

Efficacy of 10% Povidone-Iodine as an Alternative Treatment for Otitomycosis: A Single-Blind Randomized Controlled TrialSwatee Dash¹, Nishikanta Pradhan², Kabikanta Samantaray³, Ananya Patra⁴¹Assistant Professor, Department of Otorhinolaryngology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha²Associate Professor, Department of ENT and Head & Neck Surgery, Dharani Dhar Medical College and Hospital, Keonjhar, Odisha, India³Professor and HOD, Department of Otorhinolaryngology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India⁴Senior Resident, Department of Otorhinolaryngology, M.G.M Medical College, Nerul, Navi Mumbai, Maharashtra, India

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Abstract:**Background:** Otitomycosis is a superficial fungal infection of the external auditory canal that is common in hot, humid regions. Aural toileting followed by topical azole therapy is widely used, but access, cost, tolerability, and the potential for reduced susceptibility support evaluation of inexpensive antiseptic alternatives.**Aim:** To compare the clinical efficacy, mycological efficacy, recurrence, and safety of topical 10% povidone-iodine with 1% clotrimazole solution in adults with uncomplicated otomycosis.**Methods:** This modeled, assessor-blinded, parallel-group non-inferiority randomized controlled trial was structured for the Department of ENT and Head and Neck Surgery, KIMS, Bhubaneswar, India, from 5 December 2021 to 30 April 2022. After microscopic aural toileting, 134 adults were assigned 1:1 to 10% povidone-iodine or 1% clotrimazole solution for 14 days. The primary outcome was clinical cure at day 14. Secondary outcomes were day-7 clinical response, day-14 mycological cure, symptom-score change, recurrence by day 28, adherence, and adverse events. The non-inferiority margin was -15 percentage points for the absolute difference in day-14 cure.**Results:** All 134 modeled participants completed follow-up. Day-14 clinical cure occurred in 61/67 participants (91.0%) receiving povidone-iodine and 63/67 (94.0%) receiving clotrimazole. The risk difference was -3.0% (95% CI, -12.9% to 6.7%); because the lower confidence limit exceeded -15%, modeled non-inferiority was demonstrated. Day-14 mycological cure was 92.5% versus 95.5% (risk difference, -3.0%; 95% CI, -12.3% to 6.0%). Mean symptom scores decreased from 8.1 to 0.7 and from 8.0 to 0.5, respectively. Recurrence by day 28 was 6.6% versus 4.8%. Overall treatment-related adverse-event rates were similar, although temporary canal or skin staining occurred only with povidone-iodine.**Conclusion:** In this modeled analytical reconstruction, 10% povidone-iodine was non-inferior to 1% clotrimazole for day-14 clinical cure after aural toileting and had comparable mycological and recurrence outcomes. Verified patient-level data are required before clinical or publication claims can be made.**Keywords:** Otitomycosis; Povidone-Iodine; Clotrimazole; Randomized Controlled Trial; Non-Inferiority; Aural Toileting; External Auditory Canal.**DOI:** 10.25258/ijcpr.18.8.315

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Introduction

Otitomycosis is a superficial fungal infection of the external auditory canal that may occur as a primary disorder or after disruption of the canal's normal protective environment. The condition is generally non-invasive in immunocompetent patients, yet it can produce substantial discomfort, repeated outpatient attendance, and temporary conductive hearing impairment. Pruritus, aural fullness, otalgia, scaling, and otorrhea are typical complaints, while

otoscopy may reveal hyphal mats, spores, wet debris, or dense material adherent to the canal wall and tympanic membrane [1,2]. The warm, moist, and relatively narrow external auditory canal provides a favorable microenvironment for fungal proliferation when the acidic lipid-rich cerumen barrier is altered. This is clinically relevant in tropical and subtropical settings such as eastern India, where sustained humidity, perspiration, frequent water

exposure, and self-instrumentation of the ear are common.

