Asian Journal of Oral and Maxillofacial Surgery 22 (2010) 68–73

Contents lists available at ScienceDirect

Asian Journal of Oral and Maxillofacial Surgery

journal homepage: www.elsevier.com/locate/ajoms

Original research

The influence of causes of hyposalivation on clinical outcome of nizatidine in patients with dry mouth

Takashi Ogawa[a,*], Kouji Takada[a], Yuichi Sato[a], Hiroshige Chiba[b]

[a] Department of Oral and Maxillofacial Surgery, Tokyo Medical University Hachioji Medical Center, 1163 Tate-machi, Hachioji, Tokyo 193-0998, Japan
[b] Department of Oral and Maxillofacial Surgery, Tokyo Medical University, Tokyo, Japan

ARTICLE INFO

Article history:
Received 16 April 2009
Accepted 10 December 2009

Keywords:
Nizatidine
Dry mouth
Salivary flow rate
Improvement rates of subjective symptoms

ABSTRACT

It was reported that nizatidine, a histamine H_2-receptor antagonist, promoted salivation by inhibiting acetylcholinesterase and increasing acetylcholine in cholinergic nerves. However, little is known concerning the appropriate usage of the drug for dry mouth. Therefore, the relationship between the causes of dry mouth and the effects of nizatidine was investigated in order to examine the indication of the drug in dry mouth.

In the study, 45 patients who came to the Department of Oral and Maxillofacial Surgery, Tokyo Medical University Hachioji Medical Center, with a chief complaint of dry mouth during the 1-year period from August 2006 to August 2007, were given nizatidine at 300 mg/day continually for 4 weeks. At 2 weeks and 4 weeks of administration, gum tests were conducted on the patients, and the effect of nizatidine was evaluated on a visual analog scale. The cases were divided into groups according to the causes of hyposalivation, and the effect of nizatidine was examined for each group. As a result, the group with aging as the cause, and the group with drug side effects as the cause, was observed to have increased salivary secretion and improvement in subjective symptoms.

1. Introduction

Nizatidine is a histamine H_2-receptor antagonist that has the action of inhibiting the secretion of gastric acids. Its original usages are to treat gastric and duodenal ulcers, reflux esophagitis, and gastritis [1]. With this action, nizatidine stimulates parasympathetic nerves, which are cholinergic nerves, to promote digestive movements [2]. The mechanism of this action stimulates muscarinic receptors at the same time, and thus, it was assumed that it would increase the secretion of saliva [3]. A basic experiment on rats reported significant increases in saliva production [4], and clinical effectiveness has also been reported in patients with dry mouth [1,5,6]. Nizatidine, however, was not originally developed as a salivator, and little is clear as to its appropriate usage in patients with dry mouth. In this light, the effectiveness of nizatidine administration was examined in four groups of patients with different causes of dry mouth: aging, drug side effects, psychogenesis and Sjögren syndrome, for the purpose of investigating the appropriate usage of the drug for the treatment of dry mouth.

2. Patients and methods

2.1. Patients

Forty-five patients who came to the Department of Oral and Maxillofacial Surgery, Tokyo Medical University Hachioji Medical Center, with a chief complaint of dry mouth, during the 1-year period from August 2006 to August 2007, excluding those with a history of radiation therapy treatment, those with a history of drug hypersensitivity, and those with a complication of grave hepatopathy were selected as subjects. Full explanation of the research objectives was given to each of the patients, and the consent to the research program was obtained in writing.

2.2. Methods

Nizatidine was administered to the patients at 300 mg/day continually for 4 weeks. The effect of the administration was evaluated in terms of the salivary flow rate and the improvement of the subjective symptoms by measuring the stimulated salivary flow rate by means of gum test and recording subjective symptoms by means of a visual analog scale (VAS) before, and at 2 weeks and 4 weeks of, administration. In the gum test, subjects were asked to chew gum (Xylitol, Lotte Co. Ltd.) for a period of 10 min, after which the saliva

* Corresponding author. Tel.: +81 426 65 5611; fax: +81 426 65 5639.
E-mail address: oga-taka@Tokyo-med.ac.jp (T. Ogawa).

0915-6992/$ – see front matter © 2010 Asian Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.ajoms.2009.12.002

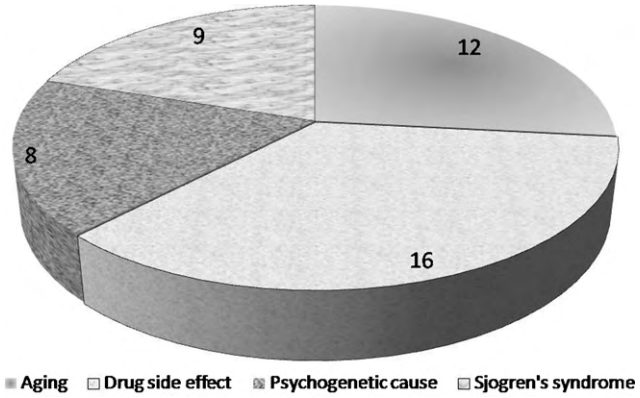

Fig. 1. Number of cases by cause.

secreted was collected in a graduated cylinder for measurement. On the VAS scale, "not dry" was set at 0 mm and "dry" at 100 mm. Patients were asked to plot their subjective symptoms of dry mouth on the VAS scale.

