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The Efficacy of Burow's Solution as an Ear Preparation for the Treatment of Chronic Ear Infections

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Objective: To determine the efficacy of Burow's solution as an otologic preparation for the treatment of chronic ear infection.
Study Design: Two studies were included: 1) a prospective clinical study and 2) a laboratory study on antibacterial and antifungal effects.
Setting: A private otology practice and a laboratory study.
Patients: Fifty-eight patients with refractory otorrhea.
Intervention: Diagnosis by otoscopy, audiometry, and bacteriology.
Methods: Burow's solution was mixed in solutions with four organisms: methicillin-resistant *Staphylococcus aureus*, penicillin-resistant *Streptococcus pneumoniae*, *Candida albicans*, and *Aspergillus*. Soon after Burow's solution was mixed in the solutions with organisms, and 5, 10, and 20 minutes thereafter, the mixtures were cultured on agars. The numbers of the bacterial or fungal colonies were counted to evaluate the effect of Burow's solution.
Main Outcome Measures: Changes in the clinical findings of the ears, the symptom of otorrhea, and side effects were assessed.
Results: Thirty-five (70%) of the 50 ears assessed were "cured" and 10 (20%) ears assessed were "improved." No significant side effect was observed. Regarding the laboratory study, the four organisms disappeared within 20 minutes after Burow's solution was mixed.
Conclusion: Burow's solution was considered to be an effective otologic preparation. **Key Words:** Acid—Biofilms—Burow's solution—Infections—Therapy.
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Chronic infection of the ear can be quite refractory because of the low concentration of antibiotics administered to the local area of the ear and the appearance of resistant bacteria. Burow's solution, named after Karl August von Burow, a German surgeon in the late 19th century, has been used as a local otologic preparation. This colorless liquid with an acetic odor is aluminum acetate of approximately 13%, with a pH of 3.06, and is considered to have antibacterial and astringent effects (1). Compared with other antibiotics, it is not used as much now as it was in the past. Recently, Thorp et al. (2,3) reported on the clinical efficacy of this solution for chronic otitis media and determined the optimal dilution for clinical usage (4). To search for a new strategy without using antibiotics for the treatment of ears with chronic infection, we investigated the clinical efficacy of Burow's solution for chronic infection of the external and middle ears of 48 patients. We also examined the antibacterial activity of this solution in vitro.

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MATERIAL AND METHODS

The Department of Pharmacy, Hokkaido University Hospital prepared Burow's solution, which was used for the studies described in this article. The ingredients and the compounding information are listed in Table 1.

Clinical Study

Fifty ears of 48 patients who had suffered from persistent otorrhea were assessed. Before the treatment with Burow's solution, they had received conventional therapies, such as systemic or local administration of antibiotics or antifungals, irrigation with 1% povidone-iodine, and cleaning with microsuction for a period of at least 1 month. The causal diseases of otorrhea were chronic otitis externa, chronic otitis media with perforation, repetitive granular myringitis, and chronic infection in the cavity after canal wall down surgery. Nine of the 10 granular myringitis cases were postoperative. The methods of local administration of Burow's solution are listed in Table 2. All patients were given explanations on Burow's solution and possible positive effects or side effects. The treatments were started after patient consent was given. Initially, we put cotton pills soaked with Burow's solution in the infected ears because we were concerned about pain that might be caused by direct dripping into the ears. If patients did not complain of any pain and the symptom of otorrhea did not completely disappear, we

TABLE 1. *The recipe for Burow's solution*

Ingredient	Amount
Aluminum sulfate	22.5 g
Calcium carbonate	10.0 g
Acetic acid	25.0 ml
Purified water	75.0 ml

1. Aluminum sulfate wrapped double in gauze is floated in purified water for 24 hr until dissolved.
2. This liquid is passed through a filter and more purified water is added to a total amount of 65 ml.
3. Calcium carbonate is levigated with 10 ml of purified water. Then, aluminum sulfate liquid made through Process 2 is added gradually.
4. Acetic acid is added to the liquid made through Process 3 and left for 3 days, with occasional stirring. The top clear layer of the liquid is passed through a filter to obtain Burow's solution.

