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Efficacy of Oxygenated Glycerol Tri-Ester (OGT) Oral Spray in Management of Psychotropic Drugs Induced Xerostomia: Systematic Review

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ABSTRACT

AIM: To assess the efficiency of oxygenated glycerol tri-ester a new oral lubricant in the management of psychotropic drugs induced xerostomia. **MATERIALS AND METHOD:** A literature search was done using PubMed, ResearchGate, Wiley online library, Journal of clinical psychopharmacology, Clinical trials.gov, Cochrane using the MeSH terms – oxygenated glycerol tri-ester, management, xerostomia. Out of the 850 articles screened, 185 were full text articles assessed for eligibility and 4 articles were taken for the qualitative analysis. The review was reported according to PRISMA guidelines. 4 randomized control trails were included in the review process. **RESULTS:** In this systematic review, 4 randomized control trails were reviewed and they all have shown indistinguishable results aiding the efficiency of oxygenated glycerol tri-ester in management of psychotropic drug induced dry mouth. Among the four included studies, all four reported statistically significant effect in reduction in scores measured from that of baseline. **CONCLUSION:** The OGT oral spray is effective in stimulating saliva secretion and hence in the management of psychotropic drug induced xerostomia.

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INTRODUCTION

The oral hygiene and health are regulated by saliva, in addition, it plays a vital role in mastication, speech, digestion. An average of 0.3–0.4 ml min^{-1} of saliva is secreted by a healthy human. Xerostomia (dry mouth) occurs when the rate of loss of moisture content in the mouth is greater than the rate of saliva produced.[1] Lactoferrin, peroxidase, and histatin are the key components of saliva which contributes to the antimicrobial, antiviral, and antifungal properties it beholds.[1] In individuals with hyposalivation, these important properties of saliva are absent, causing rapid development of dental caries and fungal infections of the throat, the mucous membrane gets dried causing pain and discomfort, delayed wound healing, difficulty in swallowing and speech, dehydration and malnutrition.[3]

Xerostomia (dry mouth) is a symptom of salivary hypofunction (decrease in the level of saliva secreted in the oral cavity), which is often seen as a common side effect of medications or drug abuse such as antidepressants, antihypertensives, opiates.[15], bronchodilators, proton-pump inhibitors, antipsychotics, antihistamines, diuretics, antineoplastics, psychotropics.[2] These drugs such as psychotropics affect the rate of saliva secreted by acting on the receptor of the sympathetic and parasympathetic pathways of the major and minor salivary glands and this in turn alters the composition of saliva.[2] But drug-induced xerostomia is generally reversible.

Psychotropic drugs are substances that affects and alters how the brain works and causes changes in mood, awareness, thoughts, feelings, or behaviour. [8] These substances may be used to purposefully improve performance or alter one's consciousness. They induce a sense of euphoria by altering a person's neurochemistry. Psychotropic drugs directly act on the sympathetic and parasympathetic pathways, thus decreasing salivary output and modifying the quality of saliva. However, the structure of the salivary gland is not affected, with effects in the oral cavity.[8] Addiction and dependency are very common and leads to substance abuse. Few of the most abused psychotropics are: cocaine, heroin, ecstasy (MDMA), methamphetamine etc and with every abuse comes the side effects, among which dry mouth has been reported to be the most communal.[5]

Sialagogues and saliva substitutes have been used in the management of xerostomia, along with conventional measures such as sipping water or chewing gum.[6] However, the expediency of many available agents is controversial, and few have been validated in controlled clinical trials. To overcome this concern, a new oral spray-DC161 with three

formulations (two aqueous and one oily) has been developed by Pierre Fabre Medical Devices, whose mechanism of action varies according the physical and chemical properties of their components. The new oral spray acts as a substitute for saliva in treatment and management of xerostomia in adults.[3] The objective of these formulations is to act as provisional substitutes for saliva by refabricating its physical action without disturbing the oral environment.[4]

