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Review Article

Prevalence of *Pseudomonas aeruginosa* in burns and the recent trend in antibiotic sensitivity pattern

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Abstract

A small critical review that affirms the omnipresence of Pseudomonas aeruginosa in burn infections worldwide that area localised on the strains screened and on their susceptibility to the antibiotics that determines the treatment regime. Thus, treatment of burn wound infections was found to be efficient when localised regionally and locally. This review discusses the emergence of ESBL resistant *Pseudomonas aeruginosa* strains that are resistance to even vancomycin and cephalosporins (expect cephamycins, cefoxitin and cefotetan) and the evolving research on novel molecular drug, nubiotics. This emphasizes the need for the judicious and cautious use of the prevalent drugs at least until the release of new generation of drugs.

Keywords: Pseudomonas aeruginosa, burns, antibiotic sensitivity pattern

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1. Introduction

The human body has an amazing and well-established first line of defense mechanism that is colonised by friendly microbes that becomes armaments and equip the organ system with an a range of immune mediators that elicits inflammatory cells to neutralise and evade the invading bacterial and fungal pathogens [1,2]. Thus after a burn incident the patient is going to suffer from the strongest defence mechanism of the body being lost until healed. Besides, the trauma and stress paves way for easy evasion by a wide range of microorganisms and their colonisation leading to sepsis [3, 4].

One of the common opportunistic pathogen—microbes that are normally abode in the skin, which becomes a pathogen once their immune power is compromised— is *Pseudomonas aeruginosa* [5]. These organisms are the most common organisms that are responsible in sepsis of burn wounds as they can thrive in facultative aerobic conditions. Furthermore, they can get into the blood stream and secrete numerous virulent factors that result in endotoxicity syndromes that ultimately lead to sepsis and finally death [6].

With the number of incidences of *Pseudomonas* sp infection becoming prominent and the addressal of the issue using broad-spectrum antibiotics becoming a common practice, the microbe have developed multi-drug resistance mechanisms. Some of the common drug resistance mechanisms will include impermeability to antibiotics, multi-drug efflux mechanisms and production of β - lactamases like AmpC β – lactamases [7]. Thus, this is necessary to understand the molecular and cellular mechanism of these microbes for counteracting their host interactions to cause sepsis in burn wounds to develop novel drugs and to streamline the currently used drugs by adopting standard screening procedures for relevant and targeted use on individual patients. Furthermore, knowledge on the antibiotic spectrum of these organisms will warrant efficient use of the

prevalent drugs in use in the treatment of burn wounds and prevent infection and sepsis. This short review will thus focus on the recent developments in the microbiology of *Pseudomonas* sp. in burn wound infections: drug resistance mechanisms and currently available drugs for efficient treatment.

Burns, Burn Centers and their implications:

Burn injuries are the most evasive injuries leading to major complications because they affect the first and the most powerful defence fortress of the body, the skin. Burn injuries are divided into three categories: a) first degree burns that evade the topmost layer of the skin, b) second degree burns evades the skin until the dermal layers or subcutaneous damage, and c) third degree burn injuries are the ones that penetrate deep down into the inner layers of the skin. Infection of injuries is a serious menace delaying healing of burn wounds and spread of injury due to infection [8].

The most commonly infesting microbe is Pseudomonas aeruginosa that area facultative and affect individuals using quorum sensing method for invasion with the production of virulence factors like proteases, exotoxin A, hemolysins and pyocyanin for invading the tissues. The protease system is the first mode of system in action, the products of which elicits the second phase of quorum sensing system, the hemolysin system. A research by a group of researchers in Auburn University showed that the presence of quorum sensing system in these organisms makes them more virulent.

Almost worldwide, owing to the seriousness and the need for quarantine to prevent spread of infections and to transfer of infections from these burns patients, burn centres are established. The normal hospital flora and those prevalent in the burn patients are routinely screened for prevalence, antibiotic susceptibility and resistance.

