

Assessment of antibacterial activity of some topical otological solutions

Bazı topikal otik solüsyonların antibakteriyel aktivitesinin değerlendirilmesi

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Objectives: Otological solutions have long been used in the treatment of the bacterial and fungal infections of the ear. We investigated antibacterial activity of some otic solutions against the most common bacteria isolated from discharging ears.

Study Design: Three solutions were used (Castellani's, Burrow's, and 2% salicyl alcohol) for 20 fresh isolates of each of the following organisms: *Staphylococcus aureus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Enterobacter* spp.. The activity of each solution was determined by the size of the zone of inhibition of bacterial growth.

Results: The Castellani's solution showed significantly larger average inhibition zones than the other solutions did ($p < 0.001$).

Conclusion: The Castellani's solution may be considered a good option against bacterial or mixed infections (bacterial and fungal) of the ear.

Key Words: Administration, topical; anti-bacterial agents; bacterial infections/drug therapy; otitis externa; otitis media/drug therapy; *Proteus mirabilis*/drug effects; *Pseudomonas aeruginosa*/drug effects; *Staphylococcus aureus*/drug effects.

Amaç: Otolojik solüsyonlar uzun zamandır kulağın bakteriyel ve fungal enfeksiyonlarında kullanılmaktadır. Bu çalışmada, kliniğimizde akıntılı kulaklardan en sık izole edilen bakterilere karşı bazı otik solüsyonların antibakteriyel etkinliği araştırıldı.

Çalışma Planı: Çalışmada *Staphylococcus aureus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli* ve *Enterobacter* türlerinden 20'şer adet suş için üç farklı solüsyon (Castellani, Burrow ve %2 salisil alkol) kullanıldı. Kullanılan her bir solüsyonun etkinliği bakteriyel büyüme alanında oluşturduğu inhibisyon alanının büyüklüğü ile değerlendirildi.

Bulgular: Castellani solüsyonu ile elde edilen inhibisyon alanı, diğer solüsyonlarla elde edilen alandan anlamlı derecede büyüktü ($p < 0.001$).

Sonuç: Castellani solüsyonunun bakteriyel veya bakteriyel ve fungal birliktelik gösteren kulak enfeksiyonlarında iyi bir tedavi seçeneği olabileceği düşünüldü.

Anahtar Sözcükler: Uygulama, topikal; antibakteriyel ajan; bakteriyel enfeksiyon/ilaç tedavisi; otitis eksterna; otitis media/ilaç tedavisi; *Proteus mirabilis*/ilaç etkisi; *Pseudomonas aeruginosa*/ilaç etkisi; *Staphylococcus aureus*/ilaç etkisi.

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Castellani's, Burow's, 2% salicyl alcohol solutions have long been used as topical otological preparations in the treatment of bacterial and fungal infections of the ear.^[1,2] Burow's solution prepared by adding glacial acetic acid to aluminum subacetate solution and diluting the mixture with water to final concentration of approximately 13 per cent aluminum acetate. Salicyl alcohol (2%) is prepared with salicylic acid 2g, alcohol 90% 50 mL, freshly boiled and cooled water to 100 mL.^[3] Castellani's contains Resorcinol 10 gr, phenol 4.5 gr, boric acid 1 gr, Fuchsin 0.3 gr, acetone 5 cc, 70% alcohol 10 cc; this solution is raised to 100 cc with an addition of distilled water.^[1] pH values of these solutions are 4.01, 2.91 and 2.55, respectively.

Although Burow's solution is bactericidal on *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Streptococcus pyogenes*, *Staphylococcus aureus*, the other solution's action on bacteria commonly associated with infections of the ear is not known.^[2] The mode of action is thought to be the alteration of the pH of the external auditory canal and middle ear and hence the bacterial profile and inflammatory response of the mucosal lining.^[4]

The aim of this study was to determine the antibacterial activity of three topical otic solutions against a range of commonly occurring organisms believed to be pathogenic in chronic suppurative otitis media.

MATERIALS AND METHODS

Organism: The study was carried out on 100 isolates that belong to five common species which were most frequently isolated in our laboratory from discharging ears. These species were as follows: *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Enterobacter spp*, *Escherichia coli*.

Ear swab samples were taken from patients and streaked onto blood agar, eosin methylene blue agar and MacConkey agar for primary isolation.^[5] After an incubation period of 48 hours at 37 °C, microorganisms were recovered and then identified to species level by API Staph, API 20E and API 20NE identification systems (bioMerieux, France).

Twenty strains from each organism were used in order to detect the antibacterial effect of each solution against mentioned bacteria.

Susceptibility testing procedure: Organisms were plated onto Mueller Hinton agar using inocula

criteria according to NCCLS standards (National Committee for Clinical Laboratory Standards-USA).^[6] Four wells in 0.5 cm diameter were cut into the agar and each was filled with the solutions of 2% salicyl alcohol, Burrow's and Castellani's. Plates were then incubated at 35 °C for 24 hours and the diameters of the zones of growth inhibition were measured in mm and recorded.

