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Original Research Article

Role of hemithyroid preservation in total laryngectomy for laryngeal/hypopharyngeal malignancy

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ABSTRACT

Background: Thyroid gland invasion in advanced laryngeal/hypopharyngeal malignancy is not uncommon. The preservation of the contralateral lobe of thyroid and associated parathyroid glands with its blood supply, in suitable patients, can be beneficial in reducing the incidence of both hypothyroidism and hypoparathyroidism. The aim of the study was to assess the functionality of the contralateral preserved hemi-thyroid gland with its parathyroid glands, during total laryngectomy with or without partial/total pharyngectomy (TL/TLP), with or without post-operative radiation therapy.
Methods: A retrospective study of patients with advanced laryngeal or hypopharyngeal malignancy who underwent TL/TLP with contralateral hemi-thyroid and parathyroid gland preservation, between January 2012 and May 2019 were included in this study. Pre-operative thyroid/parathyroid function was assessed by estimation of blood levels of T3, T4, TSH and calcium. The same were evaluated at 1week and 6 weeks following surgery and 4 weeks following radiotherapy.
Results: 72.7% patients developed hypothyroidism and only 22.7% developed hypocalcemia following surgery alone at the end of 6 weeks post-surgery. 60% developed hypothyroidism and 10% had hypocalcemia in the group of patients who underwent surgery followed by radiotherapy.
Conclusions: Preservation of contralateral hemi-thyroid with parathyroid glands, significantly reduces the incidence of hypoparathyroidism in patients undergoing TL/TLP. Though incidence of hypothyroidism in such cases is still high, reduced dose of thyroid hormone supplementation was achieved. Post-operative radiotherapy did not significantly alter the thyroid and parathyroid function in such cases.

Keywords: Total laryngectomy, Hypothyroidism, Hypoparathyroidism, Hypocalcemia, Laryngeal malignancy

INTRODUCTION

Head and neck cancers form a major contributor to the cancer burden in the world. Laryngeal malignancies form the 2nd most common type of head and neck cancer (2% of all cancers). Higher incidence is noted among males in South Asian countries in the ratio of 9:1.[1] Majority of the patients in India present in advanced stages due to lack of awareness of cancer, illiteracy, poor socioeconomic status and poor healthcare facilities. Advanced malignancies can be defined either by virtue of an advanced primary tumor or by the presence of regional lymph node metastasis. The thyroid gland invasion in advanced laryngeal malignancy is not common. The lymphatic drainage to the nodes in the central compartment occurs in close proximity to the thyroid and para-thyroid glands. The involvement of central compartment nodes is more common in malignancy involving the subglottis, apex of the pyriform fossa and the post-cricoid area. This has led to removal of the entire thyroid gland with the

parathyroid glands along with total laryngectomy necessitating life-long thyroid hormone and calcium supplementation.[2] The preservation of the contralateral lobe of thyroid and associated parathyroid glands with is blood supply, in suitable patients, can be beneficial in reducing the incidence of both hypothyroidism and hypoparathyroidism in such patients.

Hypothyroidism contributes to delayed wound healing, salivary fistula, difficult speech rehabilitation, cardiac morbidity, and depression. The common blood supply to parathyroid glands can affect the parathyroid functionality leading to hypocalcemia as well. Adult thyroid tissue is known to be radio-resistant up to around 30Gy of radiation exposure beyond which the hormonal production of the gland can get affected. Hypothyroidism following radiotherapy to the head and neck region is one of the well-known side effects.[3,4] This study is intended to assess the functionality of the smaller volume of thyroid gland left behind following surgery as well as the effect of radiation on the same. The objective of this study was to compare the serum levels of thyroid hormones and serum calcium of patients undergoing total laryngectomy/total laryngopharyngectomy (TL/TLP) pre and post operatively as well as among recipients and non-recipients of post-operative radiotherapy.

METHODS

Retrospective observational study on patients with laryngeal/hypopharyngeal malignancy who underwent TL/TLP with or without post-operative radiation therapy in our tertiary hospital affiliated to a university setting, between January 2012 and May 2019 using the case records including the laboratory values available in the hospital.

