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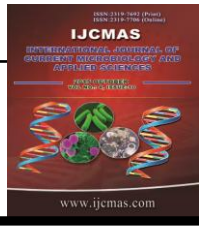

Original Research Article

Incidence and Clinical Significance of Coagulase Negative *Staphyloocci* in Blood Culture

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A B S T R A C T

Coagulase-negative staphylococci (CoNS) are a group of micro-organisms that are increasingly implicated as a cause of significant infection and the leading cause of bacteremia. One important predictor of true bacteremia is the isolation of CoNS from multiple blood cultures, presuming that the isolates represent the same species. Thus the objective of this study was to determine the significance of repeated CoNS isolated from blood cultures. The study was conducted in a teaching tertiary care hospital. The study period was between January 2013 and June 2014. A total of 1500 samples were received from medicine and pediatric wards including intensive care units. Of the 1500 blood samples 480 were from adults, 360 from pediatric and 690 from NICU. Blood cultures were performed by Castaneda's method using Hi-Media. Out of 1500 blood samples cultured from different age groups, 182 (12.3%) yielded bacterial growth, of which 86 (5.73%) were coagulase negative staphylococci, which represented 47.25% of the total isolates. Repeated isolation and antibiotics susceptibility testing from blood cultures are strongly recommended. This practice will reduce irrational use of the antibiotics and reduce the emergence of resistant strains that indirectly reduce total hospital costs.

Keywords

Coagulase negative Staphylococci (CoNS), Blood culture, Bacteremia, Contaminant, Castanedas method

Introduction

Septicemia is a clinical syndrome which is characterized by fever, chills, malaise, tachycardia, hyperventilation and toxicity or prostration, which results when the circulating bacteria multiply at a rate that exceeds their removal by phagocytosis (Washington Winn *et al.*, 1997). During septicemia, organisms are released into the blood stream at a fairly constant rate and also during the early stages of certain specific infections, bacteria continuously present in the blood stream (Forbes *et al.*, 2007). The mortality rate from septicemia may be 40% or higher and hence, the timely recovery of bacteria from the patients' blood can have a great diagnostic and prognostic importance. Hence, it becomes mandatory that every precaution must be taken to minimize the percentage of contaminated blood cultures. The critical factors which must be decided by the laboratory include the type of collection, the number and timing of the blood cultures, the volume of

blood, the amount and the composition of the culture medium, when and how frequently to subculture and the interpretation of the results (Washington Winn *et al.*, 1997).

Coagulase-negative staphylococci (CoNS), the most frequent blood culture isolates, are predominantly blood culture contaminants, but they are also a significant cause of bacteremia'. The vast majority of infections (or diseases) assumed to be caused by CoNS are a significant consequence of hospitalization. Recent reports taken from the National Nosocomial Infections

Surveillance System (NNIS) during the late 1980s and early 1990s have indicated that CoNS are among the five most commonly reported pathogens" (National Nosocomial Infections Surveillance System, 2004), This survey and others revealed that CoNS accounted for 36, 51 and 38 percent of all blood stream isolates in Medical, Neonatal and Pediatric Intensive 138 Care Units respectively" (Wisplinghoff *et al.*, 2004).

Clinical criteria in predicting whether CoNS isolated from blood cultures are associated with bloodstream infection are neither sensitive nor specific (Herwaldt *et al.*, 1996). Repeated CoNS should be of the same strain to be clinically significant, and should be confirmed by genotyping, which is not widely available (Singh *et al.*, 2006). These uncertainties regarding the significance of CoNS isolated from blood cultures may result in over-diagnosis and, indirectly, overuse of anti-staphylococci drugs, especially vancomycin, which may contribute to the development of resistance that will amplify the likelihood of morbidity, mortality and total hospital costs (Beekmann *et al.*, 2005). Thus the objective of this study was to determine the significance of repeated CoNS isolated from blood cultures.

Materials and Methods

The study was conducted in a teaching tertiary care hospital. The study period was between January 2013 and June 2014. A total of 1500 samples were received from medicine and pediatric wards including intensive care units. Of the 1500 blood samples 480 were from adults, 360 from pediatric and 690 from NICU (Table 1). Blood cultures were performed by Castaneda's method using Hi-Media. These bottles were incubated at 37ºC for 7 to 10 days and subcultures were performed after 24 hours of incubation, 72 hours of incubation, 120 hours of incubation and 240 hours of incubation on Mac Conkey's agar, chocolate agar, and blood agar. These plates were incubated for 18 to 24 hours at 37ºC and the growth, if any, was identified by the standard CLSI procedures (Washington Winn *et al.*, 1997). Susceptibility testing was performed by a disc diffusion method according to the Clinical Laboratory and Standard Institute (CLSI) recommendations and was interpreted accordingly (Washington Winn *et al.*, 1997). The following antibiotics were tested: erythromycin (15 µg), gentamicin (10 µg), clindamycin (2 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), oxacillin (1 µg) and vancomycin (30 µg). Two samples of blood cultures were obtained from all the groups, except neonates, from which only one sample was obtained.

