



Study of Combination the Antifungal with the Antibacterial against Bacteria *Staphylococcus aureus* Isolated from Skin Infection

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Abstract

Bacteria are one of the factors that cause skin infections. *Staphylococcus aureus* was the most prevalent type and because of the frequent use of antibacterial, many of them have become resistant. From this principle, it is necessary to test new ones. The combination of the antifungal itraconazole with the antibacterial amoxicillin, norfloxacin and trimethoprim was tested, and some results gave a higher effect compared to the antibacterial. It is possible to use these synergies for skin infections.

Keywords: Antifungal; Antibacterial; Skin Infection; *Staphylococcus aureus*

Abbreviations

AM: Amoxicillin; NOR: Norfloxacin; TRI: Trimethoprim; IT: Itraconazole

Introduction

Skin infection is an infection of the skin in humans and other animals, that can also affect the associated soft tissues such as loose connective tissue and mucous membranes [1]. skin infections include: Cellulitis, a diffuse inflammation of connective tissue with severe inflammation of dermal and subcutaneous layers of the skin [2] Causes of skin infections Bacteria [3] infections [4]. Fungal infections [5] Parasitic infections [6]. Viral infections [3]. Common Bacteria in Skin Infections Staphylococcus, they are normal flora of human skin and mucous membranes and their spread is either endogenously or from infected skin [7]. *Staphylococcus aureus* is one of the most important a most opportunistic pathogens of hospital-acquired infection [8]. The way it arrives mostly through the skin and causes inflammatory damage filled with pus

called abscesses and severity of the affected tissue is called pustule abscess pustule (inflammation of the hair follicle) and called boil if the inflammation spread from the hair follicle to the adjacent tissue called carbuncle or chamber, often caused by post-operative wounds and accident wounds, although it causes normal dermatitis [9,10]. Antibiotics are used to treat or prevent some types of bacterial infection many mild bacterial infections get better on their own without using antibiotics [11]. The mechanism of action of antimicrobial agents is categorized based on the function that is affected by the agents, these generally include the following inhibition of the cell wall synthesis, inhibition of ribosome function, inhibition of nucleic acid synthesis, inhibition of folate metabolism, inhibition of cell membrane function [12]. Antifungal effect on some bacteria such as lactic acid bacteria [13].

Materials and Methods

This study was conducted at the College of Medical Technologies/Islamic University from September 2020 to April 2021.

88 samples were collected from patients with skin infection such as acne, wounds and skin ulcers, after their visit to the specialist doctor at Al-Sadr Teaching Hospital.

All collected swabs were incubated with brain heart infusion broth for 24 hours at 37°C to encourage bacterial growth [14]. Identification of bacteria and diagnosis depended [15,16].

Antibiotics used in research from the Indian company Ajanta: Amoxicillin (AM) Anti-bacterial, Norfloxacin (NOR) Anti-bacterial, Trimethoprim (TRI) Anti-bacterial, Itraconazole (IT) Anti-fungal.

One gram of powder (antibiotic) was dissolved by 1 ml of distilled water. After that, equal quantities of each solvent were mixed to form the anti-mixture. Four antibiotics were tested in addition to mixing all two together by the method of drilling (6 mm) Cork Borer was used in the middle of Muller-Hinton which contains the bacteria and the dishes were incubated in the incubator at a degree 37 for a period of 24 hour. The inhibition zones around the hole were measured [17].

Results and Discussion

From figure 1, *Staphylococcus aureus* bacteria are the most prevalent, 40 isolates compared to other species, *Escherichia coli*, 31 isolates of *Pseudomonas aeruginosa*, 7 isolates, *Staphylococcus epidermidis* 5 isolates, and *Klebsiella pneumoniae* 4 isolates, while *Proteus mirabilis* is only one, and this dominance may be due to its presence in areas close to the skin, such as the mucous membranes [18,19].

