Iran J Nucl Med. 2024;32(1):16-25 [Serial No. 62]

Homepage: https://irjnm.tums.ac.ir/

ORIGINAL RESEARCH ARTICLE

Possible protective effect of *Zataria multiflora* Boiss. on salivary glands in patients with differentiated thyroid carcinoma treated with radioiodine: A randomized, double-blind, placebo-controlled clinical trial

Farinaz Farhoudi[1,2,†], Mohammad Ebrahim Zohalinezhad[1,†], Mohammad Mehdi Zarshenas[3], Nahid Masoudi[4], Ebrahim Fallahzadeh Abarghooei[1], Mahdi Haghighatafshar[4]

[1]*Research Center for Traditional Medicine and History of Medicine, Department of Persian Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*

[2]*Student Research Committee, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*

[3]*Department of Phytopharmaceuticals (Traditional Pharmacy), Shiraz University of Medical Sciences, Shiraz, Iran*

[4]*Department of Nuclear Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*

[†]*These authors shared first authorship*

ARTICLE INFO

Article History:
Received: 09 August 2023
Revised: 30 September 2023
Accepted: 02 October 2023
Published Online: 21 November 2023

Keyword:
Persian medicine
Radioiodine
Salivary gland scintigraphy
Thyroid cancer
Zataria multiflora Boiss

*Corresponding Author:
Dr. Mahdi Haghighatafshar
Address: Department of Nuclear Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
Email: afsharm@sums.ac.ir

ABSTRACT

Introduction: The standard treatment for differentiated thyroid carcinoma is post-surgical radioiodine ablation; however, salivary gland damage is prevalent. This study aimed to evaluate the efficacy of *Zataria multiflora* Boiss. (ZM) aerial part essential oil in protecting salivary glands from post-radioiodine therapy damage in differentiated thyroid cancer patients.

Methods: In this randomized clinical trial, 24 patients with differentiated thyroid cancer were randomly allocated to two groups: 11 patients in the ZM essential oil group and 13 in the placebo group. Patients in the intervention and placebo groups received 20 oral drops three times a day of ZM essential oil or placebo respectively, starting from one week before radioiodine therapy to 4 weeks afterward. Salivary gland function was assessed using scintigraphic parameters before and six months following radioiodine therapy.

Results: Follow-up scintigraphy demonstrated significant decrease in parotid UI in the placebo group (P=0.032) while significant increase in UI (P=0.025) and EF (P=0.042) of the parotid was observed in the ZM group. Comparing changes in functional indices of salivary glands between the two groups after six months revealed significantly better function in parotid UI (P=0.005) and parotid EF (P=0.006) in the ZM group. Substantial damage to parotid UI was significantly less in the ZM group (P=0.044).

Conclusion: Results of this study demonstrated that administration of ZM essential oil to patients with differentiated thyroid cancer may protect the salivary glands from radioiodine injury.

Use your device to scan and read the article online

How to cite this article: Farhoudi F, Zohalinezhad ME, Zarshenas MM, Masoudi N, Fallahzadeh Abarghooei E, Haghighatafshar M. Possible protective effect of *Zataria multiflora* Boiss. on salivary glands in patients with differentiated thyroid carcinoma treated with radioiodine: A randomized, double-blind, placebo-controlled clinical trial. Iran J Nucl Med. 2024;32(1):16-25.

https://doi.org/10.22034/IRJNM.2023.129359.1572

Copyright © 2024 The Authors. Published by Tehran University of Medical Sciences.
This work is published as an open access article distributed under the terms of the Creative Commons Attribution 4.0 License (http://creativecommons.org/licenses/by-nc/4). Non-commercial uses of the work are permitted, provided the original work is properly cited.

result of the difference in RAI doses, follow-up duration, SGS indices, and sample sizes.

Changes in functional SGS parameters in the ZM group

Given the functional parameters of the parotid and submandibular glands in the ZM group, a significant increase was shown in UI and EF of parotid glands after radioiodine therapy. Our study also showed that the function of salivary glands in the ZM group after the intervention was less affected by RAI therapy.

Among different strategies proposed for the prevention of post-RAI therapy salivary gland damage, using antioxidants has attracted the researchers' concern in recent decades [48]. Several studies have shown the antioxidant property of thymol and carvacrol as ZM essential oil main components [49]. An animal study that used thymol at a dose of 50 mg/Kg demonstrated the protective effect of thymol on post-radiotherapy salivary glands damage in rats according to SGS parameters [34]. Results of an animal study on 47 veterans exposed to sulfur mustard treated with ZM extract showed an increase in antioxidant biomarkers and a decrease in oxidant biomarkers [50].

