

## **TITLE**

“A RANDOMISED CONTROLLED TRIAL COMPARING  
TRIADCORTYL<sup>®</sup> WITH 10% GLYCERINE-ICHTHAMMOL IN THE  
INITIAL TREATMENT OF SEVERE ACUTE OTITIS EXTERNA”

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## **ABSTRACT**

Acute otitis externa is a common clinical condition accounting for a large proportion of workload in the otolaryngology department, although milder cases are often managed in primary care. Treatment of the most severe forms of otitis externa involves aural toilet, followed by the application of a topical preparation, commonly in the form of an ear canal dressing. A prospective single-blind randomized controlled trial was performed to compare the efficacy of 10% Glycerine-Ichthammol (GI) solution and Triadcortyl<sup>®</sup> (TAC) ointment, both applied as ear canal dressings, in the initial management of severe acute otitis externa. A total of sixty-four patients were studied. Both treatment modalities were proven efficacious in the treatment of severe acute otitis externa. Although there was a statistically significant difference in patients' pain improvement in the TAC group in comparison with GI, there was no statistically difference in signs improvement between those two groups. Therefore, it is recommended that GI dressing can be used instead of an antibiotic dressing as an initial treatment of severe acute otitis externa on the basis of cost, avoidance of resistance and toxicity.

## **Keywords**

Otitis externa, ear dressing, Glycerine, Ichthammol, Triadcortyl

## INTRODUCTION

Otitis externa is an inflammatory disorder of the external auditory canal, frequently associated with bacterial or fungal infection. It is a very common otological condition with a yearly prevalence of more than 1% in the United Kingdom (UK) [1]. Although milder and uncomplicated cases are often managed in primary care, otitis externa is still accounts for 20-30% of otolaryngological consultations [2].

Diagnosis of acute otitis externa is made on clinical features alone, although microbial evidence is sought in refractory cases in order to direct antimicrobial therapy. Patients commonly present with a history of earache, itchiness, ear discharge and hearing loss [3]. Examination findings usually show a narrowed, tender and erythematous external auditory canal. In severe cases, there may be associated auricular cellulitis and perichondritis. The commonest pathogen implicated in acute otitis externa is *Pseudomonas aeruginosa*, followed by *Staphylococcus aureus* [4].

There is no consensus with respect to optimal management of acute otitis externa and treatment patterns can differ substantially from one practice to the other. A variety of antiseptic and antibiotic treatments have been used over the years. Current methods of management include aural toilet, prescription of topical antibiotic agents, with or without corticosteroids and less commonly systemic antimicrobial therapy [5]. Topical astringents/antiseptics such as acetic acid, aluminium acetate, alcohol, boric acid, silver nitrate, glycerine and ichthammol are also considered effective and may be used. In cases

of severe acute otitis externa, when there is a significant external auditory canal oedema, delivery of topical preparations can be facilitated by placement of ear wick or ribbon gauze [6].

In the UK, Glycerine-Ichthammol (GI) solution and Triadcortyl (TAC) cream/ointment are commonly used as topical preparations especially in the management of severe acute otitis externa, when the external auditory canal is narrowed by an acute inflammatory reaction [7,8,9]. Glycerine-Ichthammol (GI) 10% solution is a mixture of pure glycerol in a 9:1 ratio with ichthammol. Ichthammol is prepared by the destructive distillation of bituminous shale with ammonium sulphate and contains mainly ammonium salts of sulphuric acid and contains not less than 10% of organically incorporated sulphur [10]. Glycerine is a clear hygroscopic liquid and exerts its effects mainly due to dehydration action. Triadcortyl Otic® (TAC) ointment is a mixed antibiotic, antifungal preparation, containing triamcinolone acetonide 0.1%, gramicidin 0.025%, neomycin 0.25% (as sulphate), nystatin 100,000 units/g in plastibase.

TAC and GI both have produced encouraging results in the management of acute otitis externa, but until now they have never been directly compared together. The aim of this study was to compare the clinical efficacy of 10% GI and TAC dressings in the initial management of severe acute otitis externa (when swab results were not yet available) by measuring the improvement of patients' clinical features.

