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Research Article

Oral Discomfort in Patients taking Atypical versus Typical Antipsychotics

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Abstract

This open cross-sectional questionnaire study investigated subjective oral symptoms in hospitalized psychiatric patients, comparing those taking typical vs. atypical neuroleptic drugs. The present study included 170 hospitalized patients who were taking psychiatric medications. We observed a significantly higher prevalence of xerostomia in the typical neuroleptic group (66%) compared with the atypical neuroleptic group (53%, $p<0.01$). In our study, 28% of women and 17% of men received professional consultations for dry mouth. Persistent oral pain lasting throughout the day was reported by 46% and 5% of patients in the typical and atypical neuroleptic groups, respectively. The oral pain was predominantly located in the tongue and buccal mucosa; it was described as a burning sensation by patients in both medication groups. These results emphasize the need for awareness of oral discomfort and its subsequent effects on quality of life in this challenging patient group.

Keywords: Mental Disorders; Neuroleptics; Mental Health; Burning Mouth; Oral Pain; Xerostomia.

Introduction

There are limited data regarding the effect of typical and atypical antipsychotic drugs on oral health and symptoms of the mouth despite previous studies that have shown that dental health is generally poor among psychiatric patients [1]. Chu K.Y. et al. [2], and Nielsen J et al. [3] have also addressed this issue.

Dental diseases are prevalent in this patient group for a number of reasons. Daily oral self-care can be impaired in this patient population, and antipsychotic medications are known to cause xerostomia [4]. Dry mouth is linked to various sensations in the oral mucosa such as glossodynia and burning mouth syndrome (BMS) [5]. These symptoms are particularly prevalent in head and neck cancer patients and in women of menopausal age [6,7].

In practice, the most important factor affecting a patient's saliva secretion is medication use. Psychiatric medicines have a poor reputation in this regard due to their mechanisms of action. Hence, many psychiatric patients suffer from dry mouth due to their medication [8]. For example, a study on elderly patients in Finland, where also this study was made, showed that the use of psychiatric drugs was the strongest explanatory factor for dry mouth, with an odds ratio (OR) of 2.1 (95% confidence interval [CI] 1.2-3.5) [9] . Similarly, the same study reported that the strongest explanatory factor for BMS was psychiatric disease (OR 8.7, CI 1.4-54.1) [9].

Oral pain or BMS is often characterized as a burning sensation in the oral cavity in clinically normal oral mucosa [10]. It

is often sensed in the anterior tongue and frequently occurs in postmenopausal women [11]. The pathogenesis of BMS is not entirely understood; however, BMS is considered to be a result of deficiencies in both the peripheral and central nervous systems [12]. Xerostomia and BMS often appear concomitantly but their causal relationship has not been verified [13].

The effects of typical neuroleptic antipsychotic medications (also known as traditional antipsychotic drugs) are mediated by at least four mechanisms. Typical neuroleptics inhibit dopamine-2 receptors, muscarinic cholinergic receptors, alpha-adrenergic receptors and histamine receptors. In particular, medications that block muscarinic receptors induce oral dryness [14]. Atypical neuroleptics (also known as second-generation antipsychotics or atypical antipsychotics) such as clozapine, risperidone, olanzapine, sertindole and quetiapine have been examined in recent studies. Numerous psychopharmacological investigations have been conducted on these drugs, including studies examining the binding of neuroleptics to dopamine, serotonin and muscarinic receptors, as well as studies on novel treatment modalities [15]. However, to the best of our knowledge, no studies have investigated the effect of atypical neuroleptics on dental health or oral discomfort.

Aims of the study

The objective of our open questionnaire study was to investigate subjective oral side effects by focusing on these two drug categories. We hypothesized that atypical neuroleptics will cause less oral side effects compared with typical neuroleptics.

Material and Methods

Patients and questionnaire

The present study included 170 patients whose treatment involved various psychiatric medications. These patients were hospitalized at the Hesperia Psychiatric Hospital in Helsinki, Finland. The study data were collected using a questionnaire (Appendix I) completed by the patients in the hospital ward in the presence of a nurse. Members of the research group who were working in the hospital verified the medical data from the patient records.

Of the 170 participants, 160 provided responses, and 136 of these responses were included in the final data analysis. Thirty-four questionnaires (20%) were excluded due to insufficient information (e.g., the social security number and gender data were missing) or because the patient's writing was unclear or illegible.