The increase in SGS parameters following RAI ablation in our study has been demonstrated in other studies as well [47]. One of the illustrations of this compensatory mechanism is the proliferation of undamaged cells, which is shown to be enhanced by pretreatment with vitamin E and pilocarpine [12, 51].

Given that differentiated thyroid cancer has an excellent prognosis, it is essential preventing damage to the salivary gland to improve the patients' quality of life. ZM essential oil is a natural antioxidant with high lethal dose of its main ingredient, thymol. No serious adverse event has been reported regarding therapeutic doses of ZM products [24, 52]. In the current study, there was no report of severe side effects of ZM essential oil consumption that might be the result of the small sample size.

CONCLUSION

To the best of our knowledge, this was the first human study that assessed the radioprotective effect of ZM. In addition to the strengths of the present study such as prospective design, using a placebo against ZM, and double blinding the study, there were some inherent limitations. Small sample size, administration of one dose of ZM, and lack of assessment of related clinical symptoms that might present minor salivary gland damage were among the most noticeable limitations. This study revealed that using ZM essential oil might protect the salivary glands from post-radioiodine injury in differentiated thyroid cancer patients. However, further human studies with the similar reference values and SGS indices, larger sample sizes, and follow-ups in different stage to evaluate the effects on acute and chronic damages, along with assessing clinical symptoms, are recommended.

Acknowledgment

This study has been part of a Ph.D thesis at the Research Center for Traditional Medicine and History of Medicine of Shiraz University of Medical Sciences. The Research Consultation Center, and the Center for Development of Clinical Research of Nemazee Hospital are acknowledged for their invaluable consultations. Our study was financially supported by Shiraz University of Medical Sciences (grant No. 20601).

REFERENCES

1. Farhood B, Geraily G, Alizadeh A. Incidence and mortality of various cancers in iran and compare to other countries: a review article. Iran J Public Health. 2018 Mar;47(3):309-16.
2. Hollingsworth B, Senter L, Zhang X, Brock GN, Jarjour W, Nagy R, Brock P, Coombes KR, Kloos RT, Ringel MD, Sipos J, Lattimer I, Carrau R, Jhiang SM. Risk factors of 131I-induced salivary gland damage in thyroid cancer patients. J Clin Endocrinol Metab. 2016 Nov;101(11):4085-93.
3. Jung JH, Lee CH, Son SH, Jeong JH, Jeong SY, Lee SW, Lee J, Ahn BC. High prevalence of thyroid disease and role of salivary gland scintigraphy in patients with xerostomia. Nucl Med Mol Imaging. 2017 Jun;51(2):169-77.
4. Baudin C, Lussey-Lepoutre C, Bressand A, Buffet C, Menegaux F, Soret M, Broggio D, Bassinet C, Huet C, Armengol G, Leenhardt L. Salivary Dysfunctions and Consequences After Radioiodine Treatment for Thyroid Cancer: Protocol for a Self-Controlled Study (START Study). JMIR Res Protoc. 2022 Jul 22;11(7):e35565.
5. Moreddu E, Baumstarck-Barrau K, Gabriel S, Fakhry N, Sebag F, Mundler O, Chossegros C, Taïeb D. Incidence of salivary side effects after radioiodine treatment using a new specifically-designed questionnaire. Br J Surg . 2017 Jul 1;55(6):609-12.
6. Fard-Esfahani A, Fallahi B, Karimi M, Beiki D, Saghari M, Emami-Ardekani A, Fard-Esfahani P, Ansari M, Eftekhari M. Changes in salivary gland function following radioiodine therapy of thyroid diseases: A comparison of high-dose therapy for thyroid cancer and low-dose therapy for benign thyroid disease. Iran J Nucl Med. 2015;23(1):1-7.
7. Verburg FA, Hänscheid H, Luster M. Radioactive iodine (RAI) therapy for metastatic differentiated thyroid cancer. Best Pract Res Clin Endocrinol Metab. 2017 Jun 1;31(3):279-90.
8. Charalambous A. Seeking optimal management for radioactive iodine therapy-induced adverse effects. Asia-Pac J Oncol Nurs. 2017 Oct 1;4(4):319-22.