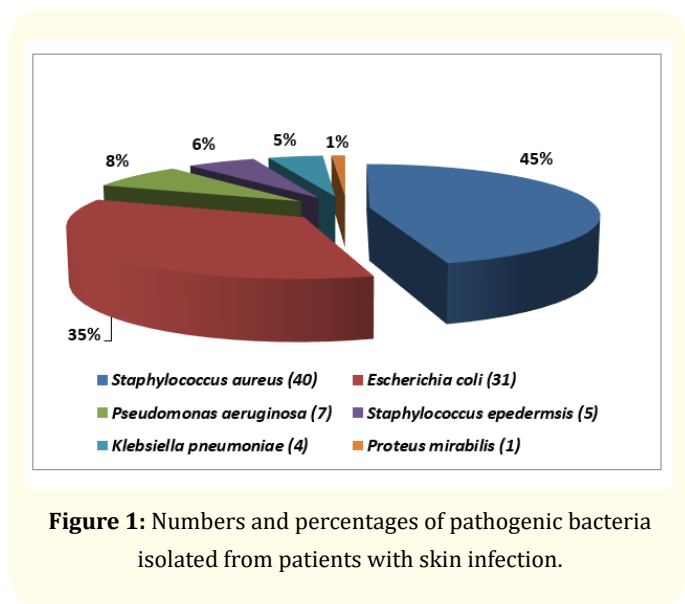


Figure 1: Numbers and percentages of pathogenic bacteria isolated from patients with skin infection.

Three antibacterial were used: (AM) act by binding to penicillin-binding proteins that inhibit a process called transpeptidation (cross-linking process in cell wall synthesis), leading to activation of autolytic enzymes in the bacterial cell wall [20], (NOR) involves inhibition of the A subunit of the important bacterial enzyme DNA gyrase, which is essential for DNA replication [21] and (TRI) binds to dihydrofolate reductase and inhibits the reduction of dihydrofolic acid (DHF) to tetrahydrofolic acid (THF). THF is an essential precursor in the thymidine synthesis pathway and interference with this pathway inhibits bacterial DNA synthesis [22].

In addition to the antifungal (IT) that has no effect on *Staphylococcus aureus* bacteria - it was tested on 6 isolates - and as shown in the table 1, all two antifungals were mixed with each other and according to the apparent results, it was found that the average diameter of the inhibition diameter of mixing (IT) with (AM) (33 mm) was better. Effective when (AM) was alone (18.7 mm), as well as when (IT) was mixed with (NOR), the rate of inhibition was (34.3 mm), while the inhibition rate of (NOR) was (33.2 mm), while when mixed (IT) with (TRI), the result was similar to (TRI), but in some isolates (3.4.6). I gave more inhibition

Since antibiotics are chemical structures, when mixed, I think they form a new chemical compound and its effect is not on one target of the bacteria, but more. Or the lack of resistance of the bacteria to it is due to the lack of recognition of it.

N. o	Antibiotic	Zone of inhibition (mm)						Range
		S 1	S 2	S 3	S 4	S 5	S 6	
1	(AM)	20	21	10	24	24	13	18.7
2	(NOR)	28	26	42	40	23	40	33.2
3	(TRI)	28	30	45	41	25	44	35.5
4	(IT)	0	0	0	0	0	0	0.0
5	(AM)+ (NOR)	30	29	48	41	30	45	37.2
6	(AM)+ (IT)	33	30	35	35	25	40	33.0
7	(AM)+ (TRI)	28	23	38	22	23	45	29.8
8	(TRI) + (NOR)	25	24	47	50	29	42	36.2
9	(IT)+ (NOR)	23	29	40	40	25	49	34.3
10	(TRI) + (IT)	26	22	43	45	22	55	35.5
11	Control (D.W)	0	0	0	0	0	0	0
(S) Sample of <i>Staphylococcus aureus</i> bacteria								

Table 1: Zone of ambition for *Staphylococcus aureus*.

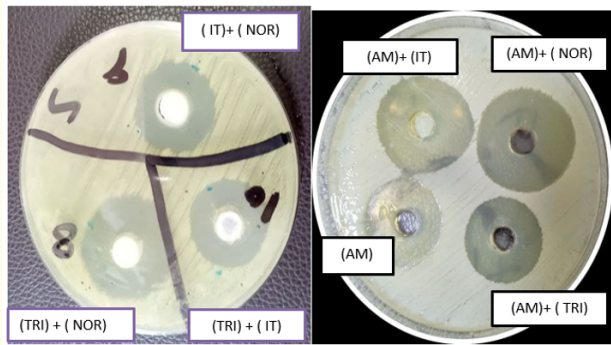


Figure 2: Antibiotics combination activity against *S. aureus*.

Conclusion

An increase in the number of cases of skin infections with staphylococcus may be due to its spread among the medical staff and thus may be transmitted to the patients, whether they are patients or accompanying them. Bacteria of *S. aureus* which have different resistance mechanisms, and therefore when mixing two antibiotics, the effect on two targets in the bacteria, for example on the cell wall and DNA, as when mixing (AM) with (NOR), and when mixing a fungal antibiotic with an antibacterial, a new antibiotic is formed that the bacteria did not have mechanisms of resistance to. Previously, this is more effective than the antidote used previously.

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