RESULTS

According to the evaluation in consideration of all bacteria isolated from chronic suppurative otitis media by making use of variance analysis and Duncan multiples range test, these solutions ranged from Castellani, 2% salicyl alcohol to Burow's in terms of their effectiveness ($p < 0.01$). Salicyl alcohol was the most influential on *Proteus mirabilis* and the least on *Staphylococcus aureus* ($p < 0.001$). No statistically significant difference was found in the effectiveness of Burrow's solution on isolates (Table I). Castellani, however, was found as the most influential on *Staphylococcus aureus* ($p < 0.001$).

DISCUSSION

The important factors to be considered in the treatment of the acute attacks of chronic otitis media are the high likelihood of controlling the disease to be treated, its easy application and its failure to cause the risk of ototoxicity.^[7]

Treatment of this disease can be time-consuming and difficult. Treatment options include aural toilette, local insufflation of antiseptic powders, an array of topical otic drops and sprays, systemic antibiotics and surgery.^[4] Treatment of this condition with expensive systemic and topical antibiotics is often not possible due to the constraints of limited health budgets in such situations. Cheap and effective topical ear drops have a very high capacity of treating in such cases.

Clayton et al.,^[8] indicated that there was no difference between the use of a topical antiseptic (aluminum acetate) and a topical antibiotic (gentamicin sulfate) for the initial of otorrhea, whether it be caused by otitis externa, acute otitis media or chronic otitis media. These authors favored the use of a topical antiseptic rather than a topical antibiotic in the initial treatment of purulent otic discharge on the grounds of cost, avoidance of resistance and toxicity.

TABLE I
RANGE AND AVERAGE GROWTH INHIBITION ZONE SIZE FOR EACH
ORGANISM AND AGENT

Organism (20 culture of each)	%2 salicyl alcohol range in mm (average)	Burow's range in mm (average)	Castellani's range in mm (average)
<i>Pseudomonas aeruginosa</i>	0-15 (7.75)	0-15 (2.75)	0-20 (9.2)
<i>Staphylococcus aureus</i>	0-20 (3.2)	0-30 (2)	14-35 (19.9)
<i>Proteus mirabilis</i>	0-18 (9.0)	0-15 (1.7)	0-15 (10.7)
<i>Escherichia coli</i>	0-10 (5.8)	0-10 (4.1)	0-12 (7.8)
<i>Enterobacter spp</i>	0-10 (7.69)	0-15 (1.7)	0-15 (7.8)

Various topical ear drops are used for this purpose. Thorp et al.^[2] in a study where they determined the antibacterial influence of acetic acid and Burrow's solution on pathogen bacteria frequently observed in otitis externa and otitis media, found out that Burrow's solution and acetic acid inhibits growth of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus mirabilis* and *Streptococcus pyogenes*. In this study Burrow's solution produced an even more effective preparation for the inhibition of growth of the four most common organisms isolated from discharging ear.

The study by Aminifarshidmehr^[9] shows that irrigation with 2% acetic acid resolved the otorrhea in 74 patients (77%), and 19 of them (19%) had spontaneous closure of the tympanic membrane. To him, the advantages of this treatment are important from socioeconomic view of the patients and the cost of this therapy is very low, compared with antibiotic treatment.

In their study in which they compared the ciprofloxacin and tobramycin in the treatment of chronic suppurative otitis media, Kaygusuz et al.^[10] determined that both drugs have similar qualities and that the healing period of the patients who were given siprofloksasin was shortened after an addition of steroid to the treatment.

In their study in which they investigated the effectiveness of topical siprofloksasin in the acute

attacks of chronic suppuratif otitis media, İköz et al.^[7] acquired full success in 87.5% of the patients and partial success in 12.5% of them. For this evaluation, the patients whose draining was found to be completely stopped in the control of the 11th day were accepted as full success and the ones whose draining was stopped more than 50% were regarded as partial success.

Aminifarshidmehr,^[9] in his study, reported that changing the pH media of the ear canal interrupts the growth of the bacteria by affecting the amino acids, which causes alteration in the bacterial enzymes three-dimensional structures. Extreme change in pH can cause protein denaturation. It has been postulated that the antibacterial effectiveness of these preparations is largely due to their acidity. On the other hand, Burrow's solution was found more influential in Thorp et al's^[2] study investigating the activity of acetic acid and Burrow's solutions. In the same study, acidity of Burrow's solution was found less than that of acetic acid. It was, however, thought that this effectiveness of Burrow's solution is partly due to the aluminium acetat it contains.^[9]

Although there are no reported cases of ear drop related ototoxicity in humans, there is mounting evidence that sensorineural hearing loss can occur in patients treated with antibiotic containing and especially aminoglycoside-based topical preparations for prolonged periods.^[11,12]

Considering the ear drops, which contain antibiotics such as ciprofloxacin, tobramycin and gentamicin, and which are currently on market, it was observed that 2% salicyl alcohol was seven times as cheap, Burrow's solution was four times as cheap, and Castellani's solution was twice as cheap as them.

That Castellani's solution, more frequently used for fungal infections, also has antibacterial influence makes us think that this solution can also be used for bacterial infections or bacterial and fungal mixed infections.

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