of clinical infection, an initial silver sulfadiazine cream and repeated cultures. Lines were routinely changed to minimize risk of infection. Nonetheless the level of expertise of the doctor caring for all casualties, whether all patients were under the care of same physician and techniques used to insert lines and catheters are not mentioned. These factors introduce risk of observer bias.

Statistical analysis is very limited. The unpaired t-test was used to analyze continuous variables and a statistically significant level was set at 0.05. There is no univariate or multivariate analysis hence one cannot ascertain whether results are due to significance or covariance. This implies poor statistical rigor [32].

The main outcome of the study indicated the commonest pathogens in burn wounds, with Staphylococcus species and Enterococcus faecalis being the commonest organisms cultured in the first week while multiple drug-resistant Acinetobacter baumannii was the commonest pathogen cultured thereafter. A delay to first blood stream infection was noted. Results were compared to a similar study by Sherry et al. [33] stating that microbiology of wildfire burn victims differs significantly from other burns mainly due to the difficult preventative measures in a burn disaster. SAP prevented transmission of rare human pathogens and the rate of infection overall and delayed the first episodes of blood stream infections. High incidence of fungal and multiple drug-resistant organisms was noted in SAP strategies.

In conclusion, the study implies that SAP is beneficial in burn wounds. However, results are limited to mass burn casualty incidents and applicable on a very small population. Given the high risk of bias, the study may be graded as 2- according to Harbour & Miller classification [11]. Further studies with greater numbers over more centers are required to obtain transferable results.

Conclusion

All studies relating to prophylactic antibiotics in burns analyzed in this review have inconclusive results [1,7,12]. Ramos et al. [7] described no benefit in systemic antibiotic prophylaxis. This is also supported by Muthukumar et al. [1]. Contrastingly, Yeong et al. [12] suggested that systemic antibiotic prophylaxis is beneficial in burns. However, it must be noted that this study was carried out following a mass burn casualty incident. All authors were aware and exhibit the limitations of their studies namely single centered studies with lack of power calculation and non-standardized data collection techniques.

The studies have a score of 1- or 2- on Harbour & Miller [11] classification given the high degree of bias. This urges for more rigorously conducted studies, ideally from multiple centers with greater numbers.

Acknowledgements

None.

Conflict of Interest

No conflict of interest.

Reference

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Citation: Jessica Dowling*. An update on the role of antibiotic prophylaxis for preventing burn wound infections in burn patients. Anaest & Sur Open Access J. 5(4): 2024. ASOAJ.MS.ID.000617. **DOI:** 10.33552/ASOAJ.2024.05.000617.