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Burow's solution in the treatment of active mucosal chronic suppurative otitis media: determining an effective dilution

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Abstract

Burow's solution (13 per cent aluminium acetate) has been found to inhibit *in vitro* the growth of most commonly occurring bacteria found in the discharging ear. An *in vitro* study has shown that the minimum inhibitory concentration of Burow's solution for these organisms lies between a 1:80 and a 1:160 dilution. This paper reports on a clinical trial that incorporated 67 discharging ears to establish the most effective strength of aluminium acetate solution. There was no statistical difference in the effectiveness of full strength Burow's solution compared to 3.25 per cent aluminium acetate solution (a quarter strength Burow's solution). Response rates of 80.8 per cent and 75 per cent respectively following a two-week treatment period were achieved using these two solutions. A 1.3 per cent aluminium acetate solution (1/10 strength Burow's solution) was found to be markedly inferior. Bacteriological and audiological profiles were recorded for each patient.

Key words: Otitis media, suppurative; Therapy

Introduction

The management of chronic suppurative otitis media (CSOM) also known as active mucosal chronic otitis media can be both 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.

Burow's solution, named after Karl August von Burow (1809–1874), has been used as a local otological preparation since the late 19th century.[1] It is a clear, colourless liquid with a faint acetous odour and a sweet taste made by adding glacial acetic acid to aluminium subacetate solution and diluting with water to give a final concentration of approximately 13 per cent aluminium acetate.[2,3] It has been found *in vitro* to effectively inhibit the growth of commonly occurring organisms found in CSOM including *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Proteus mirabilis*.[4] Acid medium ear drops are effective in treating CSOM[5] but the low pH makes them uncomfortable to use especially in the presence of acute inflammation. Although Burow's solution is not as acidic as two per cent acetic acid,[4] it can also cause discomfort on application. *In vitro* determination of a minimum inhibitory dilution of Burow's solution has shown that dilutions ranging from 1:80 to 1:160 will inhibit growth of all commonly occurring organisms found in CSOM.[6]

The aim of this study was to determine the clinical efficacy of Burow's solution in the treatment of CSOM and to investigate whether a diluted solution would cause less discomfort whilst remaining as effective. This was achieved by prospectively randomizing a group of children with active mucosal CSOM to receive either full strength Burow's solution or a dilution thereof and document the response to treatment. Neither the patient nor the treating physician was aware of which solution had been allocated. Pure tone hearing threshold assessment prior to and on completion of therapy was also documented.

Materials and methods

All patients presenting with active mucosal CSOM to the Otolaryngology outpatient clinic at the Red Cross War Memorial Children's Hospital over a six month period were assessed. Active mucosal CSOM was defined as a defect of the pars tensa, inflamed oedematous middle ear mucosa and a mucopurulent discharge for more than four weeks. Patients were excluded if systemic antibiotics or any topical ear drop preparations had been administered within the preceding two weeks, or if there was any evidence of cholesteatoma or aural polyps.

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TABLE I
DEMOGRAPHIC DATA OF PATIENTS COMPLETING THERAPY

	Ears	Age	SD	Male	Female	Left	Right	Unilateral	Bilateral
Solution B (Burow's solution)	26	5.00	3.52	16	7	15	11	20	3
Solution C (3.25% alumimiun acetate)	20	5.24	3.23	12	5	11	9	14	3
Solution A (1.3% aluminium acetate)	10	4.60	3.87	7	2	5	5	8	1
Total	56	5.42	3.61	35	14	31	25	42	7

The frequency and duration of the discharge was noted. The ear was thoroughly cleaned with micro-suction toilette or dry mopping prior to a swab of the middle ear being taken for microscopy and culture. The degree of inflammation and the size of the perforation were recorded. All patients had pure tone air conduction audiometry prior to and after the treatment period. Patients old enough to tolerate headphones had bone conduction thresholds recorded as well.

The first 30 patients were randomized to receive either solution A (1.3 per cent aluminium acetate – 1/10 strength Burow's solution) or solution B (Burow's solution – 13 per cent aluminium acetate). At this stage a preliminary assessment of the results indicated a poor response to treatment with solution A. Thereafter patients were randomized to receive solution B or solution C (3.25 per cent aluminium acetate – quarter strength Burow's solution). The pH of each solution was measured following preparation, prior to packaging.