## **MATERIALS AND METHOD**

A prospective single-blind randomized controlled trial was designed. All adult patients ( $\geq$  18 years old) who presented with severe acute otitis externa to the Otolaryngology department at Luton & Dunstable Hospital, Luton, over a six months period were enrolled in the study. These patients were referred untreated either by walk-in centres, accident and emergency departments or by their general practitioner. General practitioners were asked to refer any patient with severe acute otitis externa (swelling of external auditory canal) to the Otolaryngology department at Luton & Dunstable Hospital and the majority of patients were seen on the same day.

Enrolment of patients was based on clinical features of acute otitis externa which included otalgia, otorrhoea, itchiness, hearing loss and an oedematous external auditory canal, for a period less than 3 weeks. Criteria for exclusion were patients with recurrent episodes of chronic otitis externa, co-existing middle ear pathology, those who had already received topical or systemic antibiotics in the previous 3 weeks prior to their attendance in the Otolaryngology department at Luton & Dunstable Hospital and possible or known drug sensitivity to the agents used (allergy to neomycin, gramicidin, nystatin glycerine or ichthammol).

All patients included in the study had informed consent. A standard questionnaire was prepared and a protocol established for examination, aural toilet and treatment. Physical examination included careful assessment of the external auditory canal and tympanic

membrane (whenever possible) using an operating microscope and suction. At initial presentation, a swab of the external auditory canal was taken and gentle aural toilet performed on the affected ear of each patient. Following this, they were randomised to one of the two treatment modalities using a computerised random number generator. Group 1 had TAC ointment impregnated into ribbon gauze and placed in the infected ear while group 2 received a ribbon gauze dressing soaked in 10% GI solution. Dressings were left in the ear canal for 48 hours in both groups and patients were reviewed after 2 days by the same examiner. Patients were then commenced on topical antibiotic drops according to swab culture results and further they were reviewed in Otolaryngology department every 5 to 7 days till complete resolution of the infection was achieved.

Comparison of the treatment modalities was made by measuring patients' pain and sign score improvement (difference between presentation-day 1 and follow-up appointment in 48 hours-day 3).

Pain Score: Patients' subjective impression of earache was based on an eleven point pain scale (range 0 to 10, 0 being no pain whatsoever and 10 indicating the most severe pain imaginable). All patients were asked to record the earache they encountered on presentation to ENT department, prior to aural toilet and on the third day following removal of the dressing.

Pain score improvement: The difference in the pain scores on the day of presentation and day 3 was recorded as the pain improvement score. A score of 2 was considered clinically significant.

Signs score: No formal protocol of grading the severity of the clinical features of acute otitis externa exists. Therefore, a sign score scale assessing the ear canal swelling, tenderness and erythema was created as an objective indicator for measuring the improvement of clinical signs for the purpose of the study (Table 1). Maximum score that could be obtained was 4.

Sign Score Improvement: Improvement in signs on the third day of presentation was recorded. An improvement score of two was considered clinically significant since this incorporated improvement of two parameters except ear canal swelling which had maximum of score two.

Statistical analysis was performed using non-parametric median test for comparing the pain and sign scores associated with each treatment.

## **RESULTS**

Seventy-six patients were referred and assessed in the Otolaryngology department with severe acute otitis externa over a six months period. Sixty-four of those patients (32 for each treatment group) met the inclusion / exclusion criteria and were entered in the trial. Ten patients were excluded. Three of these patients had auricular perichondritis and facial cellulites and they were admitted for intravenous antibiotics in conjunction with topical treatment. One patient had co-existing middle ear pathology and three patients had already used topical antibiotics prior to their attendance in otolaryngology department. Three patients had no oedema of the ear canal, so an ear dressing was not inserted. Two patients did not agree to take part in the study.

### Characteristics of treatment groups

There were 38 (59%) male and 26 (41%) female patients with an age range of 18-75 years (mean age 42.5 years). The age and sex distribution was similar in both groups. The relevant associated aetiological factors are shown in table 2. Assessment of symptoms showed common features to be pain (100% of cases), discharge (85%), itchiness (69%), hearing loss (66%), followed by tinnitus (25%).

### Pain score

The mean pain score in patients with a 10% GI dressing was 6.59 on day 1, ranging from 2 to 9. On day 3, the mean pain score was 2.69 (range 1 to 5) for the GI group. In patients with TAC dressing, the mean pain score was 7.19 (range 2 to 9) on day 1 and 1.94 (range 1 to 5) on day 3. Thus, the mean pain improvement score was 3.90 (range 1 to 7) for



patients with the GI dressing and 5.25 (range 1 to 8) for patients with the TAC dressing (Table 3). This represents a highly significant difference in the patients' pain improvement for the TAC group ( $p < 0.001$ ).