Inclusion criteria

All consecutive patients as above, who were available for a minimum follow-up period of 6 weeks post-surgery and 4 weeks post RT. Patients who succumbed to post-surgical complications or lost to follow up after 6 weeks following surgery were included in this study as their biochemical parameters as per the protocol was available.

Exclusion criteria

Patients with preoperative thyroid disease. Patients with second primary or those who received radiotherapy prior to surgery for any cause.

Methodology

This study was conducted after obtaining the approval of the Institutional Ethics Committee of our medical college hospital. As per the pre-existing protocol for all laryngeal/hypopharyngeal cancers, a pre-operative thyroid and parathyroid function status work up was done by assessing levels of T3, T4, TSH and serum calcium levels. These tests were repeated one- and six-weeks post-surgery and 4 weeks following radiotherapy.

Using the available case records the demographic details, history and clinical findings, extent of the loco-regional disease as per CT imaging, histopathological report, type of surgical treatment and post-operative treatment received and follow-up details were collected. Statistical analysis of the data was done using Fischer's exact testing by comparison between two groups (Group A - Only Surgery and Group B - Surgery with Radiotherapy).

RESULTS

A total number of 42 patients were studied out of whom 22 underwent only surgery and 20 underwent surgery followed by external radical radiotherapy using a linear accelerator. Age of the patients ranged from 41 years to 80 years with a mean of 60.8 years. Majority of the patients were males with sex ratio being 38:4. All the patients had stage 4 squamous cell carcinoma, out of whom 27 had laryngeal and 15 had hypopharyngeal malignancy. Among cases with laryngeal malignancy 37% were supraglottic and rest were transglottic and glottic lesions. Majority of the hypopharyngeal cancers were arising from the pyriform sinus (60%) and 40% patients had post-cricoid malignancy.

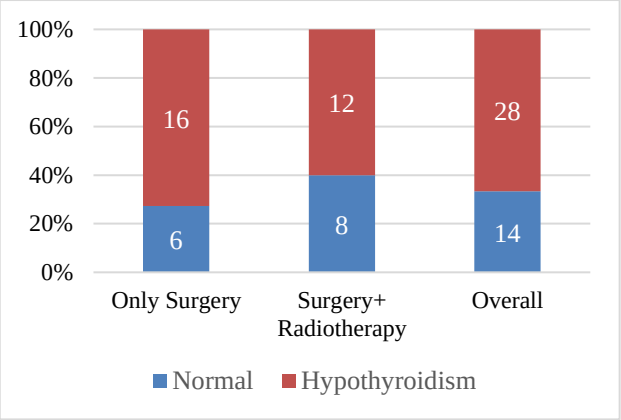

Figure 1: Incidence of hypothyroidism in study population.

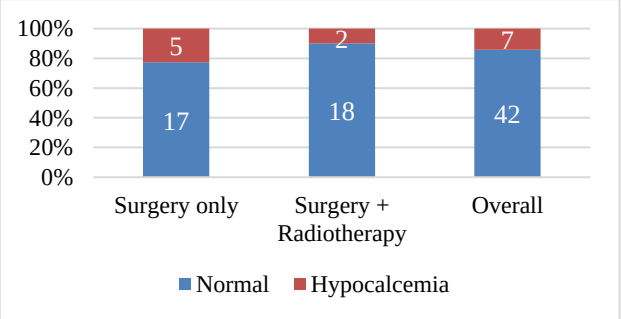

Figure 2: Incidence of hypocalcemia in study population.

Table 1: Fisher's exact test for count data for hypothyroidism.

Comparison of final TSH between groups					
Variables	**Hypothyroidism**	**5**	**No hypothyroidism**	**%**	**P value**
Only surgery (22)	16	72.72	6	27.28	0.515423
Surgery + RT (20)	12	60	8	40	

Table 2: Fisher's exact test for count data for hypocalcemia.

Comparison of final calcium between groups					
Variables	**Hypocalcemia**	**%**	**No hypocalcemia**	**%**	**P value**
Only surgery (22)	5	22.7	17	77.3	0.41433
Surgery + RT (20)	2	10	18	90	

Table 3: Statistical analysis of various factors affecting the incidence of hypothyroidism/hypocalcaemia.