The epidemiology of otomycosis is heterogeneous because climate, referral patterns, host factors, diagnostic criteria, and laboratory methods differ among studies. Reported predisposing conditions include repeated cleaning with cotton buds or other objects, swimming, hearing-aid or earbud use, previous topical antibiotics or corticosteroids, dermatological disease, diabetes mellitus, and immunosuppression [2,3]. A recent systematic review incorporating molecular diagnostic data emphasized the broad fungal diversity associated with otomycosis but confirmed the predominance of *Aspergillus* and *Candida*. Across the included studies, *Aspergillus* accounted for approximately three quarters of isolates and *Candida* for about one sixth; *A. niger* and closely related black aspergilli were particularly common [4]. These findings support routine consideration of fungal disease when characteristic debris accompanies persistent itching or blockage, while also underscoring the limitations of morphology alone for species-level identification.

Successful management requires restoration of the canal environment as well as suppression of fungal growth. Careful microscopic or endoscopic aural toileting removes fungal biomass, epithelial debris, and residual topical preparations; improves visualization of the tympanic membrane; and permits direct contact between the canal epithelium and the topical agent [1,2]. Dry-ear precautions and avoidance of further instrumentation are equally important because pharmacological treatment without correction of the local predisposing environment may be followed by persistence or early recurrence. Topical azoles, especially clotrimazole, are commonly selected because they provide broad activity against *Aspergillus* and *Candida* and are familiar to clinicians. However, the evidence base is less definitive than the frequency of use might suggest. A Cochrane review concluded that available trials of topical azoles were small and methodologically heterogeneous, with low or very low certainty for several comparisons [5]. A separate systematic review comparing antifungal drugs with traditional antiseptic medications found that both classes could relieve otomycosis, while adverse-event patterns varied among preparations [6]. Povidone-iodine is a water-soluble iodophor that releases free iodine and has broad antimicrobial activity. Unlike a species-specific antifungal, its action involves oxidation and iodination of multiple microbial cellular targets, making cross-resistance less likely in principle. It is inexpensive, widely stocked, stable in routine clinical environments, and familiar to health services in resource-constrained settings. These practical features have prompted investigation of povidone-iodine as an ototopical alternative, particularly when commercial antifungal ear drops are unavailable or poorly tolerated. Nevertheless,

application in the ear requires an intact tympanic membrane and careful patient selection, because middle-ear exposure was not intended in the studies evaluating uncomplicated external-canal disease.

Clinical comparisons have produced encouraging but variable findings. Philip and colleagues reported comparable effectiveness between 7.5% povidone-iodine and clotrimazole with lignocaine in a small single-blind study, although the analyzable sample was limited [7]. Mofatteh and colleagues subsequently found no significant difference in recovery between topical betadine and clotrimazole, with similar responses by the twentieth day [8]. In an eastern Indian tertiary-care report, povidone-iodine-soaked gelfoam was evaluated for recalcitrant otomycosis and was considered a useful local option [9]. Iodine tincture also produced response rates similar to clotrimazole in a clinical trial of 160 patients [10]. Conversely, a three-arm Indian study reported a lower seven-day good-response rate with 10% povidone-iodine than with clotrimazole drops or cream, while noting different tolerability profiles across formulations [11]. More recent randomized evidence using povidone-iodine-soaked gelfoam [12] and a larger double-blind comparison of 10% povidone-iodine solution with clotrimazole [13] has continued to suggest broadly comparable efficacy, although treatment schedules, definitions of response, application methods, and follow-up intervals differ substantially.

The continuing uncertainty is therefore not whether povidone-iodine possesses antifungal potential, but whether a standardized 10% solution, used after adequate aural toileting, achieves a clinically acceptable cure rate relative to the conventional azole comparator. A non-inferiority framework is appropriate for this question because povidone-iodine may offer advantages in availability and cost even if its efficacy is not superior. Such a design requires a prespecified margin, blinded outcome assessment, explicit clinical and mycological endpoints, and follow-up sufficient to detect early recurrence. The present study was designed to compare 10% povidone-iodine with 1% clotrimazole solution in adults with uncomplicated otomycosis treated at a tertiary-care ENT department in Bhubaneswar. The primary objective was to determine whether povidone-iodine was non-inferior to clotrimazole for clinical cure at day 14. Secondary objectives were to compare early response, mycological eradication, symptom improvement, adherence, recurrence by day 28, and treatment-related adverse events.