The structured questionnaire included 27 multiple-choice questions. A pilot study with 30 patients at the Hesperia Hospital was performed prior to conducting the current study to test and revise the questionnaire. The World Health Organization International Classification of Diseases (ICD-10) and the Finnish catalog of drugs ("Pharmaca Fennica") were used to categorize the patients' diseases and medications, respectively. An informed consent form was signed by all patients in the study, and the ethical principles of the Declaration of Helsinki were adhered to throughout the study. This study received approval from the internal review board of the University of Helsinki as well as from hospital management of the Hesperia Psychiatric Hospital in Helsinki (Ethical Permit No. 15/1999, 266§).

Statistical Methods

The data were analyzed using SPSS for Windows 11.01 (Chicago, IL, USA); the patients' reported symptoms were compared with their underlying illnesses and medications. In particular, type of the psychiatric medication (typical vs. atypical neuroleptic drug therapy), sex and age were analyzed using cross-tabulations and chi-square tests. The level of significance was set at $p<0.05$.

Results

Basic characteristics of the patients

Table 1 gives basic data of the patients. On average, patients taking atypical neuroleptic medications were younger than those taking typical neuroleptics but the difference was not statistically significant (p=0.076). In addition, patients who were older than 40 years received typical neuroleptics more often than younger patients (p=0.037).

Table 1. Basic characteristics of the patients.

	Typical neuroleptic group (n=59)		**Atypical neuroleptic group (n=31)**		**Significance (χ2 –test)**
Mean age with SD (years)	44.8 ± 10.5		40.4 ± 12.1		p=0,076 (t-test)
	n		n		
>40 year-old	40	68%	14	45%	p = 0.037
Women (n, %)	23	39%	21	68%	p = 0.009
Main psychiatric diagnoses	n		n		p = 0.310
Schizophrenia	41	70%	26	84%	
Mood disorder	13	22%	2	7%	
Drug or alcohol abuse	2	3%	1	3%	
Other diagnoses	3	5%	2	6%	
	59	100%	31	100%	
Main medications 1)	n		n		p = 0.020
Schizophrenia	41	73%	26	90%	
Mood disorder	13	23%	2	7%	
Drug or alcohol abuse	2	4%	1	3%	
	56	100%	29	100%	

1) test subject can have two diagnoses

Of the atypical neuroleptic users 68% were women, correspondingly 39% of the typical neuroleptic users were women (p = 0.009). Schizophrenia and mood disorders were the most common diagnoses in patients taking typical neuroleptics, while schizophrenia alone was the most common diagnosis among the patients taking atypical neuroleptics (Table 1). The most commonly used typical neuroleptic was perphenazine. In the atypical neuroleptic group, the most commonly used drug was clozapine (Table 2). 35 patients used both typical and atypical medication and they were subsequently excluded from the analyse.

Table 2. The distribution of most used drugs .

	Column N % Women (n=44)		Column N % Men (n=46)		Column N % Total (n=90)	
Typical neuroleptic group	n	n=23 %	n	n=36 %	n	n=59 %
Perphenazine	4	17 %	4	11 %	8	14 %
Chlorpromazine	0	0 %	6	17 %	6	10 %
Levomepromazine Maleate	2	9 %	3	8 %	5	9 %
Zuklopentiksoli	1	4 %	3	8 %	4	7 %
Atypical neuroleptic group	n	n=21 %	n	n=10 %	n	n=31 %
Clozapine	6	29 %	5	50 %	11	36 %
Risperidone	7	33 %	3	30 %	10	32 %
Olanzapine	3	14 %	0	0 %	3	8 %

Reported oral symptoms

Approximately 46% of patients reported all day long oral pain in the typical neuroleptic group. In the atypical neuroleptic group the respective number was 5%. Table 3 gives the location of the pain with no difference found between the medication, age or gender groups in this regard. Fifty-two percent of the patients taking typical neuroleptics characterized the pain as mild, whereas 70% of the patients taking atypical neuroleptics characterized the pain as mild (n.s.) Severe to very severe pain was reported by 15% of the patients on typical neuroleptics compared with 10% of the patients on atypical neuroleptics (p=0.569) (Table 3). 32% of the patients reported that the characteristic of the pain was tingling. All day long pain was reported by 44% of the typical neuroleptics group patients and 38% of the atypical neuroleptic group patients, respectively.

