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Diagnosis, treatment and prevention of *Staphylococcus aureus*

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Abstract
Samples from pus, abscess, nasal swab, ulcer, burn area, sputum, and blood in cases of bacteremia, and urine, feces, vomit, spinal fluid, and joint fluid in cases of septicemia can be used. An appropriate sample for diagnosis of endocarditis due to artificial valves is blood drawn from the portal vein. In infections of joints and artificial organs, joint washing with sterile fluids and aspiration from the joint and in urinary tract infections sampling by clean-catch midstream technique leads to obtaining the desired organism. Samples from pus, purulent fluids, sputum, and urine should be inoculated directly on the surface of the blood agar culture medium or the thioglycollate broth tube. Staphylococci grow easily on typical laboratory media, especially if sheep blood is added. The sensitivity of *Staphylococcus aureus* to antimicrobial medicines is different. 90% of strains isolated from patients or carriers are resistant to penicillin due to beta-lactamase (Penicillinase) production or to changes in the nature of penicillin binding proteins (PBPs). Methicillin-sensitive β-lactamase-producing strains can be treated with oxacillin, cloxacillin, and nafcillin; however, for the treatment of methicillin-resistant strains, vancomycin, teicoplanin and mupirocin are used). Staph VAX vaccine that has conjugated capsular polysaccharides is at the clinical trial stage. These tests are conducted on dialysis patients and a group of patients exposed to severe *Staphylococcus aureus* infections (12).

Keywords: *Staphylococcus aureus*, treatment, prevention, diagnosis

Introduction

Sampling

Samples from pus, abscess, nasal swab, ulcer, burn area, sputum, and blood in cases of bacteremia, and urine, feces, vomit, spinal fluid, and joint fluid in cases of septicemia can be used. Sampling and transfer conditions should be considered to collect the samples. To collect the sample from the skin, the sampling site should be cleaned well and the samples should be transferred to the laboratory immediately [1]. An appropriate sample for diagnosis of endocarditis due to artificial valves is blood drawn from the portal vein. Blood cultures are useful in diagnosis of bacteremia. In infections of joints and artificial organs, joint washing with sterile fluids and aspiration from the joint and in urinary tract infections sampling by clean-catch midstream technique leads to obtaining the desired organism. For sampling using the clean-catch midstream method from neonates, children and patients with clinical signs, it is recommended to culture the collected sample immediately in a culture medium containing 5% sheep blood agar or TSA culture medium due to the low number of bacteria in the sample. Samples collected from high-infected areas such as feces or sputum should preferably be cultivated in selected medium [2].

In the microscopic test of purulent discharge, the presence of gram-positive cocci with irregular grapevine clusters indicates possible presence of staphylococcus; however, its definitive diagnosis is based on culture and isolation in laboratory culture media. Microscopic examination, catalase test, coagulase test, and cultivation in mannitol salt agar media are used to detect *Staphylococcus aureus* [3].

Methods

Search strategy

Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. After the MEDLINE strategy was finalized, it was adapted to search in other databases. Accordingly, PROSPERO was searched for ongoing or recently related completed systematic reviews. The key words used in the search strategy were "Diagnosis, Treatment, Prevention, *Staphylococcus aureus*" and Iran which were combined with Boolean operators including AND, OR, and NOT.

Study Selection

Results of the Literature review were exported to Endnote. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening. Formal screening process of titles and abstracts were conducted by two researchers according to the eligibility criteria, and consensus method was used for solving controversies among the two researchers. The full text was obtained for all titles that met the inclusion criteria. Additional information was retrieved from the study authors in order to resolve queries

regarding the eligibility criteria. The reasons for the exclusion criteria were recorded. Neither of the review authors was blinded to the journal titles, the study authors or institutions.

Culture

Samples from pus, purulent fluids, sputum, and urine should be inoculated directly on the surface of the blood agar culture medium or the thioglycollate broth tube. In the case of culture from the blood sample, about 10 ml of venous blood is inoculated into 50 ml of tryptose phosphate broth [4]. Staphylococci grow easily on typical laboratory media, especially if sheep blood is added. For primary culture of samples, it is possible to use nutrient agar and thioglycollate. Samples with small amount of staphylococcus can be cultivated in a broth containing 6-12% sodium chloride and then transferred onto a suitable solid medium. Staphylococcus colonies after 18-24 hours incubation at a temperature of 35-37° C on agar media are round, protruded, and white to cream color. *Staphylococcus aureus* may have a hemolysis aura around the colony, as well as yellow or orange pigment; of course, staphylococci cannot be identified based on their colony color [5, 6].

