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Hot Topic

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Mouthwash for Gonorrhea, Does it Work?

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This episode reviews some studies evaluating mouthwash as an intervention for oropharyngeal gonorrhea.

Topics:

- Gonorrhea
- STI
- STD
- Neisseria gonorrhoeae

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Disclosures

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[00.00] Introduction

Hello everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STD [sexually transmitted disease] literature review for health care professionals who are interested in remaining up-to-date on the diagnosis, management, and prevention of STDs.

[00.22] Background
In this episode, we'll discuss an interesting topic and that's the idea of using mouthwash to prevent or cure bacterial sexually transmitted infections. Early advertisements for Listerine in the 1880s said the product actually cured gonorrhea. Now, the claims by developers were unsubstantiated, but people used Listerine for this infection during that time. In this episode, we'll go through some of the literature on this topic and two recent articles released in *Lancet Infectious Diseases* on antiseptic mouthwash for gonorrhea prevention.

[00.55] Paper #1

Chow EP, Howden BP, Walker S, et al. Antiseptic mouthwash against pharyngeal *Neisseria gonorrhoeae*: A Randomised controlled trial and an in vitro study. Sex Transm Infect. 2017 Mar;93(2):88-93.
[PubMed Abstract]

The first article for review was published in the journal *Sexually Transmitted Infections* in March of 2017, and this was published by Dr. Chow and colleagues. It was titled "Antiseptic mouthwash against pharyngeal *Neisseria gonorrhoeae*: A randomized controlled trial and an in vitro study." So, the study had two parts:

1. In the first part, it was an in vitro study that evaluated the amount of bacterial growth. And, that was measured in colonies on a plate after a suspension of a clinical pharyngeal isolate of *Neisseria gonorrhoeae* was added to dilutions of two different types of Listerine mouthwashes. And this was then compared also against a saline control.

2. The second part of the study was a trial that enrolled 196 MSM [men who have sex with men] at Melbourne Sexual Health Centre. These were MSM who had already tested positive for pharyngeal gonorrhea by NAAT [nucleic acid amplification test] and were returning to the clinic for antibiotic treatment. The men were randomized to gargle for one minute with serial dilutions of alcohol-containing Listerine mouthwashes (either Cool Mint or Total Care), or a saline placebo. Pharyngeal swabs were taken before and after gargling, and then they were evaluated for *Neisseria gonorrhoeae* growth by culture.

3. So what the authors found is that:

- For the in vitro study, Listerine at dilutions up to 1:4 resulted in a significant reduction of total *Neisseria gonorrhoeae* counts compared to saline. Saline had no inhibitory effect.
- Now, when the authors took a look at the randomized control trial, they found that out of the 196 *Neisseria gonorrhea* NAAT-positive participants, 30% (or 58 participants) were culture-positive for *Neisseria gonorrhea* on the swab sample that was taken before gargling—so this is to begin with. This included 33 participants who were culture-positive in the Listerine group and 25 participants who were culture-positive in the saline group.
- After gargling, the authors found only 52% of participants (or 17 men) had gonorrhea culture positivity on the pharyngeal surface with Listerine mouthwash compared to 84% of participants (or 21 men)—a much higher number—who gargled with a saline solution, and that had a P value of .01.
- They found that men in the Listerine group were less likely to be culture-positive for gonorrhea on the pharyngeal surface compared with those in the saline group after rinsing and gargling, and that had an odds ratio of 0.2.
- So these are promising findings. But it's important to mention, swabs of the oropharynx were taken only five minutes after gargling with solution, so the study evaluated the immediate impact of mouthwash on *Neisseria gonorrhea* and not whether this impact would be sustained.

Wouldn't it be wonderful for this low-cost, easily accessible intervention be able to prevent or treat gonorrhea in the oropharynx? It would help to potentially decrease transmission of this organism, but could also reduce the need for antibiotic therapy. The 2017 study by Dr. Chow was an exciting pilot study that really propelled further research in this area.

[04.02] Paper #2

Chow EPF, Williamson DA, Hocking JS, et al. Antiseptic mouthwash for gonorrhoea prevention (OMEGA): A randomised, double-blind, parallel-group, multicentre trial. Lancet Infect Dis. 2021 May;21(5):647-656. **[PubMed Abstract]**

So now let's go to May 2021, when Dr. Chow and colleagues published an article in the *Lancet Infectious Diseases,* and this was titled "Antiseptic mouthwash for gonorrhoea prevention (OMEGA): A randomized, double-blind, parallel-group, multicentre trial."