The composition of Oxygenated glycerol tri-ester contains no pharmacological ingredients but a lubricant compound, OGT (94.4%), silicon dioxide (1.5%), and alimentary-grade flavouring agents (4.1%). OGT spray has the characteristics of adherence to the oral buccal mucosa due to the presence of OGTs and silicon dioxide, forming a lipid film that protects against mechanical trauma and helps to reduce oral tissue moisture loss and inflammation.[8] The traces of flavouring agents present in OGT spray may stimulate saliva production up to a lesser extent.[8] It is prone to be effective in the subjective relief of signs and symptoms of dry mouth in patients with xerostomia instigated by long-term administration with psychotropic drugs by lubricating the entire oral cavity, including the oral mucosa, the tongue and the throat. Even though oxygenated glycerol tri-ester-oral lubricant have such features which are useful in dentistry, it's role in management of drug induced xerostomia has not been documented.

OBJECTIVE

To assess the effectiveness of oxygenated glycerol tri-ester as an oral lubricant in the management of psychotropic drug induced xerostomia.

MATERIALS AND METHODS

STUDY DESIGN: Systematic review of randomized controlled trials (RCT)

ELIGIBILITY CRITERIA

INCLUSION CRITERIA

- Randomized controlled trials and pilot studies.
- Full-text article available in search engine mentioned in the search strategy were included.
- Articles that are in English language.

EXCLUSION CRITERIA

- Non-randomized studies.
- Articles without full text.

SEARCH STRATERGY

Published literature on assessing the effectiveness of oxygenated glycerol tri-ester as an oral spray in the management of psychotropic drug induced xerostomia which includes original articles and randomized control trial articles in databases such as PubMed, ResearchGate, Wiley online library, Clinical trials, Journal of clinical psychopharmacology and Cochrane were taken into study for review. A literature search to collect pertinent data was done using MeSH terms such as “oxygenated glycerol tri-ester, xerostomia, management and drug induced”.

SEARCH ENGINE

- PubMed
- ResearchGate
- Wiley Online Library
- Journal of Clinical Psychopharmacology
- Clinical trials.gov
- Cochrane