Treatment

The sensitivity of *Staphylococcus aureus* to antimicrobial medicines is different. 90% of strains isolated from patients or carriers are resistant to penicillin due to beta-lactamase (Penicillinase) production or to changes in the nature of penicillin binding proteins (PBPs). β-lactam clavulanic acid (such as co-amoxiclav) was used to treat infections caused by *Staphylococcus aureus* β-lactamase-producing strains. Methicillin-sensitive β-lactamase-producing strains can be treated with oxacillin, cloxacillin, and nafcillin; however, for the treatment of methicillin-resistant strains, vancomycin, teicoplanin and mupirocin are used [7].

Trimethoprim/sulfamethoxazole may be substituted by vancomycin. Infections caused by staphylococci sensitive or resistant to methicillin respond to trimethoprim-sulfamethoxazole. Trimethoprim-sulfamethoxazole may be used in patients who are sensitive to vancomycin. In combination with rifampin, trimethoprim is used to eradicate resistant *Staphylococcus aureus* spread by nasal carriers in epidemic of nosocomial infections [8].

Fusidic acid is also active against methicillin-resistant staphylococci, and like rifampin creates resistance quickly if applied alone; therefore, it should be used in combination with a medicine such as rifampin. In addition to the mentioned drugs, two new vancomycin-like drugs, Lipopeptide LY46532 and Glycopeptide teicoplanin, are used in humans. These drugs are chemically and mechanically similar to vancomycin, and *in vitro* condition in animal models, they function against staphylococci resistant and sensitive to methicillin [9].

Vancomycin is considered a selective drug for the treatment of methicillin-resistant staphylococci; however, in case of drug allergy, the drug regimen in Table 1 can be used.

Table 1: Regimen treatment of infections caused by methicillin-resistant staphylococci

Parameter	Treatment
First selective treatment	Vancomycin, Rifampin, Gentamicin
Second selective treatment	Trimethoprim, Sulfamethoxazole
Effective diets	Trimethoprim, Sulfamethoxazole Ciprofloxacin, Ofloxacin, Fusidic acid, Rifampicin
Drugs that will respond beneficially if investigated	Teicoplanin LY146032

Safety

Humans are very resistant to *Staphylococcus aureus* infection. Billions of organisms must enter the host's body for the appearance of a visible response. Many adults have antibodies in their serum against some of the cell wall antigens and toxins of this organism, but none of these antibodies will protect the individuals completely against infection caused by *Staphylococcus aureus*. In most deep-tissue infections caused by *Staphylococcus aureus*, antibodies usually increase against peptidoglycan and teichoic acid [10].

Prevention

Various efforts have been made to produce an appropriate vaccine against *Staphylococcus aureus*. Patients undergoing treatment processes requiring intravenous strains (such as hemodialysis) are at high risk for *Staphylococcus aureus* bacteremia [11]. Staph VAX vaccine that has conjugated capsular polysaccharides is at the clinical trial stage. These tests are conducted on dialysis patients and a group of patients exposed to severe *Staphylococcus aureus* infections [12]

There is evidence of a connection between the spread of staphylococcus infections and those who carry this bacterium in their nose. The amount of infection in *Staphylococcus aureus* carriers is higher than those who are not carriers. Studies have indicated that infected people have been infected with the same strain they carry themselves in 80% of the cases [13].

Most bacteremia also occurs due to auto infection. Eradication of the carriers from the bacterium using topical mupirocin reduces the number of nosocomial infections in dialysis patients and those undergoing surgery. It has been indicated that lysostaphin can be an effective treatment for endocarditis and staphylococcal keratitis. The continuous contact of this bacterium with lysostaphin leads to the emergence of resistant strains [14]. Most researchers believe that although mupirocin may be effective in reducing nasal carriers, the use of this drug as a preventer is not appropriate according to current evidence [15].

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