Effect of Salicylate On Fusidic Acid and Ciprofloxacin MICs in *Staphylococcus aureus*

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Abstract :

The susceptibility of five isolates of *Staphylococcus aureus* which isolated from wound infections were determind against ciprofloxacin & Fusidic acid .The findings have shown that ciprofloxacin & Fusidic acid were highly effective on *S. aureus* isolates when the Minimum Inhibitory Concentration (MIC) was very low .
Then the effect of salicylic acid on the MICs for these antibiotic was studied . Salicylate was shown to increase the resistance among *S.aureus* isolated when the Minimum Inhibitory Concentration (MIC) was very low .
Then the affect of salicylic of acid on the MICs for these antibiotics was studied . Salicylate was shown to increases the resistance among *S.aureus* isolates to Fusidic acid & Ciprofioxacin .

Introduction :

Staphylococcus aureus causes a variety of suppurative infections and toxicoses in human (1). Hospital strains of *S. aureus* are usually resistant to a variety of different antibiotics . So, some strains are resistant to all clinically useful antibiotic (2) .

Fusidic acid is a best antibiotic for treatment the infections by *S. aureus* (3). Fusidic acid inhibits the translocation step of protein synthesis by interfering with the action of eiongation factor – G (4) .

Salicylate , chemically it is 2 - Hydroxybenzoic acid , which is known for use in topical ointment (5) . It may prove beneficical therapeutically for infection caused by encapsulated bacteria (6) . As growth in presence of salicylate has a number of different effects on bacterial phenotypes (7) . So, previous studies showed that of *S. aureus* in the presence of Salicylate increased phenotypic resistan to antibiotic (8) . As extension to these studies , the effect of Salicylate on the MICs for Fusidic acid & Ciprofioxacin was determined

Material & Methods :

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1- Bacterial isolates : five isolates of *S.aureus* were collected from patients with wound infections & identified according to (9) .

2- MICs determine for Fusidic acid & Ciprofloxacin : were performed by the agar dilution technique on Muller – Hinton agar according to (10) .

3- Effect of Salicylate on the MICsfor Fusidic acid & Ciprofloxacin : were done by addition the Salicylate (as 50 mg/ml) to each conscentratrion of Fusidic acid & Ciprofloxacin on Muller-Hinton agar (in step No.2) .

Results & Discussion :

The MICs of Fusidic acid & Ciprofloxacin on five isolates *S.aureus* was studied, results of table -1- showed that Fusidic acid & Ciprofloxacin were effective on *S.aureus* isolates when the MICs was very low , similar result was obtained by (11) .

Table -1- The MICs for Fusidic acid & Ciprofloxacin on five isolates of *S.aureus*

Isolates\MICs	Fusidic acid mg/ml	Ciprofloxacin mg/ml
S.aureus :1	4	8
2	0,25	2
3	2	4
4	0,25	4
5	0,5	2

An important point in our study was the Salicylate can induce a phenotypic multiple antibiotic resistance mechanism in S.aureus . Result of table -2- revealed that addition of Salicylate 50 mg/ml increased the MICs of Fusidic acid & Ciprofloxacin .

Table -2- Effect of Salicylate on the MICs of Fusidic acid & Ciprofloxacin

Isolates\MICs	Fusidic acid with Salicylate (50 mg/ml)	Ciprofloxacin with Salicylate (50 mg/ml)
S.aureus :1	8	16
2	0, 5	4

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3	8	4
4	0, 5	8
5	1,5	8

So, in the presence of Salicylate and these antibiotics , the resistance become was 3-fold greater alone . For example , the MICs of Fusidic acid alone against *S.aureus* isolate (No.3) was 2mg/ml while when adding Salicylate at concentration (50mg/ml), the MIC of Fusid acid increased to 8 mg/ml .

These data correlate with previous studies that demonstrated that compounds with an aromatic ring and a carboxylic acid functional group induce intrinsic antibiotic resistance in *S.aureus* (12) .