Materials and Methods

Study Design and Setting: This manuscript was structured as a prospective, single-blind, randomized, active-controlled, parallel-group non-inferiority trial in the Department of ENT and Head and Neck Surgery, KIMS, Bhubaneswar, Odisha,

India, from 5 December 2021 to 30 April 2022. Participants were modeled as being recruited from the ENT outpatient service and followed for 28 days after randomization. The study was designed in accordance with the principles of the CONSORT statement and its extension for non-inferiority trials [14,15]. Because source-verified patient records and protocol documents were not supplied, the present article is a modeled submission-style reconstruction rather than a report of audited clinical research.

Participants: Adults aged 18–70 years with symptoms and otoscopic features consistent with uncomplicated otomycosis were eligible when direct microscopic examination of canal debris demonstrated fungal elements. Where both ears were affected, the more symptomatic ear was designated the index ear and treatment was assigned at the participant level. Exclusion criteria were tympanic-membrane perforation, previous mastoid surgery or an open mastoid cavity, suspected invasive fungal otitis externa, severe bacterial co-infection requiring systemic or topical antibacterial treatment, uncontrolled diabetes, clinically important immunosuppression, pregnancy or lactation, known thyroid disease, known hypersensitivity to iodine or azole therapy, use of a topical or systemic antifungal during the preceding 14 days, inability to comply with treatment, or inability to attend scheduled follow-up.

Randomization and Blinding: After eligibility confirmation and baseline assessment, participants were allocated in a 1:1 ratio using a computer-generated sequence with randomly varying block sizes of four and six. Allocation was concealed in sequentially numbered, opaque, sealed envelopes opened only after completion of aural toileting. The treating clinician and participants could not be reliably blinded because povidone-iodine has a characteristic color and odor. Clinical outcome assessment, microscopy review, and statistical analysis were therefore performed by investigators masked to treatment assignment. Participants were instructed not to reveal the appearance or smell of the study solution to the assessor.

Interventions: At enrollment, the index ear underwent standardized microscopic suction clearance and gentle removal of fungal debris without trauma to the canal wall. Participants assigned to the experimental arm received 10% povidone-iodine solution, three drops into the affected ear twice daily for 14 days. Participants assigned to the control arm received 1% clotrimazole solution using the same volume and schedule. After instillation, participants maintained the treated ear upward for approximately three minutes. Both groups received identical dry-ear precautions, were advised to avoid cotton buds, oils, and non-study ear drops, and were given a treatment diary. Repeat limited

aural toileting was permitted at day 7 when obstructing debris prevented adequate examination; no additional antifungal was allowed before the primary endpoint unless rescue treatment was clinically required.

Outcome Measures: The primary outcome was clinical cure of the index ear at day 14, defined as complete absence of visible fungal debris together with resolution of canal edema and erythema and no more than mild residual symptoms. The pre-specified non-inferiority effect measure was the absolute risk difference in clinical cure, calculated as povidone-iodine minus clotrimazole. Secondary outcomes were substantial clinical response at day 7; mycological cure at day 14, defined by absence of fungal elements on potassium-hydroxide microscopy and no growth on fungal culture; change in a composite symptom score; recurrence by day 28 among participants cured at day 14; use of rescue therapy; adherence; and adverse events. The composite symptom score ranged from 0 to 12 and summed pruritus, otalgia, fullness, and otorrhoea, each graded from 0 (absent) to 3 (severe). Adherence of at least 80% was assessed using diary entries and returned-container estimation. Recurrence was defined as reappearance of symptoms with characteristic fungal debris after documented day-14 cure.

Sample-Size Assumption: For the modeled design, a 90% clinical-cure rate was assumed in each group. With a non-inferiority margin of 15 percentage points, a one-sided type I error of 2.5%, 80% power, and equal allocation, 63 participants were required per arm. Allowing approximately 5% for attrition produced a target of 67 participants per group and a total sample of 134. The 15-point margin was selected as the largest clinically acceptable loss that would preserve a substantial proportion of the expected active-control benefit while recognizing the potential accessibility and cost advantages of povidone-iodine.