On the basis of previous studies on coagulase negative staphylococcus (CoNS) (Souvenir *et al.*, 1998; Zaidah Abdul Rahman *et al.*, 2013) clinical criteria for true bacteremia were developed for this study. Essential clinical criteria for true bacteremia included one or more of the following (Souvenir *et al.*, 1998): persistent temperature of ~38°C or body temperature below 36°C, hypotension (BP <90mmHg), Leucocytosis or neutropenia with left shift

differential or disseminated intravascular coagulopathy (DIC). In addition major risk factors for potential infection caused by skin flora was required which included: long term intravascular catheterization (mainly used in critical care units) and immunocompromised patients with central lines. Laboratory criteria for classification of true bacteremia included: patients with the same bacteria isolated from at least two sets of blood cultures, or patients with the same species isolated in one set of the initial blood cultures and additional blood cultures in the presence of systemic inflammation reaction syndromes. Patients who were receiving antibiotics therapy prior or during blood culture sampling were excluded from the study.

Results and Discussion

Out of 1500 blood samples cultured from different age groups, 182 (12.3%) yielded bacterial growth, of which 86 (5.73%) were Coagulase negative staphylococci, which represented 47.25% of the total isolates. The isolation was seen maximum in the pediatric age group (12.77%), followed by adults (3.75%) and NICU 9(3.18%) patients. According to the clinical classification, there were 09 patients out of 86 isolates with significant bacteremia (10.46%), 11 patients (12.79%) could not be ascertained as having blood stream infection (pseudobacteremia) and 66 patients with contaminated blood cultures (76.74%). The total contamination rate was calculated to be 4.4% of the total blood cultures performed during the study period.

Resistance rate was very high to penicillin (98%), followed by erythromycin (91.4%), cotrimoxazole (82.3%), gentamicin (74%), amoxicillin-clavulanic acid (76%) and clindamycin (62%). Sensitivity was 100% to vancomycin.

Blood for culture is a routine procedure for investigating the cause of fever or suspected infection in the majority of hospitalized patients and certain patients attending an emergency department. Isolation of a true pathogen from blood culture ultimately warrants treatment with an appropriate antibiotic. Problems occur when the isolated organism is of doubtful significance, such as CoNS, which require further clinical assessment and extra laboratory tests to help the physician in appropriate patient management. For a clinical microbiologist, interpretation of the clinical significance of isolated CoNS from blood culture continues to be complex. The isolation of CoNS from blood on more than one occasion and clinical parameters are used habitually in determining the clinical significance of the isolate (Zaidah Abdul Rahman *et al.*, 2013). However, a gold standard for such differentiation still does not exist (Weinstein, 2003).

As per our study, the contamination rate of the blood culture was 4.4 %, which correlates with two other studies (Weinstein, 2003; Chandrasekar and Brown, 1994). The actual rates for the contamination vary widely from institution to institution, ranging from 0.6% to over 6% (Chapnick *et al.*, 1991; Hall and Lyman, 2006).

The incidence of true bacteremia in the literature is reported to be 10% to 30% (Souvenir *et al.*, 1998; Ching-Chi Lee *et al.*, 2007). Although the incidence of positive blood cultures for CoNS is being increased due to many factors, including the advances in microbiology techniques, changes in therapeutic modalities and patient population with an increase in the use of intravascular devices; the vast majority of CoNS is still encountered as contaminants of blood cultures.

Table.1 Total number of samples & isolates in different age group

Age group	Number of samples	Number of isolates
Adults	480	18 (3.75%)
Pediatric	360	46 (12.77)
Neonates (NICU)	690	22 (3.18%)

Table.2 Antibiotic susceptibility pattern of CoNS isolates of blood cultures

Antimicrobial drug	Percentage sensitivity
Erythromicin	91.4%
Gentamicin	74%
Clindamycin	62%
Trimethoprim-sulfamethoxazole	82.3%
Penicillin	98%
Amoxycillin–clavulanic acid	76%
Oxacillin	26%
Vancomicin	100%

This should be borne in mind and patients with isolates of CoNS from blood cultures should be carefully evaluated before starting therapy to avoid unnecessary use of antibiotics, especially vancomycin and the consequent increase of antibiotic resistance in hospitals (Souvenir *et al.*, 1998). There is a tendency for clinicians to overuse antibiotics in patients with CoNS from blood cultures. In this study, 93.5% of the study patients with positive blood cultures for CoNS were treated with multiple antibiotics. Of the study patients with CoNS contamination, 28.7% were unnecessarily treated with vancomycin. Other specific CoNS antibiotics were used frequently and unnecessary. For this reason, CoNS has become resistant to many commonly used antibiotics. The high level of bacterial resistance to oxacillin in this study reflects the inappropriate use of such treatment modality.

In conclusion, this study shows that only 46% of repeated isolation of CoNS represents significant isolates; therefore, repeated isolation and antibiotics susceptibility testing from blood cultures are strongly recommended. This practice will reduce irrational use the antibiotics and reduce the emergence of resistant strains that indirectly reduce total hospital costs. Ideally, the molecular approach is for the most part a consistent method in determining the significant isolates of CoNS. However, in countries with inadequate resources, repeated isolation and antibiogram are recommended when determining significant isolates.

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