dropped the solution into the ear or injected it through a perforation on the eardrum to make the solution contact with the local region more effective. All patients were treated at our outpatient clinic from 1 to 3 days per week. Any discharge from the patients was taken with otologic plus swabs and cultured to investigate the infectious organisms. All patients were examined for their hearing thresholds by a pure-tone audiometer before and after the treatment period. The results of the treatment were categorized as follows: if the local area became totally dry, it was categorized as "cured"; if the local area became partially dry and subjective symptoms of otorrhea disappeared, it was categorized as "improved." Finally, others were categorized as "no change."

Study of Antibacterial and Antifungal Activity

Four organisms—methicillin-resistant *Staphylococcus aureus* (MRSA), penicillin-resistant *Streptococcus pneumoniae* (PRSP), *Candida albicans*, and *Aspergillus*—cultured from patients' otorrhea in daily otolaryngologic practice were tested. Once the organisms were standardized to 1.0 McFarland, 0.5 ml of this solution was placed into nine respective test tubes. Burow's solution (0.5 ml) was added to each of the first three test tubes. Soon after a couple of shakings, the mixture was taken with a platinum loop to inoculate on three respective agars. Then, after 5, 10, and 20 minutes, the same procedures were performed. As a control study, 0.5 ml of saline was added to each of the second three test tubes, and this mixture was inoculated onto three agars soon thereafter and after 5, 10, and 20 minutes. To compare the antiseptic activity of Burow's solution, 1% povidone-iodine solution, which was used to irrigate the infected ears, was added into the third three test tubes and the same procedures were performed. As testing agars, Muller-Hinton agar with 5% sheep blood was used for PRSP, and Muller-Hinton agar was used for the other three organisms. All inoculated organisms were incubated at 35°C for a period of 36 hours. The numbers of colonies were counted to evaluate the effectiveness of each solution on the organisms tested.

TABLE 2. *Methods of local administration of Burow's solution*

Method	No. of cases
Cotton pills	30
Ear drops	18
Injection through the perforation on the eardrum	2
Total	50

TABLE 3. *Results of the effectiveness of Burow's solution*

Disease	No. of ears	Cured	Improved	No change
Chronic otitis externa	12	10	2	0
Chronic otits media with perforation	14	8	3	3
Granular myringitis	10	7	2	1
Chronic infection in the postoperative cavity	14	10	3	1
Total	50	35	10	5

RESULTS

Clinical Study

Patients had suffered from otorrhea before using Burow's solution for 1 month to 20 years, with a mean period of 33.5 months. The treatment periods were from 1 day to 4 weeks. The number of treatments ranged from 1 to 10. The clinical results are listed in Table 3. Thirty-five (70%) of the 50 ears assessed were cured, and 10 (20%) ears assessed were improved. Posttreatment cultural tests by otologic plus swabs were performed on 30 of the 35 ears that were assessed to be cured, all of which were proven to be negative. The percentage of cured and improved ears was 83.3% for otitis externa, 78.6% for chronic otitis media with perforation, 90.0% for granular myringitis, and 92.9% for infection of the open cavity. Table 4 lists the results of the effectiveness on the organisms identified. Twelve ears showed fungi, and they all turned dry. MRSA was identified mostly as a sole organism and was cultured from 14 ears. Ten (71.4%) ears were cured and three (21.4%) ears were improved. Twenty-three ears were found to have other bacteria. Twenty-one ears were cured or improved.

Regarding side effects, 13 patients complained of an irritating feeling locally and 6 patients complained of a moderate pain in the local area of the ears. The other patients did not complain of any uncomfortable symptoms. No patient showed any signs of hearing impairment on audiometric tests. Furthermore, no taste disorders were observed.