Parameters		Age (years)			Addictions			Type of surgery			Comorbidities		
		<60 (n=18)	**>60 (n=24)**	**P value**	**P* (n=36)**	**A (n=6)**	**P value**	**TL/TLP (n= 34)**	**With pull-up (n=8)**	**P value**	**P* (n=19)**	**A (n=23)**	**P value**
Hypothyroidism	N	14	14	0.32	25	3	0.382	24	4	0.406	12	16	0.7483
	%	77.7	58.3	41	69.4	10.71	5	70.58	50	44	63.15	69.56	33
Hypocalcemia	N	3	4	1.0	7	0	0.566	4	3	0.112	3	4	1.0
	%	16.6	16.6	-	19.64	0	8	11.76	37.5	9	15.78	17.39	-

Note: P-p value; P*-present; A-absent.

Table 4: Dosage of thyroid supplementation in two groups.

Dose of thyroid hormone supplementation (L-thyroxine) per day	Surgery alone (n=22)	Surgery + RT (n=20)	Total	P value
<100 µg	15	7	22	0.1213
>100 µg	2	4	6	
Total	17	11	28	

All the patients had normal thyroid and parathyroid function results on pre-operative bio-chemical evaluation. Overall, on their last biochemical evaluation, 28 among 42 (66.6%) patients developed hypothyroidism and only 7 out of 42 (16.6%) patients had hypocalcemia following surgery with or without radiotherapy.

In the only surgery group, 72.7% (16/22 patients) developed hypothyroidism and 22.7% (5/22 patients) developed hypocalcemia.

In the group of patients who also received post-operative radiotherapy, 60% (12/20 patients) developed hypothyroidism (Figure 1) and only 10% (2/20 patients) developed hypocalcemia (Figure 2).

Statistical analysis performed using exact fischer test for hypothyroidism and hypocalcemia with comparison between two groups (group 1- only surgery, group 2- surgery with RT) showed p values of 0.515 and 0.414 respectively which was not statistically significant. (Table 1 and Table 2). Among the 22 patients who did not receive RT, 5 patients had expired due to post-surgical complications after 6 weeks, 7 of them refused RT and 10 were lost to follow up.

Dosage of thyroid hormone supplementation

The average dose of L-thyroxine received by patients were found to be 46.875 µg. The dosage of thyroid hormone supplementation (L-thyroxine) received by the patients were compared between the surgery alone group and surgery + post-operative radiotherapy group (Table 4). Irrespective of whether post-operative radiation was given or not, most of the patients (78.6%) received less than 100 µg of thyroid supplementation.

DISCUSSION

In our study, we found that almost 66.6% developed hypothyroidism. The literature review demonstrates the incidence of hypothyroidism among total laryngectomy patients to be in a range of 65-92%.[5,6] According to the study conducted by Hesham negm et al in Egypt in 2016 where 78% of the total sample size (n=19) developed hypothyroidism with 30% subclinical type and 70% clinical subtype of hypothyroidism.

In our study,16.6% had hypoparathyroidism following total laryngectomy with hemithyroidecomy with or without post operative radiotherapy. The occurrence of hypocalcemia was found to be lesser in comparison to the other studies. Hesham Et al study revealed that 42% had hypoparathyroidism among which all were hypothyroid as well, emphasising on combined gland dysfunction.[7] The manipulation and ligation of superior and inferior thyroid vessels is attributed to be one of the most common reasons.[8-10]

When we compared the development of hypothyroidism among groups who received combined modality (surgery + radiotherapy) versus surgery alone, it was noted that 60 % showed positive results in the former group whereas 72.7 % had hypothyroidism in the latter group. This is in stark contrast to the Hesham et al study where almost 88% developed hypothyroidism in the combined modality group in comparison to 63% in surgery alone category.[7] The study conducted by Garcia-Serra et al in 2005 about thyroid function monitoring following RT has shown that radiotherapy possess an additive damaging effect on both thyroid as well as parathyroid glands in post-surgical patients.[11-14]