Randomization was effected using a computer generated randomization sequence. Parents were instructed to dry mop the ear prior to insertion of six drops of solution three times per day for a two week period, or until the discharge had stopped. Delivery of solution to the middle ear was assisted by pulsed tragal pressure following administration of the drops.

If the ear was dry at the follow-up visit, the degree of inflammation, audiometric change and any discomfort experienced due to administration of the eardrops was noted.

If at follow-up the ear was still discharging a repeat pus swab was taken for culture and the patient placed onto routine treatment. The degree of inflammation, audiometric change and discomfort of medication were also recorded. Compliance was assessed by the amount of remaining solution combined with the child's response to dry mopping by the clinician.

All data was tabulated and statistical analysis was performed where appropriate.

Results

Most children with discharging ears seen at the clinic had to be excluded because of treatment within the two weeks prior to consultation. A total of 60 patients and 67 discharging ears were randomized into the trial. The data of 11 patients was excluded, due to poor compliance in five and failure to attend the follow-up visit in six. Of the 49 patients that fulfilled the trial criteria, 14 were female and 35 were male, with an average age of 5.42 (3.61) years. The data on 56 discharging ears were included for analysis.

Demographic data is shown in Table I.

The response of each organism to treatment is shown in Table II. Preliminary response data was assessed after 30 patients had completed treatment. It was noted that Solution A (1/10 strength Burow's solution) was clinically less effective than had been anticipated from *in vitro* studies and a stronger dilution of aluminium acetate, Solution C (3.25 per cent aluminium acetate – quarter strength Burow's solution) was substituted in mid-trial. Patients therefore received solution B or solution C for the remainder of the trial.

The treatment responses to each strength of aluminium acetate dispensed, as well as the pH are shown in Table III. Not included in this table was the observation that, of patients receiving solution B, three patients closed their perforations and five

TABLE II
THE RESPONSE TO TREATMENT OF THE ORGANISMS CULTURED FROM THE DISCHARGING EARS AT THE FIRST VISIT

Organism	*n*	Response to solution A (%)	Response to solution B (%)	Response to solution C (%)
Pseudomonas aeruginosa	20	1/2 (50)	5/5 (100)	9/13 (69.2)
Staphylococcus aureus	12	2/6 (33.3)	3/3 (100)	2/3 (66.7)
Proteus mirabilis	6		3/4 (75)	2/2 (100)
Streptococcus pyogenes	2		0/1 (0)	1/1 (100)
Streptococcus pneumoniae	1			1/1 (100)
Haemophilus influenzae	5	0/1 (0)	2/4 (50)	
Escherichia coli	3		3/3 (100)	
Klebsiella oxytoca	2		1/2 (50)	
Providencia	1		1/1 (100)	
Mixed skin flora	4	1/1 (100)	3/3 (100)	

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TABLE III
THE RESPONSE TO EACH OF THE TREATMENT SOLUTIONS (PERCENTAGES IN PARENTHESES WHERE APPROPRIATE)

	n	Dry ears	Average time taken (days)	Improved inflammation	pH	Initial eardrop discomfort	Continuous discomfort
Solution B (Burow's solution)	26	21 (81)	3.8	24 (92)	3.06	6 (26)	17 (74)
Solution C (3.25% aluminium acetate)	20	15 (75)	4.9	19 (95)	3.50	11 (65)	6 (35)
Solution A (1.3% aluminium acetate)	10	5 (50)	6.2	7 (70)	3.73	8 (89)	1 (11)
Total	56	41	4.78	50		25	24

developed a crystalline deposit in the external auditory canal although the otorrhoea and inflammation had resolved.

Analysis of treatment failures is shown in Table IV.

All ears treated received audiological assessment and air conduction pure tone audiological results are shown in Table V. No patients showed any deterioration in air conduction thresholds. Bone conduction studies were performed on 37 ears and no change in any individual thresholds was noted over the treatment period.

Discussion

Browning *et al.*[7] emphasize the importance of controlled trials in establishing the efficacy of treatment in CSOM. Smith *et al.*[8] have demonstrated that dry mopping alone in CSOM is no more effective than no treatment at all. As this was one aspect of treatment in this study, it was not felt necessary to include a no treatment group as a control.