TABLE 4. *Effectiveness of Burow's solution of microorganisms identified*

Microorganism	No. of cases	Cured	Improved	No change
Fungi	12	12	0	0
Aspergillus	6	6	0	0
Candida albicans	3	3	0	0
Others	3	3	0	0
Bacteria	37	25	9	3
MRSA	14	10	3	1
S. epidermidis	5	3	2	0
P. aeruginosa	4	3	1	0
Others	14	9	3	2
Total	49	37	9	3

MRSA, methicillin-resistant *Staphylococcus aureus; S. epidermidis, Staphylococcus epidermidis; P. aeruginosa, Pseudomonas aeruginosa.*

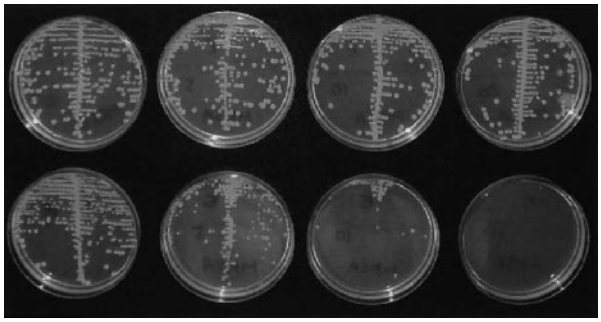

FIG. 1. Comparison of the results of control saline and Burow's solution on MRSA is displayed. Culture results at 0, 5, 10, and 20 minutes (from the left to the right) after saline (upper) and Burow's solution (lower) were added into MRSA solution are displayed. It is observed that the colonies of MRSA disappeared 20 minutes after Burow's solution was added.

Study of Antibacterial and Antifungal Activity

Figure 1 shows the comparison between the results of control saline and Burow's solution on MRSA. It was observed that MRSA was not colonized in 20 minutes after contact with Burow's solution. Similar bactericidal effects were observed in the other organisms examined. The time of disappearance for each organism was 20 minutes for MRSA, 5 minutes for PRSP, 10 minutes for *Candida albicans*, and 5 minutes for *Aspergillus*. The relationships between the time and the numbers of colonies of each organism by saline, Burow's solution, and 1% povidone-iodine solution are listed in Tables 5 through 8. It was observed that the bactericidal effect of 1% povidone-iodine solution was expressed more rapidly for each organism examined.

DISCUSSION

Burow's solution has been used in the treatment of chronic suppurative otitis media and chronic otitis externa since the late 19th century (5). Compared with other antibiotics, it is not used as much now as it was in the past. In the current study, positive effects of Burow's solution on chronic infection of the middle and external ears that were resistant to every conventional treatment were observed. Thorp et al. (3) reported on the efficacy of this solution for the treatment of chronic suppurative otitis media in children. In addition, our experience has shown the efficacy of Burow's solution on other chronic diseases such as otitis externa, granular myringitis, and infections in the postoperative cavity.

Two important points required for topical otologic preparations are the effectiveness on the causative microorganisms and safety. These causative organisms grow best in a narrow range of pH from 6.5 to 7.5 (6). Burow's solution with a pH of 3.06 is considered to have positive effects on the organisms. Considering the biochemical bases of bacterial resistance to antibiotics (7,8) and the effects of acids on bacteria (9), the bactericidal effects of acids are still expected on the antibiotic-resistant bacteria. Actually, in the current study, the ears infected by resistant bacteria such as MRSA or PRSP were cured fairly well. Our experimental results also support these findings. Thorp et al. (3) also have postulated that the antibacterial effectiveness of Burow's solution is largely due to its acidity. However, in their study, Burow's solution showed stronger inhibitory effects on the bacteria tested than either 1%, 2%, or 3% acetic acid, which were more acidic than Burow's solution (3). That would seem to support the suggestion that the effective-

TABLE 5. *Results of antibacterial activity of Burow's solution and 1% povidone-iodine solution on methicillin-resistant* Staphylococcus aureus

Solution	Agar	Minutes after mixture 0	5	10	20
Burows' solution	1	320	150	40	0
	2	380	130	0	0
	3	370	120	70	0
1% povidone-iodine solution	1	100	0	0	0
	2	30	0	0	0
	3	16	0	0	0
Saline (control)	1	420	390	370	370
	2	390	390	380	350
	3	400	320	410	380

The numbers of bacterial colonies of each agar are listed.