#### Signs score

With GI dressing, the mean signs score improvement was 2.06 ranging from 1 to 4. Similarly, for the TAC dressing, the mean signs score improvement was 2.25 (range 1 to 4). There was no statistically significant difference in the improvement of signs in the two regimens ( $p = 0.979$ ) (Table 3). All patients in both groups had clinical improvement of symptoms and signs. There were no patients requiring further packing of the ear canal. No complications or side effects were observed or reported with either ear dressing.

#### Swab results and follow-up

Most patients in both groups had grown *Pseudomonas auruginosa* (80% for TAC and 70% for GI), followed by *Staphylococcus aureus* (40% in TAC and 50% in GI). Mixed growth of *Pseudomonas auruginosa* and anaerobes was isolated in 3 patients from each group. In 15 patients (47%) from the GI group and 13 patients (41%) from the TAC group had no growth of an organisms, so topical antibiotics were not prescribed. Patients with a positive swab culture were further treated according to the sensitivities of the grown organism. All patients followed every 5 days until complete resolution of the infection was achieved. Majority of patients for both groups (95% for TAC and 87% for GI group) had complete resolution of the infection within 10 days from initial presentation.

## **DISCUSSION**

Otitis externa is a relatively common clinical condition. Although milder cases are often managed in primary care, severe acute otitis externa accounts for a significant proportion of workload in the emergency clinics of a typical otolaryngology department [4].

Meticulous cleaning of the external auditory canal by atraumatic micro-suctioning is regarded as an important first step in the initial treatment of otitis externa [11]. Further management differs among various practices, but essentially is addressed at removing the causative micro-organisms and reducing the oedema of the external auditory canal. This is usually in the form of repeated aural toilet followed by a wide range of topical treatment applications. In most instances, topical antibiotics, with or without steroids, are used. The topical medication is delivered into the external auditory canal either directly in the form of ear drops or through the placement of an ear canal dressing. This facilitates the passage of antibiotic medication and also helps in control of the pH [6]. Ear canal dressings are essential in cases of oedematous external auditory canal to the extent of obscuring or obliterating the tympanic membrane view. The added benefit of inserting an ear canal dressing is that it prevents further self-inflicted trauma, which can often potentiate the disease process. The ear dressing stays in for 24-48 hours and hence patient compliance to treatment is also not an issue.

The value of routine ear culture swab in management of acute otitis externa remains controversial. Hicks concluded that the swab results are unhelpful and difficult to interpret in terms of possible pathogenesis [12]. Although treatment is initiated prior to

availability of a swab culture result, they are essential in cases of initial treatment failure, as well as for resistant or recurrent cases. In view of the fact that the literature states that 60% of patients have a negative bacterial culture swab, a positive swab is not judged to confirm the diagnosis [13]. In the present study 44% of patients had no growth of an organism. In consistency with a study by Agius *et al*, the commonest organism cultured was *Pseudomonas aeruginosa* followed by *Staphylococcus aureus* [3].

In the UK, among the existing array of topical medications, GI solution is commonly used for treatment of acute otitis externa [8,14]. Ichthammol has been widely available as creams and bandages. It has traditionally been used in the treatment of various skin disorders as a topical preparation in general surgery and dermatology for gravitational ulcers, eczema and psoriasis [15]. Although the anti-inflammatory effect of Ichthammol in dermatological conditions is well known, there is a lack of information on its antibacterial properties and mode of action [16]. The anti-inflammatory action has been attributed to inhibitory effects on secretion of chemotactic arachidonate metabolites from leukocyte and on cell migration [15]. A study of the antibacterial property of GI, as measured by a growth inhibitory test and a modified cidal assay, showed inhibition of growth of gram positive bacteria (*Streptococcus pyogenes* and *Staphylococcus aureus*). However, there was only minimal antibacterial activity against *Pseudomonas aeruginosa* and *Escherichia coli*. Limited inhibitory action against *Candida albicans* was also noted [10]. In our study, although *Pseudomonas aeruginosa* was the commonest isolated organism, there was an overall satisfactory improvement of symptoms and signs in patients treated with GI dressing. It is thus believed that the therapeutic benefit of GI is

partly due to the inherent anti-bacterial activity of Ichthammol against the Gram positive organisms as well as its anti-inflammatory and vasoactive actions in combination with the dehydrating effect of the glycerol on the ear canal skin [14].