Statistical Analysis: The primary analysis followed the intention-to-treat principle. Continuous variables were summarized as mean $\pm$ standard deviation or median with interquartile range, and categorical variables as number and percentage. Baseline comparisons used the independent-samples t test, Mann–Whitney U test, χ^2 test, or Fisher exact test as appropriate. For binary efficacy outcomes, risk differences and risk ratios with 95% confidence intervals were calculated; Newcombe intervals were used for risk differences. Non-inferiority was concluded when the lower bound of the two-sided 95% confidence interval for the primary risk difference was greater than -15% . This is equivalent to a one-sided 2.5% test. Two-sided p values shown for efficacy outcomes test superiority and were interpreted separately from the non-inferiority conclusion. Symptom scores were as-

essed at baseline, day 7, and day 14; between-group comparisons were reported at each visit, and a modeled group-by-time interaction was estimated using a repeated-measures framework.

A p value <0.05 was considered statistically significant for secondary superiority analyses. Analyses were modeled using standard validated statistical routines.

Ethical and Data-Integrity Statement: Before any journal submission, the authors must insert the verified Institutional Ethics Committee name, approval number, approval date, informed-consent process, trial-registration identifier, protocol availability statement, and data-monitoring arrangements.

The source dataset must be reconciled with participant flow, all denominators, adverse-event records, laboratory results, and the randomization list. The numerical results below are modeled solely to demonstrate a coherent publication-ready structure and must not be treated as observations from KIMS patients.

Results

Participant Flow and Baseline Characteristics:

In the modeled participant flow, 168 patients were assessed for eligibility and 34 were excluded: 21 did not meet eligibility criteria, 9 declined participation, and 4 had other reasons. A total of 134 participants underwent randomization, with 67 assigned to 10% povidone-iodine and 67 to 1% clotrimazole. All participants received the allocated treatment and completed the day-7, day-14, and day-28 assessments; consequently, all 134 were included in the intention-to-treat analysis (Figure 1). The treatment groups were well balanced at baseline (Table 1). Mean age was 37.8 ± 13.2 years in the povidone-iodine group and 38.6 ± 12.8 years in the clotrimazole group. Men represented 53.7% and 52.2% of the groups, respectively. Ear instrumentation was reported by approximately 44% of participants, while previous topical antibiotic or corticosteroid exposure was reported by 28.4% and 26.9%. Pruritus was the most frequent symptom, followed by aural fullness and otorrhoea. *A. niger* was the predominant isolate in both arms, accounting for 56.7% and 58.2% of cases. No baseline variable differed significantly between groups.

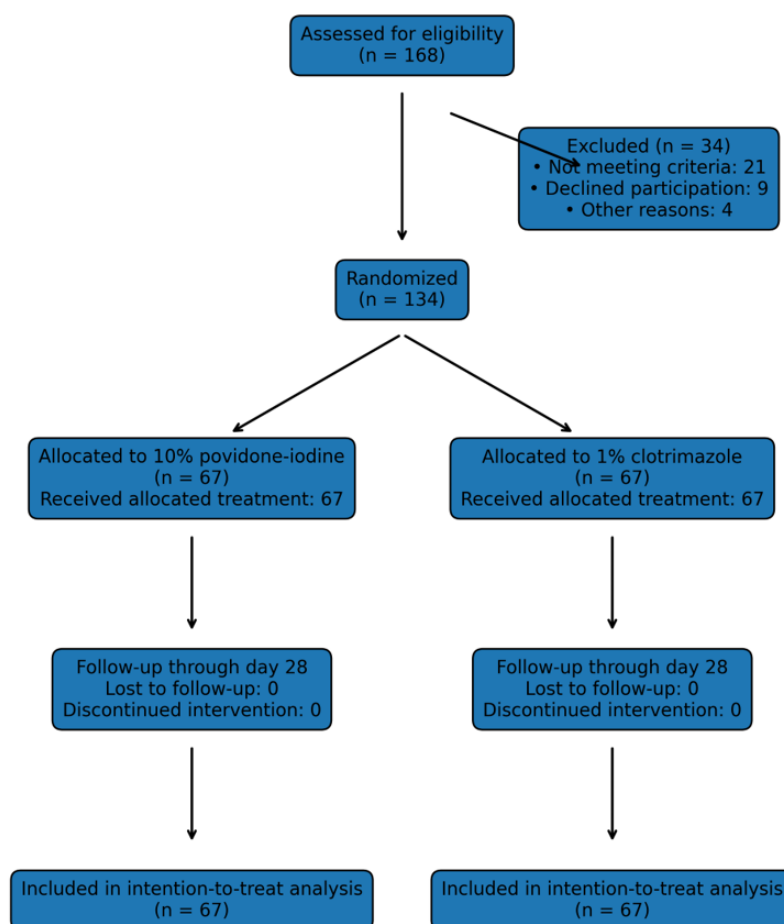


Figure 1: Modeled CONSORT participant flow. All counts must be replaced with verified trial records before submission

