

Research Journal of Pharmaceutical, Biological and Chemical Sciences

The Effectiveness of Acupuncture in Drug-Induced Hyposalivation.

Terlevic Dabic D¹, Vucicevic Boras V^{2*}, Sikora M³, Mocinic B⁴, Skrinjar I², and Gabric D⁵

¹Private Dental Practice, Ljubljana, Slovenia.

²Department of Oral Medicine, School of Dental Medicine and Clinical Hospital Centre Zagreb, Croatia.

³Clinical Hospital Centre Osijek, Croatia.

⁴Private Acupuncture Practice, Zagreb, Croatia.

⁵Department of Oral Surgery, School of Dental Medicine and Clinical Hospital Centre Zagreb, Croatia.

ABSTRACT

Hyposalivation is a lifelong problem in persons who take drugs and despite extensive research, there is a limited help. Acupuncture is known to be helpful in irradiated patients due to the head and neck malignancies, however to our knowledge there are no data with regard to the effectiveness of acupuncture in patients with drug-induced hyposalivation. Unstimulated salivary flow rate (USFR) and quality of life assessment scale (OHIP-CRO 14) before and after acupuncture treatment was determined in 24 persons with dry mouth. Acupuncture was performed by use of needles (0,16x10mm) inserted on the following points; Shen Man, Point Zero, Autonomic Point, Thirst Point, Salivary Gland F on both ears. Twenty three patients were instructed to use water (in a spray bottle) as much as they needed. Significant increase in salivary flow rate after treatment with acupuncture was found. No significant difference in USFR was found after treatment with water in the spray bottle. Significantly increased OHIP score was found after treatment with acupuncture and water. Drug-induced hyposalivation can be successfully treated by acupuncture. Treatment with water increased quality of life but not salivary flow rate in patients with drug-induced hyposalivation.

Keywords: drug-induced hyposalivation, acupuncture, water

**Corresponding author*

INTRODUCTION

Hyposalivation is a long-lasting disturbance that affects everyday activities such as eating and talking in persons with Sjögren's syndrome, who take lots of medications and in irradiated patients [1]. Furthermore, hyposalivation leads to the increased risk of cervical caries, gingivitis, candidal infection and salivary gland infections. Most salivary substitutes alleviate symptoms until the agent has been swallowed. Studies upon acupuncture treatment of hyposalivation, mostly in irradiated patients due to the head and neck malignancies confirmed beneficial effect [2,3]. Although new systematic literature review show that limited published data upon its effectiveness in cancer patients for treatment of xerostomia exist [4,5]. It is still not well known how acupuncture increases salivary function, however, three possible mechanisms have been suggested. Blom et al. [6] reported increased blood flow in the skin above parotid gland after acupuncture. Other authors suggested that acupuncture acts on sympathetic and parasympathic nerve system through incoming signals in the III and IV afferent fibers [7]. Furthermore, some authors reported that acupuncture has an effect of salivary glands by local action of released neuropeptides which act as growth factors [8]. Deng et al. [9]. on the basis of MR finding concluded that acupunctural stimulation of intestine spot 2 leads to the bilateral activation of both brain parts responsible for taste, smell and eyes and that those areas are not activated during placebo acupuncture. Furthermore, the same authors reported positive correlation between salivary flow rate and brain activation [9].

Systemic meta-analysis have shown that there are no significant differences between the topical salivary substitutes [10]. Therefore, the aim of this study was to compare traditional acupuncture and water spray in the treatment of drug-induced hyposalivation.

MATERIALS AND METHODS

Ethical committee of the School of Dentistry in Zagreb approved this study. Prior to the study every participant signed informed consent according to the Helsinki II. All patients were recruited from the Department of Oral medicine, School of Dentistry in Zagreb. Patients were allocated into either group by simple method of flipping a coin.

Prior to the either therapy as well as after the therapy every participant fulfilled quality of life assessment scale (OHIP-CRO 14, Croatian version). Salivary flow rate was measured before and after either treatment while participants were sitting into calibrated test tubes during five minutes between 8 and 11 A.M according to Wu-Wang [11].

Acupuncture was performed by use of needles (0,16x10mm) inserted on the following points; Shen Men, Point Zero, Autonomic Point, Thirst Point, Salivary Gland F [12] on both ears while the participants were sitting for 30 minutes at the acupuncturist. Participants were given press needles (0,16 x 1,4mm) on one ear at the points Shen Men and Thirst Point to be worn till the next session. Second acupuncture session was one week after the first one and the remaining three every seven days. Three patients were dropped out as one patient showed four times and two patients showed three times at the acupuncturist. Water in the spray bottle (0,5 L) was given to participants to be used as much as they want during the period of two weeks. The patients were not aware that this was pure water.

Statistical analysis

Normality of distribution was assessed by Smirnof Kolmogorov test. Due to normal distribution of the variables, parametrical statistics was used. Data were displayed as mean \pm standard deviation. Differences between groups were assessed by Student t test for independent samples. Differences before and after treatment were assessed by paired samples t test. P values lower than 0.05 ($p < 0.05$) were considered statistically significant.