Distribution of *Pseudomonas*:

Of the three most common infections of *Pseudomonas aeruginosa*, bacteremia in severe burn victims [9] has evolved multi-drug resistant strains to create havoc in providing effective treatment. Besides, being the normal flora of the body that turns opportunistic in burn patients, these strains have been the main source of infection for nosocomial infection that are transmitted through fomites, vectors and patient-patient or patient-nurse-patient (figure – 1) for any wound infection. The main reason for *Pseudomonas aeruginosa* being a menace is the production of two important enzymes: a. elastase —degrades collagen and noncollagen host proteins to disrupt the integrity of the basement membrane; and b. protease — affects the innate and acquired host immune response. Yet another reason for easy colonisation of this bacterium over others in burn patients in the presence of *lasR* gene, which is responsible for initiation of quorum sensing for the bacterium that in turn aids in production of virulence factors and biofilm formation that plays a critical role in pathogenesis [10]. However, the

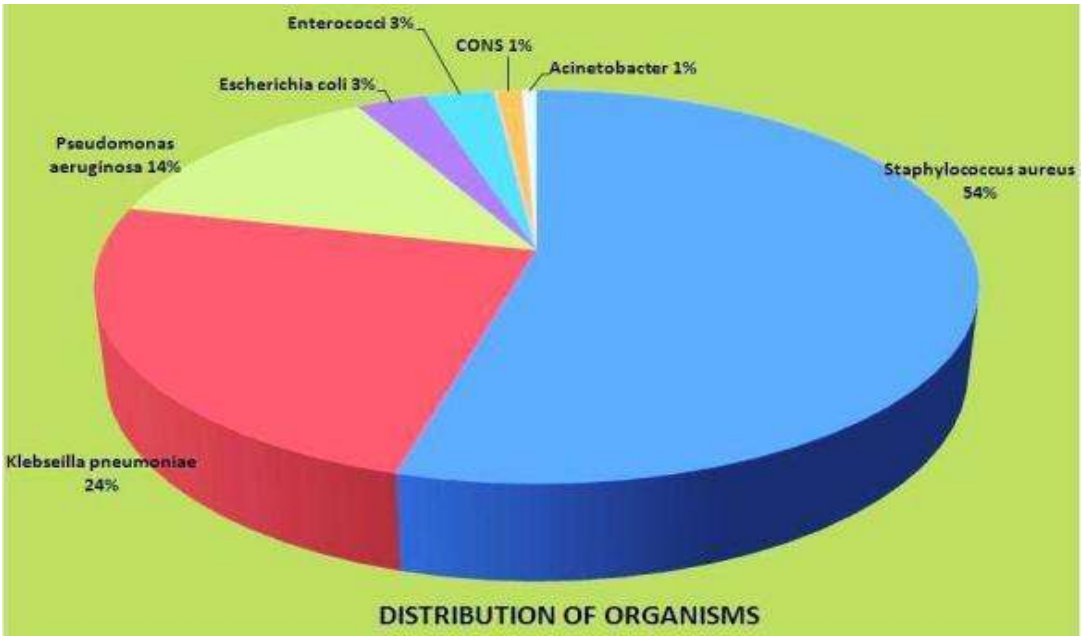

Figure 1: Distribution of micro-organism

interesting observation is the narrow range of microbes that are isolated from the wound infections when the skin's defence barrier is lost, but is best explained as monopoly of the wound infecting organism.

Drug resistance in *Pseudomonas*:

The current trend from the perusal of literature shows that *Pseudomonas* strains infecting burn patients have become completely susceptible to Ceftazidime (33.9 %) while Imipenem was the only sensitive drug that could be used against any pseudomonal strain. Furthermore, this has been observed that regular screening for antimicrobial susceptibility is essential for effective treatment at local and regional level for judicious use of antibiotics and prevent development of new antimicrobial resistance strains [9].