TABLE 6. *Results of antibacterial activity of Burow's solution and 1% povidone-iodine solution on penicillin-resistant* Streptococcus pneumoniae

Solution	Agar	Minutes after mixture 0	5	10	20
Burows' solution	1	15	0	0	0
	2	16	0	0	0
	3	15	0	0	0
1% povidone-iodine solution	1	3	0	0	0
	2	0	0	0	0
	3	3	0	0	0
Saline (control)	1	72	65	68	73
	2	75	60	65	60
	3	68	70	66	72

The numbers of bacterial colonies of each agar are listed.

TABLE 7. *Results of antibacterial activity of Burow's solution and 1% povidene-iodine solution on* Candida albicans

Solution	Agar	Minutes after mixture 0	5	10	20
Burows' solution	1	30	0	0	0
	2	42	3	0	0
	3	32	0	0	0
1% povidone-iodine solution	1	0	0	0	0
	2	6	0	0	0
	3	2	0	0	0
Saline (control)	1	68	59	54	60
	2	92	86	78	84
	3	60	68	63	45

The numbers of fungal colonies of each agar are listed.

TABLE 8. *Results of antibacterial activity of Burow's solution and 1% povidone-iodine solution on* Aspergillus

Solution	Agar	Minutes after mixture			
		0	5	10	20
Burows' solution	1	8	0	0	0
	2	9	0	0	0
	3	4	0	0	0
1% povidine-iodine solution	1	0	0	0	0
	2	0	0	0	0
	3	0	0	0	0
Saline (control)	1	15	9	16	16
	2	13	13	12	10
	3	21	14	20	17

The numbers of fungal colonies of each agar are listed.

ness of Burow's solution, although partly due to its acidity, must lie with the aluminum acetate.

Another current concept related to infections resistant to antibiotics is biofilm. A biofilm forms when bacteria adhere to surfaces in aqueous environments. It is a slimy, glue-like substance that can anchor the bacteria to all types of materials (10). Since Mills (11) reported a biofilm within the living body, it has been a noticeable phenomenon in medical fields. The biofilm structure provides a favorable protective environment for the survival of the cells of bacteria and causes refractory infection. Some evidence has been found that bacterial biofilms are formed in otitis media (12,13). The formation of biofilms in the ears could make infections resistant to antibiotics and antiseptics. Akiyama et al. (14) proved that acetic acid could have a destructive effect on biofilms. Burow's solution, an acetic compound, might destroy biofilms and might work on the infectious organisms effectively. Interestingly enough, experimental results showed that 1% povidone-iodine worked on organisms better than Burow's solution. However, in our clinical experience, most cases that had not been cured by irrigation treatments with 1% povidone-iodine were swiftly cured by local administration of Burow's solution. This might also suggest the intervention of biofilms. Akiyama et al. (15) showed that *S. aureus* cells incubated for 24 hours in human plasma were surrounded by fibrin bundles and could not be disinfected with 10% povidone-iodine solution. They suggested that *S. aureus* cells might produce biofilm-like structures and that these structures might help the cells resist the povidone-iodine.

Another considerable effect of Burow's solution is the astringent effect. The astringent effect causes proteins to decompose and constrict the blood vessels and to tighten up the skin or the mucosa. In the present clinical study, it was often observed that the granulations or the mucosa of the ears had become partially pale and shrunken after Burow's solution was administered. The shrinkage of the granulations could produce more space in the ears, facilitating the discharge of otorrhea, and the solution could consequently work deeply in the ears.

Regarding side effects, 19 of 50 (38%) patients complained of either irritating feelings or pain in the local area. However, pain levels were still tolerable, and diluting the solution could alleviate this problem if needed. Thorp et al. (3) concluded in their serial reports that the quarter diluted Burow's solution was still effective and more acceptable for the pediatric population, although it was slightly less effective than Burow's solution taken at full strength. Regarding ototoxicity, no hearing impairment in the audiometric tests was observed in the current study. Thorp et al. reported that no hearing impairment was observed in the 67 discharging ears of children by using Burow's solution locally. From these clinical findings, it should be considered that the possibility of ototoxicity of this solution is low. However, it has been proved that weak acids can infiltrate through the round window membrane and that inflammation can increase the permeability of the membrane (16). Experiments on ototoxicity of Burow's solution with animals are needed. Furthermore, it is necessary to investigate the pathologic changes caused by Burow's solution, such as the changes on eardrums, mucosa of the middle ears, or the chorda tympani nerve.

