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The effect of mouthwashes on intra-oral halitosis (bad breath)

Submission date	Recruitment status	[ ] Prospectively registered
23/08/2024	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
19/09/2024	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
18/09/2024	Oral Health	[ ] Record updated in last year

Plain English summary of protocol
Background and study aims
Mouthwashes with a combination of different agents, claiming to reduce intra-oral halitosis, are presently available on the market. There are, however, few
randomized controlled trials comparing the effectiveness of different mouthwashes on intra-oral halitosis. We aimed to evaluate the effect of three different (commercially available) oral mouthwashes and water in a single-blind four-arm randomized clinical trial on levels of hydrogen sulfide measured by gas chromatography (OralChroma).
Particularly, the mouthwash containing zinc acetate and chlorhexidine diacetate, will be compared to: a negative control (water), a positive control mouthwash containing chlorhexidine digluconate, cetylpyridinium, a mouthwash containing essential oils. Three commercially available mouthwashes are without alcohol.
Secondary objectives were:
1. To evaluate the effect of the three mouthwashes and water on methyl mercaptan levels, as measured by OralChroma, on the total oral sulfide concentration as measured with the Halimeter device and breath odor intensity with organoleptic scores.
2. To evaluate the effect of three different mouthwashes and water on tongue coating indices.
3. To evaluate the subject's self perception of his/her own breath odor (at the baseline and end).
4. To evaluate the perception of the subject's attitudes towards the different mouthwashes used in this study (at the end).
Study design: A three weeks, single-centre, single-blind, four-arm randomized controlled clinical trial. In total there will be four visits; screening, baseline (day 0), day 7 and day 21.

Who can participate?
Non-smoking healthy adults (age 18 years or older) with intra-oral halitosis and periodontally healthy (classified according to the Periodical Periodontal Screening (PPS) tool: PPS 1 or PPS 2 with not more than 2 sites with probing pocket depths of 5mm).

What does the study involve?
This study involves a mouthwash product containing zinc acetate and chlorhexidine diacetate without alcohol compared to a negative comparison (water). There will be a positive comparison mouthwash containing chlorhexidine digluconate, cetylpyridinium chloride and zinc lactate. Another comparison mouthwash is a commercially available mouthwash containing essential oils

without alcohol. The subjects will rinse and gargle their mouth twice a day for 3 weeks according to manufacturer's instructions.

What are the possible benefits and risks of participating?
There are no risks expected involved in participating in the study. The expectation is that the participants' breath odor will benefit from the use of the mouthwashes. Neither immediate nor long-term physical risks are involved.

Where is the study run from?
Academic Centre for Dentistry Amsterdam (ACTA), the Netherlands.

When is the study starting and how long is it expected to run for?
May 2022 to March 2024.

Who is funding the study?
Viatris (Mylan) and Academic Centre for Dentistry Amsterdam (ACTA), the Netherlands.

Who is the main contact?
Prof. dr. M.L. Laine, m.laine@acta.nl

Contact information

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Scientific

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Additional identifiers

Protocol serial number
NL81289.018.23

Study information

Scientific Title
The effect of different commercially available mouthwashes with active ingredients in a group of systemically and periodontally healthy subjects with intra-oral halitosis

Acronym
HALI

Study objectives
The null hypothesis is that there is no significant difference between water and anti-halitosis mouth washes in reduction of H2S levels after 3 weeks rinsing.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 26/10/2023, METC Amsterdam UMC (Meibergdreef 9, Amsterdam, 1100DD, Netherlands; +31 (0)20 4445585; metc@amsterdamumc.nl), ref: 2023.0077

Study design
Single-center single-blind four-arm randomized controlled clinical trial

Primary study design
Interventional

Study type(s)
Treatment, Efficacy

Health condition(s) or problem(s) studied
Intra-oral halitosis

Interventions
This study involves a mouthwash product containing zinc acetate and chlorhexidine diacetate without alcohol compared to a negative comparison (water). There will be a positive comparison mouthwash containing chlorhexidine digluconate, cetylpyridinium chloride and zinc lactate. Another comparison mouthwash is a commercially available mouthwash containing essential oils without alcohol. The subjects will rinse and gargle their mouth twice a day for 3 weeks according to manufacturer's instructions.