But the present study helps to highlight the fact that it is not mandatory for all cases exposed to radiation to develop thyroid dysfunction. Almost 40% of our subjects remained euthyroid. Despite the higher frequency of hypothyroidism in our study, hypocalcemia was seen in fewer patients only. While 22% developed hypocalcemia in the surgery alone category, only 10% showed evidence of hypocalcemia in the combined modality group. In other studies, 45% had hypoparathyroidism in surgery + RT group versus 38% in total laryngectomy alone subset.[7] The study conducted by us highlights the aspect that radiotherapy had less effect on development of hypoparathyroidism as only 10% showed biochemical and clinical evidence of hypocalcemia and drug therapy was commenced for the same. The intraoperative thyroid pedicle dissection and ligation is also postulated as an influencing factor in post-operative hypocalcemia.

The early commencement of correctional drug treatment for the patients who developed hypothyroidism and hypocalcemia following surgery and Radiotherapy is taken to be one of the most positive outcomes with respect to this study. The dosage of calcium and thyroid hormones required in cases of hemithyroidectomy is comparatively lesser than patients who had total thyroidectomy. 100 percentage of patients who had total thyroidectomy needed thyroid supplementations whereas only 66% took thyroid supplementation among the ones who had one lobe of thyroid preserved. In our analysis, we noticed that majority of the patients (78.57%) in both Group A and Group B took less than 100 micrograms of L-thyroxine. Both groups did not show any statistical significance suggesting that no difference was present in the dosage of L-thyroxine among recipients and non-recipients of radiotherapy.

In a study conducted by Kojima et al at Tokyo medical center, even though almost 81% were not within the standard thyroid stimulating hormone value range, 48% (n=10) required thyroid hormone therapy in the post radiotherapy category. Pharmacotherapy was initiated for 50 percent of them within 1 year and the remaining half also started drug treatment in the next 1-3 years.[15] In our study, almost three - fourth of the subjects didn't not show clinical symptoms suggestive of hypothyroidism, even though biochemical evidence of raised TSH levels were seen. The patients had commented about generalised fatigue and malaise which were attributed to the invasive surgical stress followed by radiotherapy exposure but which may in fact could have been a representation of radiation induced hypothyroidism signs.[16-18] Hence early and timely evaluation of thyroid function is crucial in diagnosing post-operative hypothyroidism which otherwise, can be missed easily.

Factors influencing the incidence of hypothyroidism/ hypocalcemia

Age (less than or more than 60 years). Hypothyroidism noted more among less than 60 years (Table 3).

Site of primary malignancy

The incidence of hypothyroidism is maximum among trans-glottic subsite (28.57%) closely followed by pyriform fossa whereas hypocalcaemia is seen more with pyriform fossa (57.1%) and post cricoid involvement. Extent of surgical resection - total laryngectomy/total laryngopharyngectomy vs TLP with gastric pull up. Addictions like smoking, alcohol consumption and tobacco chewing were assessed. Patients with addictions had more propensity for hypothyroidism and hypocalcemia. Presence of comorbidities like diabetes mellitus, hypertension and heart disease were also studied.

Male preponderance was noted in our subpopulation with mean age of 60.8 years. On pathological evaluation, majority showed moderately differentiated squamous cell carcinoma. Even though factors like addictions, comorbidities, type of surgery were analysed, results were not statistically significant due to the limited sample size. Hence, the association could not be established between the predisposing factors and development of hypothyroidism and hypoparathyroidism.

Merits of the study are early diagnosis and commencement of treatment for both clinical and subclinical hypothyroidism and hypocalcemia, dose reduction of thyroid and calcium supplements in contrast to total thyroidectomy patients as our study preserved one lobe of thyroid in all cases. Parastomal recurrence rates were negligible. Hence proving that hemithyroidectomy does not affect the oncological outcome The study also negates the general notion of development of thyroid and parathyroid dysfunction following radiation exposure as

almost 40% of patients remained euthyroid and 90 % were normocalcemic.

Limitations of the study are small sample size, long term follow up assessment not done, single institutional study, parathyroid hormone testing not carried out and used only adjusted calcium levels, which can be affected by the patient's hemodynamic status and by supplementation.