The causes of dry mouth were Sjögren syndrome, aging, drug side effect and psychogenesis, according to which the patients were divided into groups. Aging as a cause of dryness was defined as the age of 65 or more, no history of other particular diseases, and no drug dosage that could cause dry mouth. Drug side effects as a cause of dryness were defined as internal use of five different drugs, excluding Nizatidine, one or more of which had an anticholinergic action. Patients with psychogenesis as a cause of dryness were those who claimed a subjective symptom of dry mouth but had no subjectively observed reduction in salivary secretion, with a score of 10 ml/10 min or higher in the gum test before administration. Patients with Sjögren syndrome were those with a confirmed diagnosis according to the diagnostic criteria set by the European Community [7]. The resulting data was processed with the *t*-test.

3. Results

The subjects were 10 males and 35 females, with ages ranging from 29 to 91, and an average of 68.2. Regarding the divisions by cause, the aging group consisted of 12 cases, the drug side effects group 16 cases, the psychogenesis group 8 cases and the Sjögren syndrome group 9 cases (Fig. 1).

Comparison of gum test results before the administration of nizatidine among groups showed that those with Sjögren syndrome had significantly lower values than others at 1.3 ± 1.3 ml/10 min, while those with psychogenesis had significantly higher values at 15.5 ± 5.8 ml/10 min. There was no significant difference observed between the aging and drug side effect groups (Fig. 2). No significant intergroup difference was observed, either, in VAS scores on subjective symptoms before the administration of nizatidine (Fig. 3).

3.1. All subjects

The gum test showed significant increases in the salivary flow rates, changing from 7.8 ± 5.9 ml/10 min before administration to 8.6 ± 6.1 ml/10 min ($P < 0.05$) after 2 weeks and 9.6 ± 7.1 ml/10 min ($P < 0.001$) after 4 weeks of administration (Fig. 4).

Significant improvements were also observed for subjective symptoms as measured on VAS, with scores being 66.4 ± 22.1 mm before administration to 48.9 ± 26.2 mm ($P < 0.001$) and 44.1 ± 29.2 mm ($P < 0.001$) after 2 and 4 weeks of administration, respectively (Fig. 5).

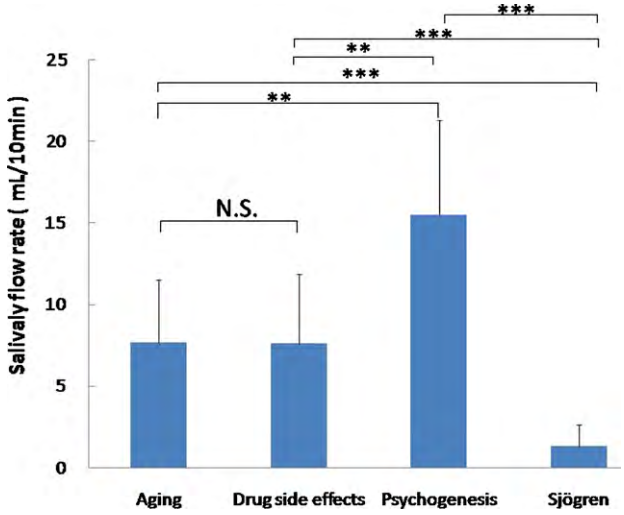

Fig. 2. Intergroup comparison of gum test values before nizatidine administration. $^{**}P < 0.01$, $^{***}P < 0.001$. N.S.: not significant.

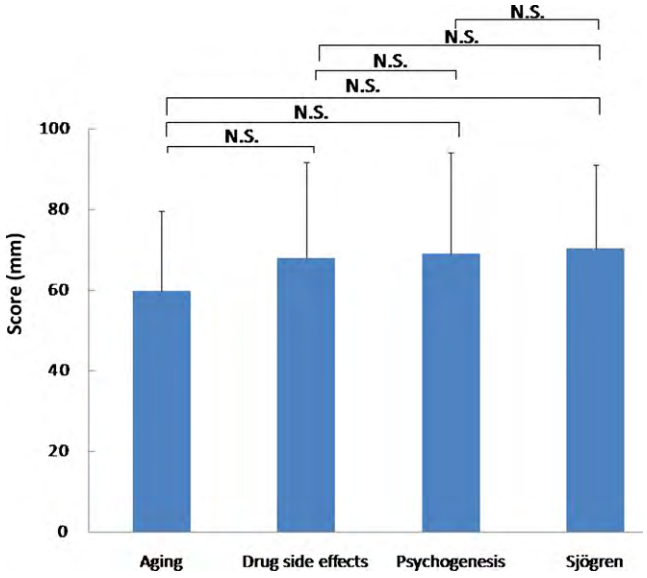

Fig. 3. Intergroup comparison of VAS scores on subjective symptoms before nizatidine administration. N.S.: not significant.

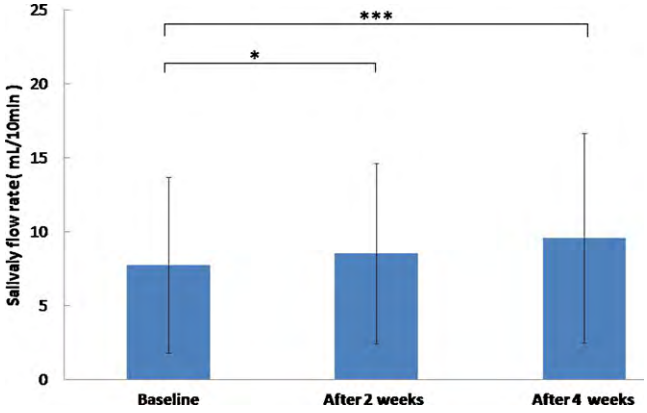

Fig. 4. Changes in the salivary flow rate in the gum tests for all cases as a whole. $^{*}P < 0.05$, $^{***}P < 0.001$ vs. before administration.