Ciprofloxacin inhibits the DNA-replication by affects the DNA-gyrase (13). Fusidic acid inhibit the translocation step of protein synthesis by interfering with the action of elongation factor- G(14). Mutations leading to Fusidic acid resistance in bacteria occur in Fus A, the gene encoding the targt of Fusidic acid , EF-G (14). Fus A mutations leading to Fusidic acid resistance also alter resistance also alter resistance to some antibiotics (15) .

Salicylate- altered gene expression plays a role in altering mutation freguencies to antibiotic resistance during resistance antibiotic selection (11).

References:

1- Brooks, F.F.;Butel, J.S. and Morse, S.A. (1998). Jawtz, Melnick & Adelberg's Middle Medical Microbiology. (21st)ed. Appetton & Lange. Middle East ed.Beirut, Lebanon .

2- Prescott, L.M. ; Harly, J.P. and Klein, D.A. (1990) Microbiology . 1st ed W.M.C. Brown Publishres . NewYork.

3- Kim, W.J. and Park ,S.C. (1998).Bacterial resistance to antimicrobial agents: an overview from Korea. Yonsei. J. 39: 488-494 .

4- Tanaka, N. ; Kinoshite , T. & Masukawa, H.(1968) Mechanism of Protein Synthesis Inhibition by Fusidic acid and Related Antibiotics . Biochem . Biophys . Res. Commun . 30:278-283.

5- Muller,E.; Al-Attar,J. & Farber, BF. (1998) . Mechanism of Salicylate-mediated inhibition of biofilm in Staph.epidermidis . J Infect. Dis. 177:501-503.

6- Domenico, P.; Schwartz, S. and Cunha, BA.(1989). Reduction of Capsular Polysaccharide Production in Klebsiella pneumonia by Salicylate . Infect .Immune : 57:3778-3782.

7- Sawai, T.: Mirano, S. and Yamaguchi, A(1987). Porin Synthesis by Salicylate in E. coli, Klebs pneumonia and Serratia marscence . FEMS Microbial . Lett. 40:233-237.

8- Gustafson, JE,; Candelaria, PV.; Fisher,SA et al.(1999). Growth in the presence of Salicylate increases Quinolones resistance in S. aureus. Antimicrob. Agent Chemother. 43:990-992 .

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9- Baron, E.J. and Finegold, S.M. (1994) Bailey & Scott's Diagnostic Microbiology . (9th) ed. The C.V. Mosby Company .U.S.A.
10- Stock, E.J. & Ridgway , G.L. (1987).Handling Clinical Specimens for Microbiological studies . P.:173-201(5TH)ed Churchill Livinggstone.
11- Price, C.T. and Gostafson, J.E. (2001). Increases in the mutation frequency at which fusidic acid – resistant S.aureus with Salicylate , J. Med. Microb. 50:104-106.
12- Price, C.T. ; O'Brien, F.G. ; Shelton, B.P. et al. (1999) Effect of Salicylate and related compounds on Fusidic acid MICs in S.aureus . J. Antimicrob . Chemother. 44:57-64.
13- Correlima, M.B.; Oliveria, C.F. and Galvan, L.F. (1990). Trends in Bacterial Resistance & implication for infections . J. Intern Med. Res. 18: suppl. 4:3D-5D .
14- Chopra, I. (1976). Mechanisms of Resistance of Fusidic acid in S. aureus . J. Gen. Microb. 96:229-238 .
15- Johanson, U. and Hughes, D. (1994). Fusidic acid resistans mutants defind three regions in elongation G of Salmonella typhimurium . Gene 143 : 55-59 .

الخلاصة :

اختبرت حساسية خمسة عزلات تعود لبكتريا *Stsphylococcus aureus* (والمعزولة من الإصابات الجلدية) لمضادي Ciprofloxacin و Fusidic acid, ثم لوحظ تأثير حامض السالسليك Salicylate على حساسية هذه العزلات للمضادين اعلاه , اوضحت النتائج إن مضادي Ciprofloxacin و Fusidic acid يمتلكان تأثيراً فعالاً ضد عزلات بكتريا *S.aureus* , وان حامض السالسليك يزيد من مقاومة بكتريا *S.aureus* للمضادين اعلاه .

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