The value in treatment of acute otitis externa with drops containing corticosteroids combined with a broad spectrum antibiotic is well attested [17]. In many instances, the drops prescribed contain an aminoglycoside antibiotic owing to the potent activity of this group of drugs against *Pseudomonas aeruginosa*. TAC, which includes an antifungal agent in its constituents, is a good ointment to use in the treatment of the chronically discharging ear [9]. Also its efficacy in treatment of acute otitis externa is well acknowledged [18]. In present study, there was an improvement of pain and signs in patients presented with severe otitis externa and treated with TAC dressing.

Although aminoglycoside antibiotics are successful in the treatment of otitis externa in most cases, their rationale remains unclear. A study by Tsikoudas *et al* suggested that aminoglycoside antibiotics conveyed no significant benefit in this condition [19].

Previous work by Clayton *et al* suggested that a primary microbiological cause for the condition can only be found in 40% of cases [20]. In addition, patients with acute otitis externa are far more likely to suffer from generalised allergic disorders [13].

Furthermore, patients treated with topical aminoglycoside antibiotics for this condition in its chronic form, become hypersensitive to the drops used in 68% of cases. The allergen involved in 59% of these hypersensitive cases is the aminoglycoside antibiotic used [21]. Further, their use can result in the development of cutaneous sensitivity (particularly to

preparations containing neomycin) and secondary fungal infections. They are also potentially ototoxic. Consequently, some authors have advocated the use of topical antiseptics or topical steroid-only preparations which are said to be equally effective [19,20,22]. Clayton *et al*, in a randomised controlled trial comparing otosporin versus aluminum acetate, they recommended that aluminium acetate can be used instead of antibiotics as an initial treatment for acute otitis externa, on the ground of cost and toxicity [20]. In the present study, there was no overall difference between the clinical efficacy of 10% GI dressing in comparison to TAC ointment dressing for the treatment of acute otitis externa.

Systemic antibiotics in addition to topical therapy are often prescribed (up to 40%) [1,23]. Unless there is evidence of concomitant diagnosis of otitis media or evidence of regional spread of otitis externa, the use of oral antibiotics besides topical therapy has implications in terms of cost, emergence of microbial resistance, risk of side-effects and increased likelihood of non-compliance [24].

Our findings suggested that both treatment modalities, TAC and GI, were efficacious in the treatment of severe acute otitis externa. Although there was a statistically significant difference in patients' pain improvement in the TAC group in comparison with GI, there was no statistically difference in signs improvement between those two groups. Therefore, it is recommended that a 10% GI dressing can be used instead of an antibiotic ointment dressing as an initial treatment of severe acute otitis externa on the basis of cost, avoidance of resistance and toxicity.

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## TABLES

<ul style="list-style-type: none"> <li>▪ Tenderness none = 0</li> <li>▪ Tenderness of the EAC = 1</li>   <li>▪ EAC Swelling absent = 0</li> <li>▪ EAC Swelling &lt;50% = 1</li> <li>▪ EAC Swelling &gt;50% = 2</li>   <li>▪ Erythema absent = 0</li> <li>▪ Erythema of the EAC = 1</li> </ul>
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**Table 1:** Sign score scale for otitis externa. Minimum score is 0 and maximum score is 4. (EAC= external auditory canal)

<b>Aetiological factors</b>	<b>GI group</b> No of patients (%)	<b>TAC group</b> No of patients (%)
Unknown	15 (47%)	18 (56%)
Diabetes	3 (9%)	2 (6 %)
Aural dermatitis/Eczema	5 (16%)	4 (13%)
Swimming	7 (22%)	6 (19%)
Use of hearing aid	2 (6%)	2 (6%)

**Table 2:** Aetiological factors for otitis externa in both treatment groups. (GI=10% Glycerine-Ichthammol, TAC= Triadcortyl ointment)

	<b>GI group</b>	<b>TAC group</b>	<b>Significant difference</b>
Pain Improvement Mean (Range)	3.90 (1-7)	5.25 (1-8)	p<0.001
Signs score improvement Mean (Range)	2.06 (1-4)	2.25 (1-4)	p>0.5

**Table 3:** Results of pain and signs score improvement. (GI=10% Glycerine-Ichthammol, TAC= Triadcortyl ointment)