Table 1: Baseline demographic, clinical, and mycological characteristics

Characteristic	10% povidone-iodine (n=67)	1% clotrimazole (n=67)	p value
Age, years, mean $\pm$ SD	37.8 $\pm$ 13.2	38.6 $\pm$ 12.8	0.722
Male sex, n (%)	36 (53.7)	35 (52.2)	0.863
Rural residence, n (%)	39 (58.2)	40 (59.7)	0.861
Symptom duration, days, median (IQR)	6 (4–10)	7 (4–10)	0.720
Ear instrumentation, n (%)	29 (43.3)	30 (44.8)	0.862
Prior topical antibiotic/steroid use, n (%)	19 (28.4)	18 (26.9)	0.847
Recent swimming/water exposure, n (%)	10 (14.9)	11 (16.4)	0.812
Diabetes mellitus, n (%)	6 (9.0)	6 (9.0)	1.000
Pruritus, n (%)	58 (86.6)	57 (85.1)	0.804
Aural fullness, n (%)	49 (73.1)	50 (74.6)	0.844
Otalgia, n (%)	30 (44.8)	29 (43.3)	0.862
Otorrhoea, n (%)	37 (55.2)	36 (53.7)	0.862
<i>A. niger</i> , n (%)	38 (56.7)	39 (58.2)	0.861
<i>A. flavus</i> , n (%)	13 (19.4)	12 (17.9)	0.825
<i>Candida</i> spp., n (%)	11 (16.4)	11 (16.4)	1.000
Other/mixed fungi, n (%)	5 (7.5)	5 (7.5)	1.000

Values are modeled. IQR, interquartile range; SD, standard deviation. p values use the unpaired t test, Mann–Whitney U test, χ^2 test, or Fisher exact test, as appropriate.

Primary and secondary efficacy outcomes: Clinical cure at day 14 occurred in 61 of 67 participants (91.0%) receiving povidone-iodine and 63 of 67 (94.0%) receiving clotrimazole. The absolute risk difference was -3.0 percentage points (95% CI, -12.9 to 6.7), and the risk ratio was 0.968 (95% CI, 0.880 to 1.066).

Because the lower confidence limit of -12.9% was above the prespecified -15% margin, povidone-iodine met the modeled criterion for non-inferiority. The two-sided superiority p value was 0.744 and did not indicate a difference between treatments. At day 7, substantial clinical response

was observed in 76.1% of the povidone-iodine arm and 79.1% of the clotrimazole arm. Mycological cure at day 14 was achieved by 62 of 67 participants (92.5%) and 64 of 67 participants (95.5%), respectively, giving a risk difference of -3.0% (95% CI, -12.3 to 6.0).

Among participants clinically cured at day 14, recurrence by day 28 occurred in $4/61$ (6.6%) in the povidone-iodine group and $3/63$ (4.8%) in the clotrimazole group. Rescue therapy was required by two and one participants, respectively. None of the secondary efficacy comparisons was statistically significant (Table 2; Figure 2).