Livermore DM (1987) [11] in his studies said that the resistance in *Pseudomonas* sp is attributed commonly against α-carboxy- and amino-penicillins, third and fourth generation cephalosporins, carbapenems, aminoglycosides, fluroquinolones and monobactams. Cephalosporin and aminopenicillin resistance is developed by mutations that cause changes in the regulation of efflux and influx of these anti-pseudomonal drugs and by hyperproduction of chromosomal AmpC β-lactamase. As most of the efficient drugs against this microbe falls in this category, treatment of *Pseudomonas* sp. becomes difficult with the evolution of resistant strains in the hospitals.

Recent studies in Iran showed that amongst burn patients, pseudomonad species were resistant to silver sulfadiazine but not to silver nitrate solution and were susceptible only to carbapenems. Similarly, resistant strains were isolated in hospitals of Greece wherein the resistance was attributed to nearly a number of chromosomal mutations causing multidrug resistance. In South Korea, resistant strains secreted hydrolysing enzymes that imparted resistance to these drugs. Thus, drug resistance in *Pseudomonas* strains has made the present generation drugs in use inefficient and is becoming a scarce to find an efficient drug that needs to be used judiciously and with fear for development of resistance. [12].

Prevention and Management of Multi-Drug Resistance:

Topical application is the best therapy for burn infections as the topical lotions than creams will be water based, thus a coolant and will have more spreading ability thereby covering the wound area giving the lost protective covering for the skin to prevent new invasion and further spread of infection. Moreover, the antibiotics present in the lotions reduce the microbial load [13]. These agents are applied directly on the dressing to decrease occurrence of new wound by the applicator and transfer of infectious agents to the container. The most common agent that is used in the treatment of burn wounds is silver that disrupts the bacterial cell's respiratory complex by binding to the thiol group of these enzymes; however, recently this was found that silver was toxic to keratinocytes and fibroblasts, thus delaying wound infections [14].
Intensive research on better medicines for treating burn wound infections led to the discovery of moisture exposure therapy to reduce surface tension caused by dehydration and the use of silver sulfadiazine being an excellent antibacterial agent for *Pseudomonas aeruginosa* and other enteric Gram-negative bacteria. Today there are ready-made dressing materials with nanocrystalline silver coats available for treating burn wound infections especially against *Pseudomonas* sp under the Acticoat AB and have antibacterial efficiency against resistant ESBL strains of *Pseudomonas aeroginosa*.

ESBLs are extended spectrum beta-lactamase enzymes (ESBLs) are the recently evolved resistance mechanisms and these enzymes are becoming a hospital menace by introducing many resistant strains as in studies by Azizi et al. (2015) [15] and Ravichandran (2015) [16]. These strains are resistant to all antibiotics including cephalosposrin excluding cephamycins, cefoxitin and cefotetan (Ravichandran, 2015) [16]. With the advent of molecular biology, came the idea of using protonated nucleic acid-based drugs, nubiotics that are administered topically at the site of administration and intravenously or subcutaneously for systemic treatment to treat burn infections against *Pseudomonas aeruginosa* (Dale, 2004) [6]. The administration of these drugs for routine use is still novice and will take time

before reaching wide use and until then the judicious use of antibiotics is the best option to treat these burn wound infections.

Conclusion

Thus, the perusal of literature affirms that along with other types of chemotherapeutic agents that rejuvenates the damaged skin to heal faster, the target specific use of antibiotics based on regular normal microflora that are regularly screened in the hospital will be effective. However, in critical cases this is necessary to choose individual specific antibiotics. While there are also under research the avenue for emerging novel drugs to treat burn wound infections like nubiotics. What more is needed is to understand the mechanism of drug resistance and the route of emergence of resistant strains of *Pseudomonas aeruginosa* like the ESBLs that will aid in the development of these novel targeted drugs. However, judicious use and regular determination of efficient antibiotics and its concentration is the unsurpassable option for ethical medical practice.

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