Although the mechanisms of Burow's solution have not yet been proven, combination therapies with antibiotics or other antiseptics might be useful. The interactions between Burow's solution and these agents should be investigated. It is no exaggeration to say that we are living in the era of antibiotic-resistant bacteria. The development of new antibiotics could lead to the appearance of new antibiotic-resistant bacteria. Therefore, the usefulness of nonantibiotic otologic preparations such as acids is quite meaningful. This solution from the past could provide an impetus in the fight against infection.

CONCLUSION

Both clinical and experimental studies suggest that Burow's solution could be an effective and safe ototopic preparation. Finally, more experiments on animals for ototoxicity and pathologic change are needed.

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REFERENCES

1. Shupack JL, Washenik K, Pak GH. Principles of topical therapy. In: Freedberg IM, Eiesn AZ, Wolff K, et al., eds. *Fitzpatrick's Dermatology in General Medicine*. New York: McGraw-Hill, 1999.
2. Thorp MA, Gardiner IB, Prescott CAJ. Burow's solution in the treatment of active mucosal chronic suppurative otitis media: determining an effective dilution. *J Laryngol Otol* 2000;114:432–6.
3. Thorp MA, Kruger J, Oliver S, et al. The antibacterial activity of acetic acid and Burow's solution as topical otological preparations. *J Laryngol Otol* 1998;112:925–8.
4. Thorp MA, Oliver S, Kruger J, et al. Determination of the lowest dilution of aluminium acetate solution able to inhibit in vitro growth of organisms commonly found in chronic suppurative otitis media. *J Laryngol Otol* 2000;114:830–1.
5. Dollery S. *Therapeutic Drugs*. London: Churchill Livingstone, 1991.

6. Aminifarshidmehr N. The management of chronic suppurative otitis media with acid media solution. *Am J Otol* 1996;17:24–5.
7. Russel AD. Microbial susceptibility and resistance to chemical and physical agents. In: Collier L, Balows A, Sussman M, eds. *Microbiology and Microbial Infections, Systemic Bacteriology*. New York: Oxford University Press, 1998.
8. Sefton AM. Mechanisms of antimicrobial resistance: their clinical relevance in the new millennium. *Drugs* 2002;62:557–66.
9. Hommais F, Laurence-Winter C, Labas V, et al. Effect of mild acid pH on the functioning of bacterial membranes in *Vibrio cholerae*. *Proteomics* 2002;2:571–9.
10. Costerton JW. Bacterial biofilm in nature and disease. *Annu Rev Microbiol* 1987;41:435–64.
11. Mills J, Pulliam L, Dall L, Marzouk J, Wilson W, Costerton JW. Exopolysaccharide production by viridans streptococci in experimental endocarditis. *Infect Immun* 1984;43:359–67.
12. Post JC. Direct evidence of bacterial biofilm in otitis media. *Laryngoscope* 2001;111:2083–94.
13. Ehrlich GD, Veeh R, Wang X, et al. Mucosal biofilm formation on middle-ear mucosa in the chinchilla model of otitis media. *JAMA* 2002;287:1710–5.
14. Akiyama H, Yamasaki O, Tada J, et al. Effects of acetic acid on biofilms formed by *Staphylococcus aureus*. *Arch Dermatol Res* 1999;291:570–3.
15. Akiyama H, Tada J, Toi J, et al. Changes in *Staphylococcus aureus* density and lesion severity after topical application of povidone-iodine in cases of atopic dermatitis. *J Dermatol Sci* 1997;16:23–30.
16. Ikeda K, Morizono T. The preparation of acetic acid for use in otic drops and its effect on endocochlear potential and pH in inner ear fluid. *Am J Otolaryngol* 1989;10:382–5.