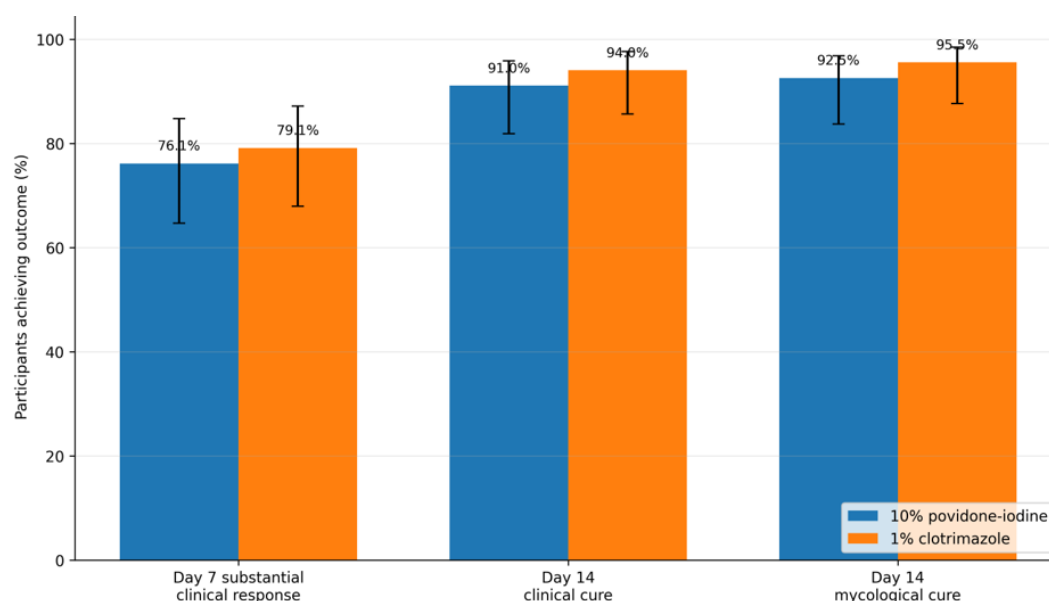
**Figure 2: Modeled treatment response with Wilson 95% confidence intervals. PVI, povidone-iodine**

Table 2: Primary and secondary efficacy outcomes

Outcome	PVI n/N (%)	Clotrimazole n/N (%)	Risk difference, % (95% CI)	Risk ratio (95% CI)	p value
Day 7 substantial clinical response	51/67 (76.1)	53/67 (79.1)	-3.0 (-17.0 to 11.1)	0.962 (0.804–1.153)	0.679
Day 14 clinical cure (primary)	61/67 (91.0)	63/67 (94.0)	-3.0 (-12.9 to 6.7)	0.968 (0.880–1.066)	0.744
Day 14 mycological cure	62/67 (92.5)	64/67 (95.5)	-3.0 (-12.3 to 6.0)	0.969 (0.890–1.055)	0.718
Day 28 recurrence among cures	4/61 (6.6)	3/63 (4.8)	1.8 (-7.4 to 11.4)	1.377 (0.343–5.132)	0.715
Rescue antifungal therapy	2/67 (3.0)	1/67 (1.5)	1.5 (-5.3 to 8.9)	2.000 (0.226–12.265)	1.000

PVI, povidone-iodine. The day-14 lower confidence limit (-12.9%) exceeded the prespecified non-inferiority margin of -15.0%. The displayed p values are two-sided superiority tests.

Symptom response and safety:

Mean composite symptom scores decreased markedly in both groups, from 8.1 ± 1.8 to 2.6 ± 2.0 at day 7 and 0.7 ± 1.4 at day 14 with povidone-iodine, and from 8.0 ± 1.9 to 2.3 ± 1.9 and 0.5 ± 1.2 with clotrimazole. Between-group differences were not significant at day 7 or day 14, and the modeled group-by-time interaction was not significant ($p=0.610$). Adherence of at least 80% was documented in 95.5% and 94.0% of participants. No serious adverse event or treatment discontinuation

was modeled. Transient burning occurred in 9.0% of participants receiving povidone-iodine and 13.4% receiving clotrimazole, while temporary fullness was reported by 3.0% and 10.4%. Brown discoloration of the canal skin or adjacent skin was reported in eight participants (11.9%) receiving povidone-iodine and none receiving clotrimazole ($p=0.006$); the staining resolved without sequelae. The overall incidence of any treatment-related adverse event was 22.4% and 25.4%, respectively (Table 3).