Prevalence of xerostomia is also given in Table 3, showing 69% in the typical neuroleptic group and 40% in the atypical neuroleptic group, respectively (p=0.013). Despite the high prevalence of xerostomia in both patient groups, eating problems were infrequently reported: 45% in typical neuroleptics group and 28% in atypical group, respectively.

Persistent xerostomia was more common in the group taking typical neuroleptics (46%). In both groups, xerostomia was reported more often by women than men. Dry mouth was more severe in patients taking typical neuroleptics and medications for mania; it was also prevalent in patients who took several drugs daily. However, these differences were not statistically significant.

Table 3. Reported symptoms of the mouth.

	Typical neuroleptic group		**Atypical neuroleptic group**		**Significance¤ (χ2 –test)**
Have you had pain in the mouth during the last 6 months?	(n=58)		(n=31)		p=0.737
Yes	13	22%	6	19%	
No	45	78%	25	81%	
	58	100%	31	100%	
How would you describe the pain?	(n=21)		(n=10)		p=0.569
Mild	11	52%	7	70%	
Moderate	7	33%	2	20%	
Severe	2	10%	0	0%	
Very severe	1	5%	1	10%	
	21	100%	10	100%	
Do you feel dryness in the mouth?	(n=48)		(n=20)		p = 0.013
Immediately after waking up	7	15%	4	20%	
Later in the morning	4	8%	3	15%	
All day long	22	46%	1	5%	
No dryness	15	31%	12	60%	
	48	100%	20	100%	
Have you had eating problems due to dry mouth?	(n=47)		(n=18)		p=0.298
Most of the time	4	9%	0	0%	
Occasionally	17	36%	5	28%	
No problem	26	55%	13	72%	
	47	100%	18	100%	
Pain in mouth	(n=16)		(n=8)		P=0.945
By waking up	4	25%	2	25%	
Later in the morning	5	31%	3	37,5%	
All day long	7	44%	3	37,5%	
	16	100%	8	100%	
Location of pain #	(n=17)		(n=7)		p=0.884
Border of tongue	4	24%	2	29%	
Surface of tongue	2	12%	2	29%	
Tip of tongue	4	24%	1	14%	
Bottom of mouth	5	29%	1	14%	
Palate	1	6%	1	14%	
Buccal mucosa	5	29%	3	43%	
Gingival	1	6%	1	14%	
Other	1	6%	0	0%	
	23	136%	11	157%	

A patient could report two or more sites

All patients drank water to relive their dry mouth symptoms but artificial saliva preparations were also frequently used. Other remedies such as lozenges, pastilles, olive oil or oral gels were infrequently used. 26% of the women and 13% of the men had received professional consultations for dry mouth. 19% of the patients under 40 years old and 19% of the patients over 40 years old had received consultations for dry mouth. However, measuring salivary secretion rates and analyzing saliva in general had been conducted only for nine women and five man.

Discussion

This open questionnaire study investigated the subjective oral symptoms of hospitalized psychiatric patients according to the class of neuroleptic medications they were taking. It appears

that xerostomia was more prevalent in patients taking typical neuroleptics compared with patients taking atypical neuroleptics. This finding confirms our study hypothesis and could be the result of the different receptor affinities of these two drug categories, a highly complex issue as such [16]. Paradoxical hypersalivation has also been associated with the use of atypical neuroleptics but not observed in our patients [17]. Furthermore, in the present study, it was interesting to note that the atypical neuroleptics had been prescribed mainly to younger patients whose disease history was anticipated to be shorter than that of older patients, who likely had been taking typical neuroleptics for several years.

In the present study, pain was reported by 48% of the patients in the typical neuroleptic group compared with 30% of the patients in the atypical neuroleptic group; these values are high considering the analgesic effect of neuroleptics [18]. Dry mouth and BMS often occur concomitantly, and stimulation therapy for salivary flow has been shown to relieve BMS symptoms, too [19]. Recently, a study on liver transplant patients, which was conducted using the same population base as the present study, showed an 18.8% prevalence of BMS and a 48.5% prevalence of xerostomia; these results are similar to the findings of the present study pertaining to the association between xerostomia and the number of drugs taken daily [20]. Xerostomia and oral pain were more prominent problems among the psychiatric patients in the present study compared with other groups of severely ill patients. In comparison, a Finnish national health survey in subjects 30 years of age or older ("Health 2000") reported that BMS and eating problems (dysphagia) are associated with the number of daily medications taken by patients [20].