RESULTS

Fourty seven participants (43 females and 4 males, average age 67.66 ± 9.4) participated in the study. Twenty three participants were assigned in the water group while 24 patients were assigned in the acupuncture group. Baseline characteristics of the participants are displayed in the Table 1.

Table 1. Baseline characteristics of the participants

	Water	Acupuncture	p
Gender N(%)			
Female	23 (100%)	20 (83.3%)	0.041
Male	0	4 (16.7%)	
Age (mean ± SD)	68 ± 8.9	67.4 ± 9.9	0.829
Duration months (mean ± SD)	15.83 ± 8.92	16.64 ± 9.83	0.730
Salivary flow rate ml/min; (mean ± SD)	0,11 ± 0,11	0,10 ± 0,12	0.732
Quality of life (OHIP score)	24.1 ± 9.5	29.5 ± 14.84	0.146

No significant difference in gender, age, duration, baseline salivary flow rate and baseline quality of life was found between the two treatment groups (Table 1).

No significant difference in salivary flow rate after treatment was found in the water group. Significant difference in salivary flow rate after treatment was found in the acupuncture group ($p < 0.001$) (Figure 1).

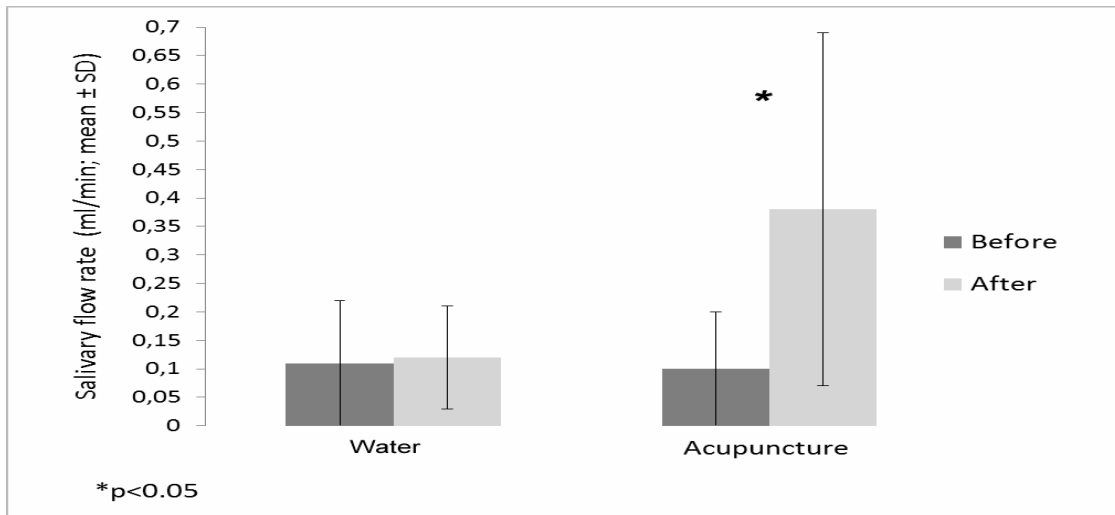


Figure 1. Salivary flow rate before and after both treatments

Significant difference in OHIP score was found after treatment with water and acupuncture group, respectively ($p = 0.003$; $p = 0.007$, respectively) (Figure 2).