1. This was a double-blind, randomized, controlled trial among MSM that were seen at three sexual health and one general practice clinic in Australia, and it compared the efficacy of Listerine and Biotene mouthwash to prevent gonorrhea infection.
2. The reason they compared these two antiseptic mouthwashes is that a previous study they had done showed that Listerine, which contains an alcohol, prevents the growth of gonorrhea in vitro but the alcohol-free Biotene mouthwash did not, or had a minimal effect on gonorrhea growth.
3. The men in this study were eligible to participate if they had a history of oropharyngeal gonorrhea in the previous 30 days or were ages 16-24 years old (and therefore considered a high-risk group for STIs [sexually transmitted infections]).
4. Participants rinsed and gargled with 20 mL of mouthwash for one minute every day for 12 weeks, and oropharyngeal specimens and saliva samples were collected to test for *Neisseria gonorrhea* by NAAT and a quantitative PCR [polymerase chain reaction].
5. The authors analyzed 227 men in the Biotene group and 219 men in the Listerine group and found oropharyngeal gonorrhea in 4% of participants (or 10 men) in the Biotene group and in 7% of participants (or 15 men) in the Listerine group—so really no difference between these two mouthwashes.
6. The self-reported mouthwash adherence was high and the majority (or 85% of participants) reported using the mouthwash for at least 80% of days over the 12-week period.
7. Now, one could say, maybe the participants needed to use the mouthwash around the time of sexual contact to get the best effect. And so in this study, the authors looked at a subset of individuals and they actually did not find a difference in oropharyngeal gonorrhea in those MSM who used the mouthwash before and after kissing. They also did not find a difference in those MSM who used the mouthwash before and after oral sex. In fact, the numbers actually show an increase in oropharyngeal cases in those who used Listerine, although this was not found to be significant.

This report is a large randomized study of MSM at high risk for STIs in which Listerine did not reduce the incidence of oropharyngeal gonorrhea when used daily. Therefore, this OMEGA trial tells me that the daily use of mouthwash is really not an effective intervention in preventing oropharyngeal gonorrhea in MSM.

[06.49] Paper #3

Van Dijck C, Tsoumanis A, Rotsaert A, et al. Antibacterial mouthwash to prevent sexually transmitted infections in men who have sex with men taking HIV pre-exposure prophylaxis (PReGo): A randomised, placebo-controlled, crossover trial. Lancet Infect Dis. 2021 May;21(5):657-667. **[PubMed Abstract]**

There was another large trial published in *Lancet Infectious Diseases* on the same topic in May 2021, and this was published by Dr. Van Dijck and colleagues, titled "Antibacterial mouthwash to prevent sexually transmitted infections in men who have sex with men taking HIV pre-exposure prophylaxis (PReGo): A randomized, placebo-controlled, crossover trial." This trial more specifically looked at persons using mouthwash around the time of sexual exposure.

1. This study enrolled those MSM on PrEP [preexposure prophylaxis] who had an STI in the past two

years in a randomized, double-blind, placebo-controlled crossover trial in Antwerp, Belgium.
2. Participants were assigned to use either Listerine Cool Mint or a placebo mouthwash daily *and* before and after sex for three months. The participants then crossed over to the second intervention (Listerine or placebo mouthwash) for another three months. The individuals also asked sexual partners to use the mouthwash before and after sex.
3. Now, the trial was terminated prematurely due to the COVID-19 pandemic, but they did have 151 participants who completed the entire study.
4. In these 151 participants, the authors found that the Listerine-placebo group, the group that first used Listerine and then used placebo, the STI incidence rate was 140 per 100 person-years during the Listerine period and 103 per 100 person-years during the placebo period, so the opposite of what one would expect if Listerine was, in fact, an effective intervention.
5. In the group that started with the placebo mouthwash first and then used Listerine, the STI incidence rate was 134 per 100 person-years during the placebo period and then 148 per 100 person-years during the Listerine period. So, again, not looking great for the Listerine group.
6. Overall, they noted a significantly higher proportion of participants had oropharyngeal gonorrhea when using Listerine than when using placebo, and that had an odds ratio of 5.78 with a P value of .02. There was no association between specific mouthwash use and the cases of chlamydia or syphilis.
7. This study was another large, randomized trial that indicates Listerine is just not a great way to prevent STI acquisition in persons at risk for acquiring pharyngeal gonorrhea, even when the mouthwash is given around the time of sexual exposure. This was despite good adherence and a high incidence of STIs in the cohort of participants. In fact, the study results suggest Listerine potentially increased the risk of acquiring oropharyngeal gonorrhea. The authors note this might be due to a change in the oropharyngeal microbiome but, really, further studies are needed in this area.

[09.46] Summary
To conclude, I'd like to summarize some key points from this session:

1. A two-part study in 2017 was really exciting because it suggested that Listerine mouthwash inhibits the growth of *Neisseria gonorrhoeae* in vitro as well as in MSM.
2. However, two large, randomized, control studies recently published in May 2021 showed no reduction in the incidence of oropharyngeal gonorrhea infection with Listerine mouthwash, and these studies do not support the use of this mouthwash to prevent the acquisition of pharyngeal gonorrhea in MSM.
3. Listerine might actually increase the risk of acquiring pharyngeal gonorrhea, and I would not recommend this method of gonorrhea prevention to my patients right now just based on this data.

Thank you for listening and have a great day.

[10.36] Credits
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