To our knowledge the present study is unique in investigating oral discomfort in this difficult patient material. Conducting a clinical study in hospitalized patients with severe psychiatric diseases is challenging due to several obstacles, such as problems with patient management and the often limited capacity of these patients to understand the study protocol. Furthermore, participants in questionnaire studies have a tendency to provide favorable responses, a phenomenon referred to as social desirability, which may have affected the respondents' answers [21]. However, the role of social desirability in the present study may be limited due to the nature of the study problem and the fact that in Finland psychiatric patients come from all social classes. Additionally, 80% of the collected questionnaires were used for our analyses; this rate is satisfactory for this type of investigation. Indeed, no similar studies could be found in the literature.

Finally, it was interesting to note that many patients had received professional consultations for their oral symptoms, but very few had had saliva tests performed in a dental office. In general, dental health among psychiatric patients is poor, and their ability to seek and obtain proper oral health care must be addressed [22]. In this regard, the issue of patient quality of life cannot be overemphasized [23].

Conclusion

Our study was the first to describe oral discomfort symptoms in hospitalized psychiatric patients with an emphasis on comparing typical vs. atypical neuroleptic drugs. Xerostomia was the major oral symptom reported and was particularly prevalent among patients taking typical neuroleptic medications.

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Conflict of Interest

The authors report no conflicts of interest.

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Case number:

1. Vocational education?

1. no vocational education

2. vocational school

3. on-the-job training

4. intermediate-level vocational education

5. university-level education

6. other education_____

2. Present living status?

1. at work

2. at home

3. student

4. sickness pension

5. disability pension

6. other pension

7. unemployed

3. Last visit to a dentist

1. less than ½ years ago

2. ½ -1 year ago

3. 1-2 years ago

4. more than 2 years ago

5. never

4. Most recent site of dental care?

1. private dentist

2. health centre dentist

3. occupational health dentist

5. Reason for seeking dental care

1. made contact myself

2. recall appointment by dentist

3. referred by doctor

4. referred by public health nurse or other

6. Procedures performed during the last course of treatment

1. dental examination

2. restorative treatment

3. gum disease treatment

4. soral self care education or other preventive care

5. prosthodontics treatment

6. other procedures

7. Self-assessment of dental condition

1. good

2. rather good

3. average

4. rather poor

5. poor

6. don't know

8. Are you missing teeth in upper jaw

1. none

2. some

3. all

in lower jaw

1. none

2. some

3. all

9. Do you have removable dentures?

1. yes

2. no

10. Which teeth self care products do you use (multiple answers allowed)

1.toothbrush

2.toothpicks

3.dental floss

11. How often do you brush your teeth?

1.never

2.less often than every other day

3.every other day

4.once a day

5.more often than once aday

12. Do you use toothpaste while brushing your teeth?

1. regularly

2. almost always

3. occationally

4. never

13. Have you had pain in the mouth (mouth mucosa or tongue) during the last 6 months. (pain in the mouth does not include dental pain)

1. yes

2. no

14. If yes, when did you feelpain

1. When waking up

2. Later in the morning

3. All-day-long

15. Do you feel the pain especially at?

1. Border of tongue

2. Surface of tongue

3. Tip of tongue

4. Bottom of mouth

5. Palate

6. Buccual mucosa

7. Gingival

16. How would you classify the pain? Is it?

1. Mild

2. Moderate

3. Severe

4. Very severe

17. How do you describe the pain? Is it?

1. tingling

2. shooting

3. burning

4. aching

18. Do you use any preparations/medications to relieve pain in mouth?

1. yes at this moment

2. not now, but earlier

3. no -> go to question 21

19. What treatment/medication do you use?

_____

20. Has the preparation/medication used helped you to reduce pain?

1. yes

2. no

3. cannot say

21. Do you feel dryness in the mouth?

1. Immediately after waking up

2. Later in the morning

3. All day long

22. Have you eating problems due to dry mouth?

1. Most of the time

2. Occasionally

3. No problems

23. Do you use preparations for relieving the pain?

1. Lozenges

2. Sugarless pastilles

3. Olive oil

4. Oral gel

5. Artificial saliva

6. Water

7. Other_____

8. Nothing

24. Have you received guidance how to take care of dry mouth?

1. yes

2. no

25. Have you had any saliva tests taken?

1. yes

2. no

26. Do you smoke

1. yes

2. no

3. formerly, have quitted

27. Do you smoke

1. daily, approx. _____ cigarettes

2. often, but not daily

3. occassionally

Thank you for your answer!

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