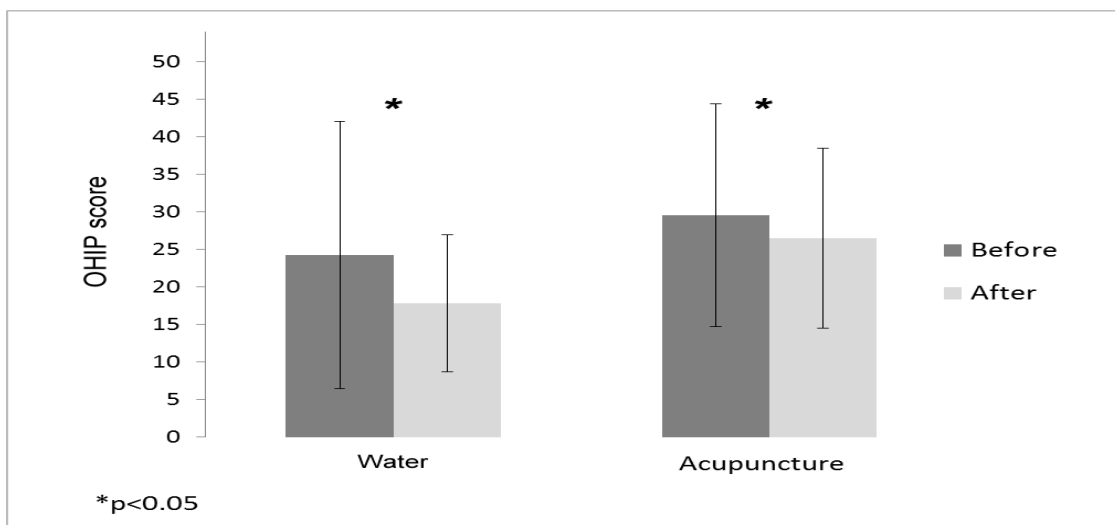


Figure 2. OHIP score before and after treatment

DISCUSSION

The result of this study show that acupuncture was beneficial in patients with drug-induced hyposalivation. So far, literature data have studied use of acupuncture in alleviating dry mouth symptoms in cancer patients and in patients with Sjögren's syndrome. However, drug-induced hyposalivation is a different entity regarding pathological process within glands. Both irradiation induced hyposalivation and one due to the Sjögren's syndrome are a result of damaging salivary serous cells within the glandular tissue which then became dysfunctional. This might be the reason why in our patients, salivary flow rate increased as glands are not permanently damaged. There are conflicting data in the literature regarding the use of acupuncture in treatment of radiation-induced hyposalivation. Many studies [2,3] have shown beneficial effect in reducing the dry mouth symptoms, however systematic review articles^{4,5} showed low quality evidence. Lovelace et al. [13] performed meta-analysis and literature review of radiation induced hyposalivation and concluded that cholinergic agonists were more effective in treating radiation-induced hyposalivation compared with salivary substitutes, hyperbaric oxygen, and acupuncture. However, their patients had radiation induced hyposalivation which damages salivary glands more than drugs. Contrary to the finding of Lovelace et al. [13], Meng et al. [14] reported that true acupuncture given concurrently with radiotherapy significantly reduced xerostomia symptoms and improved quality of life when compared with sham acupuncture. To our knowledge, there are no data regarding the use of acupuncture in drug-induced hyposalivation. As expected treatment with water had beneficial effect on quality of life of these patients, however salivary flow rate did not increase significantly.

None of the patients in this study had any unwanted side effects. As acupuncture is beneficial, cheap, minimally invasive and in rare instances with side effects we strongly support its use in patients with drug-induced hyposalivation.

REFERENCES

- [1] Skrinjar I, Vucicevic Boras V, Bakale I, et al (2015). Comparison between three different saliva substitutes in patients with hyposalivation. *Clin Oral Investig* 2015 Jan 25. [Epub ahead of print]
- [2] Zhao G, Liu L, Spelman A, Lynn Palmer J, Wei Q, Cohen L (2012). Sham-controlled, randomised, feasibility trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma. *Eur J Cancer* 48(11):1692-9.
- [3] Braga FP, Sugaya NN, et al (2008). The effect of acupuncture on salivary flow rates in patients with radiation-induced xerostomia. *Minerva Stomatol* 57(7-8):343-8.
- [4] Hanchanale S, Adkinson L, Daniel S, Fleming M, Oxberry SG (2014). Systematic literature review: xerostomia in advanced cancer patients. *Support Care Cancer* Oct 18. [Epub ahead of print]
- [5] Furness S, Bryan G, McMillan R, Birchenough S, Worthington HV (2013). Interventions for the management of dry mouth: non-pharmacological interventions. *Cochrane Database Syst Rev* Sep 5;9:CD009603. doi: 10.1002/14651858.CD009603.pub3.
- [6] Blom M, Lundeberg T, et al (1993). Effects on local blood flux of acupuncture stimulation used to treat xerostomia in patients suffering from Sjogren's syndrome. *J Oral Rehab* 2(5):541-548.
- [7] Dawidson I, et al (1998). The influence of sensory stimulation (acupuncture) on the release of neuropeptides in the saliva of healthy subjects. *Life Sci* 68: 659- 674.
- [8] Dawidson I, Blom M, Lundeberg T, Angmar-Månsson B (1997). The influence of acupuncture on salivary flow rates in healthy subjects. *J Oral Rehabil* 24;204- 208.
- [9] Deng G, Hou BL, Holodny AI, Cassileth BR (2008). Functional magnetic resonance imaging (fMRI) changes and saliva production associated with acupuncture at LI-2 acupuncture point: a randomized controlled study. *BMC Complement Altern Med* 8:37.
- [10] Furness S, et al (2011). Interventions for the management of dry mouth: topical therapies. *Cochrane Database Syst Rev* ;(12):CD008934. doi: 10.1002/14651858.CD008934.pub2.
- [11] Oleson T. *Auriculotherapy manual; Chinese and Western systems of Ear Acupuncture.*
- [12] Lovelace TL, Fox NF, Sood AJ, Nguyen SA, Day TA (2014). Management of radiotherapy-induced salivary hypofunction and consequent xerostomia in patients with oral or head and neck cancer: meta-analysis and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol* 117(5):595-607.
- [13] Meng Z, Kay Garcia M, Hu C, et al (2012). Sham-controlled, randomised, feasibility trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma. *Eur J Cancer* 48(11):1692-9.