CONCLUSION

Preservation of thyroid lobe doesn't necessarily eliminate the incidence of hypothyroidism following total laryngectomy but development of hypoparathyroidism is comparatively rarer. Radiation exposure has negligible effect on hypocalcemia. The timely analysis of serum levels of thyroid hormone and calcium helps in commencement of drug therapy for hypothyroidism and hypoparathyroidism at reduced doses at early stages itself.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Chung-Wai AH, Wai-Kuen H, Kin-Yip PL. Thyroid dysfunction in laryngectomees - 10 years after treatment; Head and Neck; 2008.
2. Sparano A, Chernock R, Laccourreye O. Predictors of thyroid gland invasion in glottic squamous cell carcinoma. Laryngoscope. 2005;115:1247-50.
3. Hancock, SLMcDougall, IRConstine LS. Thyroid abnormalities after therapeutic external radiation. Int J Radiat Oncol Biol Phys. 1995;31(5):1165-70.
4. Galbo L, Kuik AM, Lips DJ. A prospective longitudinal study on endocrine dysfunction following treatment of laryngeal or hypopharyngeal carcinoma. Oral Oncol. 2013;49(9):950-5.
5. Galbo LAM, De Bree R, Kuik DJ. The prevalence of hypothyroidism after treatment for laryngeal and hypopharyngeal carcinomas: are autoantibodies of influence? Acta Otolaryngol. 2007;127:312-7.
6. Leon X, Gras JR, Perez A. Hypothyroidism in patients treated with total laryngectomy. A multivariate study. Eur Arch Otorhinolaryngol. 2002;259:193-6.
7. Negm H, Mosleh M, Fathy H, Eur AA. Thyroid and parathyroid dysfunction after total laryngectomy in patients with laryngeal carcinoma. Arch Otorhinolaryngol. 273(10):3237-41.
8. Dadas B, Uslu B, Cakir B. Intraoperative management of the thyroid gland in laryngeal cancer surgery. J Otolaryngol. 2001;30:179-83.
9. Sinard RJ, Tobin EJ, Ernest L. Hypothyroidism After Treatment for Nonthyroid Head and Neck Cancer. Arch Otolaryngol Head Neck Surg. 2000;126(5):652-7.
10. Dutta S, Biswas KD, Ghatak S. Post-operative hypofunctioning of the thyroid gland after total laryngectomy. Ear Nose Throat J. 2016;95(8):E23-7.
11. Garcia-Serra A, Amdur RJ, Morris CG. Thyroid function should be monitored following radiotherapy to the low neck. Am J Clin Oncol. 2005;28:255-8.
12. Isaacson SR, Snow JB. Etiologic factors in hypocalcaemia secondary to operations for carcinoma of the pharynx and larynx. Laryngoscope. 1978;88:1290-7.
13. Bhandare N, Kennedy L, Malyapa R. Primary and central hypothyroidism after radiotherapy for head-and-neck tumors. Int J Radiat Oncol Biol Phys. 2007;68:1131-9.
14. Tell R, Lundell G, Nilsson B. Long-term incidence of hypothyroidism after radiotherapy in patients with head-and-neck cancer. Int J Radiat Incol Biol Phys. 2004;60:395-400.
15. Tsukahara KK, Motohashi R. Extent of thyroid resection and thyroid function after postoperative radiotherapy following total laryngectomy or total pharyngolaryngoesophagectomy. Japan Society Clin Oncol; 2017.
16. Ozawa H, Saitou H, Mizutari K. Hypothyroidism after radiotherapy for patients with head and neck cancer. Am J Otolaryngol. 2007;28:46-9.
17. Nishiyama K, Tanaka E, Tarui Y. A prospective analysis of subacute thyroid dysfunction after neck radiation. Int J Radiat Oncol Biol Phys. 1996;34:439-44.
18. Hall EJ, Cox JD. Physical and biologic basis of radiation therapy. In: Cox JD (ed) Moss radiation oncology rationale, technique, results. Mosby Co, St Louis; 1994:1-66.

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