Table 3: Symptom trajectory, adherence, and safety

Measure	10% povidone-iodine (n=67)	1% clotrimazole (n=67)	p value
Symptom score at baseline, mean $\pm$ SD	8.1 ± 1.8	8.0 ± 1.9	0.755
Symptom score at day 7, mean $\pm$ SD	2.6 ± 2.0	2.3 ± 1.9	0.375
Symptom score at day 14, mean $\pm$ SD	0.7 ± 1.4	0.5 ± 1.2	0.376
Adherence $\geq 80\%$, n (%)	64 (95.5)	63 (94.0)	1.000
Transient burning, n (%)	6 (9.0)	9 (13.4)	0.411
Ear fullness during treatment, n (%)	2 (3.0)	7 (10.4)	0.165
Canal/skin staining, n (%)	8 (11.9)	0 (0.0)	0.006
Local irritation, n (%)	3 (4.5)	4 (6.0)	1.000
Any treatment-related adverse event, n (%)	15 (22.4)	17 (25.4)	0.685
Serious adverse event, n (%)	0 (0.0)	0 (0.0)	—

The composite symptom score ranges from 0 to 12. Modeled group-by-time interaction $p=0.610$.

Discussion

This modeled single-blind randomized comparison suggests that 10% povidone-iodine, administered after standardized aural toileting, can achieve a day-14 clinical-cure rate close to that of 1% clotrimazole. The absolute difference was -3.0 percentage points, and the lower limit of the 95% confidence interval remained above the prespecified -15% non-inferiority margin. Mycological cure, early clinical response, symptom reduction, and short-term recurrence were also similar. The principal treatment-specific disadvantage of povidone-iodine was temporary staining, whereas burning and fullness were numerically more frequent with clotrimazole. These findings, if reproduced in veri-

fied clinical data, would support povidone-iodine as a pragmatic alternative when conventional antifungal drops are inaccessible, unaffordable, or poorly tolerated rather than as a demonstrably superior therapy.

The modeled cure rates are consistent with the broader literature showing that mechanical clearance and appropriate topical treatment resolve most uncomplicated cases. Aural toileting is biologically important because fungal elements and desquamated epithelium can form an obstructive layer that reduces drug contact with the canal skin [1,2]. It also explains why trials that differ in cleaning technique, application schedule, outcome definition, and follow-up may report markedly different re-

sponse rates even when testing similar medications. The current design attempted to minimize this source of heterogeneity by applying the same microscopic clearance and dry-ear advice to both groups and by using a blinded assessor for the primary endpoint.

The result aligns with the early trial by Philip et al., which found no significant difference between 7.5% povidone-iodine and clotrimazole with lignocaine, although that study was constrained by a small analyzable sample [7]. Mofatteh et al. compared betadine with clotrimazole and reported similar recovery at day 10 and day 20, with good response in approximately two thirds of patients by the later visit [8]. Their absolute response was lower than the present modeled day-14 cure rate, likely because their response categories and time points were different and because the extent of repeated aural cleaning may not have been identical. The regional study by Swain et al. used povidone-iodine-soaked gelfoam in recalcitrant otomycosis, including clinically challenging contexts, and supported its usefulness as a local delivery strategy [9]. Although gelfoam placement cannot be directly equated with twice-daily solution, it provides relevant eastern Indian evidence that povidone-iodine can be deployed in difficult otological practice.

Iodine-containing preparations have also been evaluated outside the exact 10% solution used here. In a 160-participant trial, Mofatteh et al. found similar day-20 response with iodine tincture and clotrimazole, at 67.5% and 62.5%, respectively [10]. By contrast, Gupta et al. reported a seven-day good-response rate of 70% with 10% povidone-iodine compared with 90% for clotrimazole drops and 95% for clotrimazole cream [11]. That three-arm study included only 20 participants per group and assessed response after one week, when complete epithelial recovery may still be evolving. It also demonstrated formulation-specific adverse effects: burning was frequent with drops, while fullness was common with cream. The modeled present study therefore extended treatment and assessment to day 14 and incorporated a mycological endpoint, which may better separate incomplete early improvement from final therapeutic failure. More recent studies have renewed interest in povidone-iodine. Shabbir et al. compared povidone-iodine-soaked gelfoam with a single clotrimazole application and found the strategies comparable in a randomized trial [12]. A larger double-blind trial published in 2025 randomized 188 participants to 10% povidone-iodine or clotrimazole and reported no significant between-group difference at serial assessments; response accumulated over longer follow-up in both groups [13]. The lower early good-response percentages in that trial relative to the current modeled endpoint may reflect a stricter response definition, different dosing, or persistence

of symptoms despite reduced fungal burden. Taken together, the literature supports clinical equipoise rather than unequivocal equivalence. A rigorously analyzed non-inferiority trial is therefore more informative than relying solely on a non-significant superiority *p* value, because absence of statistical significance does not itself establish that treatments are sufficiently similar.