Full strength Burow's solution proved most effective in resolving the discharge but due to its increased acidity was the most uncomfortable to use (Table III). As compliance to therapy is important, the quarter strength Burow's solution though slightly less effective proved to be more acceptable to the paediatric population used in this study. The discomfort experienced with Solutions A and C disappeared shortly after application and with resolution of the otorrhoea whereas the duration and intensity of discomfort of full strength Burow's was considerable. Both full strength and quarter strength Burow's solution were as effective as the reported success of aminoglycoside[8,9] and quinolone[10,11] containing preparations.

Assessment of the treatment failures showed that the only qualitative feature that had any bearing on response was the duration of the otorrhoea. Duration of discharge of three months or more proved most difficult to resolve. The degree of inflammation and perforation size had no effect on the outcome. Statistical analysis of treatment failures was not possible due to the small size of the groups.

To achieve a statistical difference in the efficacy of full strength and quarter strength Burow's solution an estimation of sample size to give this study statistical power showed that a further of 1700 patients would have to be randomized.

In the search for a cheap, yet effective, ototopical solution the main consideration apart from effectiveness is the potential risk of ototoxicity. Otologists have been aware of the effects of persistent CSOM on cochlear function[12–14] and hence language development[15] for some time. The pathophysiological mechanism and the clinical significance of the sensorineural hearing loss (SNHL) are as yet not definite.[16] However, MacAndie and O'Reilly[17] in a recent comprehensive retrospective review showed that SNHL is significant across the frequency range, but that the disease duration does not correlate with the severity of the SNHL. Whether greater cochlear damage is caused by the inflammatory mediators of CSOM or the topical treatment thereof, remains controversial.

The round window membrane (RWM) is thought to be integral in the pathophysiology of ototopical ototoxicity and SNHL due to CSOM.[18] Meyerhoff *et al.*[19] note that the RWM thickness of the more commonly used animal models is approximately 25 per cent of that in humans. The RWM of the chinchilla and the guinea pig are in addition vulnerably exposed in the middle ear when compared to the deeply recessed RWM in humans.[20] In

TABLE IV
TREATMENT FAILURES IN EACH OF THE TREATMENT GROUPS

	n	%	Otorrhoea duration (weeks)	Otorrhoea duration (months)	Inflammation severity: mild	Inflammation severity: moderate	Perforation size: 0–25	Perforation size: 25–50	Perforation size: >50
Solution B (Burow's solution)	5	19.2	1	4	4	1	4	1	0
Solution C (3.25% aluminium acetate)	5	25	1	4	4	1	4	1	0
Solution A (1.3% aluminium acetate)	5	50	3	2	4	1	4	1	0

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TABLE V
PURE TONE AIR CONDUCTION AUDIOLOGICAL RESULTS OF TREATMENT GROUPS

	Pure tone average improvement (dB)	Percentage audiological improvement
Solution A (1.3% aluminium acetate)	6.33	44.4
Solution B (Burow's solution)	9.68	70.8
Solution C (3.25% aluminium acetate)	8.36	63.1
Average	8.6	63.5

CSOM pathological thickening of the RWM minimizes permeability but the inflammatory process conversely increases the permeability of the RWM.[21–23] Therefore the predictive value of animal model testing is limited in ascertaining the potential ototoxicity of a preparation on a patient.

Although there are no reported cases of ear drop related ototoxicity in humans, there is mounting evidence that SNHL can occur in patients treated with antibiotic containing and especially aminoglycoside based topical preparations for prolonged periods.[24,25] Other non-antibiotic substances commonly found in eardrop preparations have shown in animal models to be ototoxic. These include propylene glycol,[26,27] ethanol,[28] povidone-iodine preparations[29] and acetic acid.[30] To date no animal studies have been performed to assess the ototoxic potential of Burow's solution.

Conclusion

In vitro studies suggest that Burow's solution may be an effective ototopical preparation for use in CSOM and this *in vivo* clinical trial serves to confirm this. It would appear that a quarter strength Burow's solution which causes less discomfort would be as effective as the full strength solution. An animal study to confirm that this would not be an ototoxic preparation is needed before recommending widespread use of this agent, which otherwise fulfils the criteria for a cheap yet effective alternative to more expensive antibiotic/steroid preparations.

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