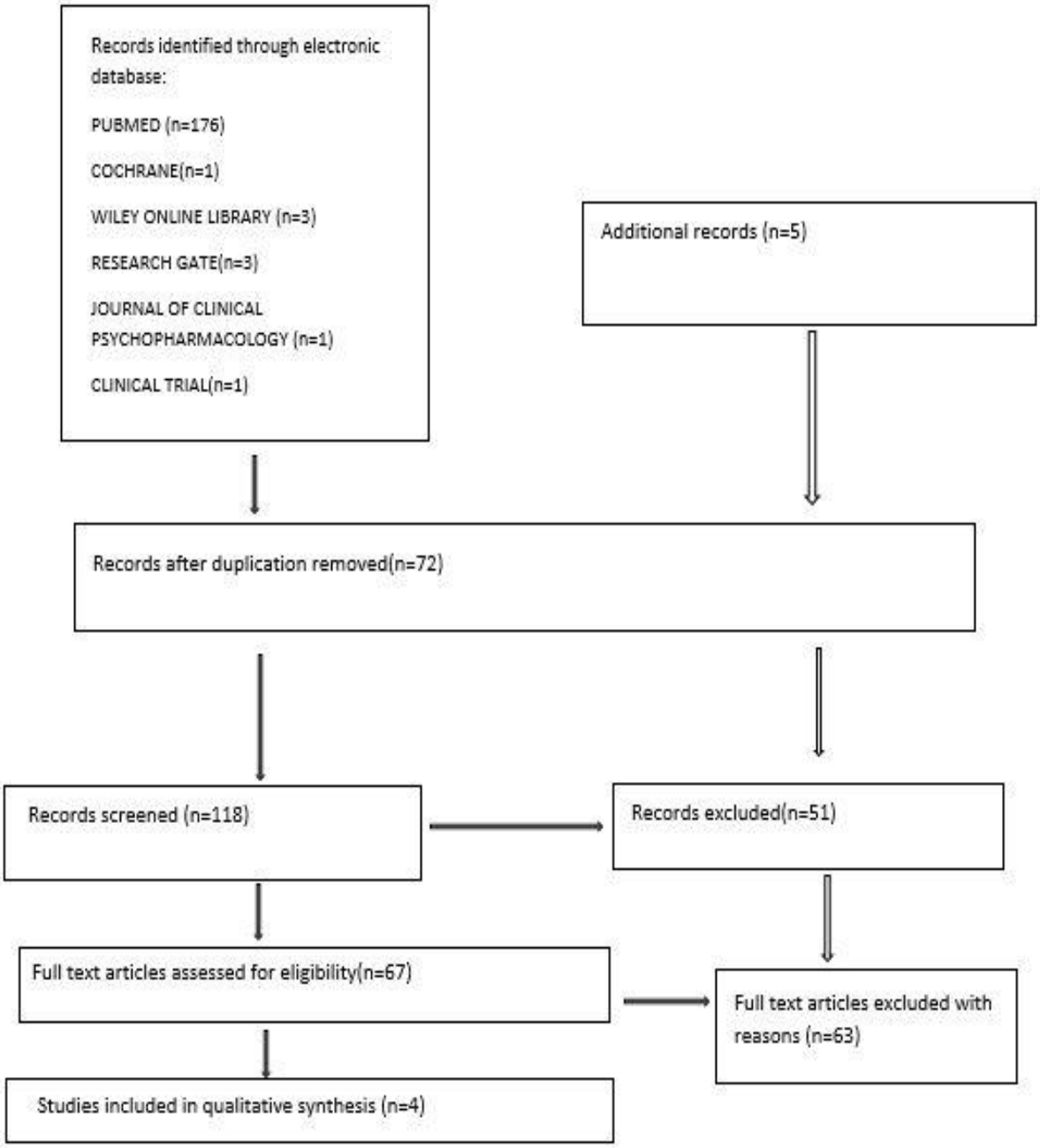

Figure No.1: Number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

Table No.1 illustrates the characteristics of the interventions in the included papers. In all the 4 studies OGT was compared with ASS and its formulations. But all the studies differed individually regarding the age and duration of the intervention.

Two of the trials were performed among individuals above the age of 18, two among individuals of age above 60 years. The subjects participated in the studies had history of psychotropic drugs and drug induced xerostomia.

Table No.1: Characteristics of the intercessions in the included papers

Name of Author	Year	Sample Number	Patient Criteria	Time Period	Groups
Stephane J. Mouly	2007	74	Adolescents aged above 18 years who were willing to participate and those who had psychotropic drug induced xerostomia.	2 weeks	Group A: ASS Group B: OGT
Frank Donath	2015	24	Adolescents aged above 18 who were willing to participate and those who had psychotropic drug induced xerostomia.	4 weeks	Group A: Aqueous Solution Group B: Aqueous Solution Group C: Oily Solution Group D: Oily Solution
Siri F. Kvalheim	2019	30	Well conscious individuals aged above 60 who were willing to participate and those who have drug induced xerostomia.	2 hours	Group A: ASS Group B: OGT
Michel Salom	2007	72	Well responsive individuals who were aged above 65 years who were willing to participate and those having xerostomia.	14 days	Group A: Oral Saliva Substitute Group B: Oral Spray OGT

Table No.2: Shows the outcome data of ASS and OGT scores in the included studies. There was a progressive decrease in the effectiveness of ASS from the baseline till end of the intervention period in 2 of the studies. Table 3 illustrates the bias assessment of the included RCT's.