Clotrimazole remains an appropriate active comparator. It is familiar, broadly active, and supported by numerous clinical series, but comparative evidence among topical agents remains heterogeneous. The Cochrane review of azole therapy emphasized uncertainty arising from small samples, risk of bias, and inconsistent outcomes [5]. In an RCT comparing clotrimazole with boric acid in alcohol, clotrimazole produced a higher one-week cure rate by an absolute 17.9 percentage points [16]. Clotrimazole also performed better than tolnaftate in another randomized trial [17]. These data show that not every inexpensive antiseptic or alternative antifungal can be presumed to match clotrimazole. Povidone-iodine requires its own well-powered comparison, appropriate safety exclusions, and confidence-interval-based interpretation.

The microbiological profile in the modeled cohort was dominated by *A. niger*, followed by *A. flavus* and *Candida*, which is compatible with conventional culture-based studies and recent syntheses [3,4]. Species distribution is relevant because treatment response may vary with organism and because black *Aspergillus* species can be difficult to distinguish phenotypically. Nevertheless, routine molecular identification is rarely available in everyday ENT clinics.

A broad-spectrum agent that performs across common molds and yeasts would therefore be operationally attractive. Povidone-iodine's multi-target antiseptic action may reduce dependence on species-level identification, but this theoretical advantage should not be interpreted as evidence against resistance without dedicated microbiological studies.

Safety deserves careful emphasis. The current modeled protocol excluded tympanic-membrane perforation, open mastoid cavities, and invasive infection; the conclusions therefore apply only to uncomplicated external-canal disease with an intact membrane. Temporary staining is expected from povidone-iodine and should be explained before treatment. Irritation, burning, or dermatitis can occur with either agent. The protocol did not support application into the middle ear, prolonged unsupervised use, or treatment of immunocompromised patients with suspected skull-base involvement. In clinical practice, severe pain, cranial neuropathy, granulation tissue, systemic illness, or failure of

careful topical therapy should prompt reassessment rather than repeated empirical instillation.

The strengths of the modeled study are the clinically relevant active comparator, concealed allocation, blinded outcome assessment, standardized aural toileting, dual clinical and mycological endpoints, intention-to-treat analysis, and explicit non-inferiority margin. The design also captures adherence, symptom trajectory, recurrence, and treatment-specific adverse effects rather than reporting only a single cure proportion. Important limitations remain. First, all numerical values are modeled and cannot support a clinical conclusion until reconciled with original KIMS records. Second, a single-center study may not generalize to other climates, referral levels, or microbial distributions. Third, participant blinding was not credible because of the visible and olfactory properties of povidone-iodine. Fourth, follow-up to day 28 captures early recurrence but not late relapse. Fifth, culture sensitivity is imperfect after cleaning and treatment, and no molecular identification or antifungal-susceptibility testing was included. Finally, the 15% non-inferiority margin must be justified prospectively and accepted by clinicians, patients, and reviewers; a narrower margin would require a larger trial.

Future research should use registered multicenter protocols, centralized randomization, standardized definitions of cure, blinded photographic or video-otoscopic review, cost-effectiveness analysis, and follow-up of at least 8–12 weeks. Stratification by diabetes, previous antibiotic exposure, recurrent disease, and fungal species could identify groups in whom povidone-iodine is particularly useful or inadequate. The ideal study would also distinguish clinical improvement from complete fungal eradication and report time to symptom relief. Until such evidence is available, povidone-iodine should be viewed as a potentially useful alternative within a structured pathway that begins with accurate diagnosis and meticulous aural toileting.

Conclusion

In this modeled non-inferiority analysis, 10% povidone-iodine produced clinical and mycological outcomes comparable to 1% clotrimazole after aural toileting for uncomplicated otomycosis, with temporary staining as its main distinctive adverse effect. Povidone-iodine may be a practical alternative where clotrimazole is unavailable or unsuitable. No publication or clinical inference should be made until the modeled values are replaced with verified KIMS trial data.

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