Randomization will be based on a randomization scheme devised by www.random.org using true random numbers, which will be generated by sampling and processing a source of entropy outside the computer. The source is atmospheric noise, which is sampled and fed into a computer, avoiding any buffering mechanisms in the operating system. The primary investigator is responsible for allocation concealment. No stratification will be applied. Every participant will receive a unique trial number. A separate CRF randomization form is used to allocate Product A, B, C or D. The randomization code is kept in a sealed envelope in the Investigator Site file, which is stored in a secured area and not accessible for the examiners. Participants will be instructed not to reveal their group assignment in any way to the clinical examiner. Any intentional or unintentional breaking of blinding will be reported in source documentation and explained, irrespective of the reason for its occurrence.

Intervention Type
Other

Primary outcome(s)
Volatile sulphur compound hydrogen sulfide level (in ppb) assessed with the OralChroma at baseline, day 7 and 21

Key secondary outcome(s))
Measured at baseline, day 7 and 21 unless noted otherwise:
1. Methyl mercaptan levels will be assessed by OralChroma
2. Total oral sulfide concentration will be measured with the Halimeter device and breath odor intensity with organoleptic scores
3. Winkel tongue coating index and the Gomez tongue index will be used to assess the tongue coating assessed
4. "Odostomia" questionnaire scores (subject's perception of his/her own breath odor) will be filled out at at baseline and day 21. As well as subjects' attitudes towards the mouthwashes used at day 21

Completion date
21/03/2024

Eligibility

Key inclusion criteria
1. Adults ≥18 years of age
2. Classified as systemically healthy as assessed by a medical questionnaire; no systemic diseases
3. Periodontally healthy classified according to the periodical periodontal screening (pps) tool: pps 1 or pps 2 with not more than 2 sites with probing pocket depths of 5mm
4. Have a minimum of 20 natural teeth
5. Having finished the necessary dental treatment(s)
6. Willing to brush twice daily and interdental cleaning as usual
7. Willing to temporary stop cleaning the tongue and use of an oral irrigator (starts from the screening until the end of the clinical trial)
8. Willing not to use any other mouthwash than the provided mouthwash of this clinical trial (starts at least two weeks before the first visit or from screening until the end of the clinical trial)
9. Willing to temporary stop using chewing gum (starts at least two weeks before the first visit or from screening until the end of the clinical trial)
10. Willing to keep calendar on use of mouthwash
11. Willing to give their mobile phone number in order to send the participant a text message to remind them of their appointments and instructions
12. Has visit their dentist on regular basis in the past 6 months – 12 months
13. Minimal scores for intra-oral halitosis assessment at screening;
13.1. Hydrogen sulfide >112 ppb as measured by OralChroma (Erovic Ademovski et al. 2017)
13.2. Total volatile sulfur compound level >160 ppb as determined with a halimeter (Erovic Ademovski et al. 2017) and
13.3. Oral organoleptic score ≥2 (Rosenberg & Mcculloch 1992)
14. Self-reported halitosis

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
59

Key exclusion criteria
1. Allergy or hypersensitive to any of the ingredients of the products; zinc acetate, chlorhexidine diacetate, cetylpyridinium chloride, essential-oils, fluoride
2. Pps 2 with > 2 sites with a probing pocket dept of 5mm
3. Pps 3

4. Open carious lesions
5. Dental students or dental care professionals
6. Self-reported pregnancy and/or lactating
7. Systemic medication related to oral dryness
8. Systemic antibiotic therapy within the preceding 3 months
9. Smoking or quitted smoking <1 year before the screening appointment
10. Extra-oral halitosis (Tangerman & Winkel 2008)
11. Night guard
12. Orthodontic brackets (retainer is allowed)
13. Removable prosthesis
14. Oral piercings

Date of first enrolment
13/11/2023

Date of final enrolment
20/02/2024

Locations

Countries of recruitment
Netherlands

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Sponsor information

Organisation
Academic Centre for Dentistry Amsterdam (ACTA)

Funder(s)

Funder type
Industry

Funder Name
Viatris (Mylan)

Funder Name
Academic Centre for Dentistry Amsterdam (ACTA)

Results and Publications

Individual participant data (IPD) sharing plan
The dataset generated during and/or analysed during the current study will be available upon request from M.L. Laine (m.laine@acta.nl) for 2 years after the publication of the study.

IPD sharing plan summary
Available on request