Table No.2: Outcome data reported in included studies

Author Name	Year	Effect Measure	Results
Stephan. J. Mouly	2007	10 cm long VAS scale	Of the 6 symptoms recorded on a VAS scale at D14 after adjustment for differences at baseline, OGT resulted in significantly better efficacy than ASS in 3 aspects, that is, mouth dryness (P = 0.006), speech difficulties (P = 0.005), and taste improvement (P = 0.02).
Frank Donath	2015	100 mm VAS, AVC – primary end point	A consistently greater mean advancement versus the comparator was noticed, especially over the 4 h after the first product application From T0 to T4h, DC161-DP0292 seemed to reduce the intensity of the associated symptoms of xerostomia.
Siri. F. Kvalheim	2019	Comparing 3 oral care products, Likert scale	A greater number of respondents treated with glycerol reported no or minimal oral dryness than those treated with Aequasyal. Two hours later, the effect of glycerol had decreased comparative to the other two products however the effects of Aequasyal largely persisted.
Michel Salom	2007	10 cm VAS scale, four point ordinal scale.	Statistical analysis of covariance with baseline value as covariable at D14 for this primary end point the result was to the advantage of the group of patients treated with OGT spray.

TABLE No.3: Bias assessment as included in studies

Author Name, Year	Random sequence Generation	Allocation Concealment	Blinding of Outcome	Incomplete Outcome data	Blinding of Participants and Personnel	Selective Reporting	Judgmental Bias
Stephan J. Mouly, 2007	+	?	?	+	+	?	?
Frank Donath, 2015	+	+	?	?	+	+	?
Siri. F. Kvalheim, 2019	-	?	+	?	?	+	+
Michel Salom, 2007	+	?	+	?	+	?	?

"+" = Low risk bias, "-" = High risk bias, "?" = Unclear risk of bias

DISCUSSION

In the recent development of various management measures in treatment of psychotropic drug induced xerostomia, the new oral lubricant OGT spray takes up the essentiality in efficient recovery. Abuse of drugs, especially psychotropic drugs such as anti-depressants, anti-anxiety medications and various illicit drugs such as heroin, cocaine, methamphetamine, ecstasy has been prevalent and according to recent studies, the most common side effect is hyposalivation.[5] On comparison with various studies it was evident that Methamphetamine had a detrimental effect on the oral cavity, like meth mouth, xerostomia, poor gingival health.[14]

In this systematic review, 4 randomized control trails were reviewed and they all have shown indistinguishable results aiding the efficiency of oxygenated glycerol tri-ester in management

of psychotropic drug induced dry mouth. Among the four included studies, all four reported statistically significant effect in reduction in scores measured from that of baseline.

Innovative approaches to treat xerostomia have been in practice for quite a long time, which includes symptomatic relief, treatment of the underlying disease, adequate hydration of the oral tissues, chewing gum, taste stimulation using gustatory substances, drugs such as pilocarpine, artificial saliva substitutes using aqueous electrolyte solutions, mucin containing saliva substitutes etc., [6] the newest addition to these effective measures is OGT oral lubricant which is mainly composed of oral lubricants, silicon dioxide and alimentary-grade flavouring agents.[8] The key components Oxygenated glycerol tri-ester and silicon dioxide helps in adherence of the spray to the oral mucosa which in turn forms a lipid layer which aids in prevention of loss of moisture and the flavouring agent stimulates the secretion of saliva. The composition plays a key role in its efficiency to treat hyposalivation caused by drugs as there are no pharmaceutical ingredients as such.

The studies shows that the OGT spray does not just stimulates saliva secretion, but also improves the taste sensation and speech difficulties that tag along with dry mouth according to Stephan J. Mouly.[1] The lubricant application is also user friendly as its in aquesal form, the spray is proven to be very conventional.

On comparison of OGT with various forms of ASS (artificial saliva substitutes), from the baseline to D14, the symptoms have effectively been decreased in the group of participants who have used OGT.

There is conclusive evidence that the new oxygenated glycerol tri-ester (OGT) oral spray is effective in the management of psychotropic drug induced xerostomia.

CONCLUSION

The aqueous electrolytic composition of the OGT oral spray is effective in stimulating saliva secretion and hence in the management of psychotropic drug induced xerostomia.

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