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Original article

Unilateral recurrent laryngeal nerve palsy post-thyroidectomy: Looking for hyperventilation syndrome

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ABSTRACT

Aims: Unilateral Recurrent Laryngeal Nerve (RLN) palsy is responsible for dysphonia and difficulties in swallowing. The role of unilateral RLN palsy on dyspnea is not fully elucidated. Our hypothesis is that air leak could be responsible for development of hyperventilation syndrome (HVS).
Objective: The objective of this study was to determine in patients with unilateral RLN palsy if dyspnea could be associated with HVS.
Material and methods: Over a 12-month period, all patients with permanent unilateral RLN palsy after thyroidectomy complaining from the onset of unexplained dyspnea were tested. Measurement of Nijmegen score, an hyperventilation test, an arterial blood gas, lung function and cardiac tests were performed. The diagnosis of HVS was defined if at least two criteria were present among: Nijmegen score > 23; reproduction of at least 2 usual symptoms during hyperventilation test; an expirated pressure of CO2 (EpCO2) < 30 mmHg or < 90% of the initial EpCO2 after a 5 minutes recovery period following a 3 minutes voluntary hyperventilation.
Results: Ten out of 366 patients with thyroidectomy for benign disease had permanent unilateral RLN palsy and dyspnea. Among 10 patients included, 8 were diagnosed having HVS on the hyperventilation test without cardiac/lung dysfunction.
Conclusion: In summary, this study is a proof of concept that HVS might be involved in dyspnea associated with unilateral RLN palsy.

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1. Introduction

The main symptom of unilateral Recurrent Laryngeal Nerve (RLN) palsy is hoarseness because of a remaining glottic gap during phonation. Patients with bilateral vocal fold paralysis typically have no impairment of the voice but inspiratory dyspnea. However, in 5–63% of cases, dyspnea also occur in unilateral RLN palsy [1,2]. The relationship between unilateral RLN palsy after surgery and dyspnea has been poorly studied. In patients with unilateral RLN palsy, the air leak could be responsible of frequent inspirations favoring the development of hyperventilation syndrome (HVS).

The HVS is defined as chronic or recurrent changes in breathing pattern, causing respiratory and non respiratory complaints of variable severity induced by physiologically inappropriate and reproducible hyperventilation [3,4]. HVS is characterized by a variety of somatic symptoms (e.g. respiratory symptoms including short of breath, tight feeling in chest, chest pain, unable to breathe deeply, and also non respiratory symptoms such as fatigue, heart palpitations, tachycardia, anxiety, feeling tense, light-headedness, dysphagia, dizziness, tetany, myalgias, cramping and paraesthesias) [3,4]. The diagnosis of HVS is oriented by the Nijmegen score

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[5]. Other suggestive parameters for HVS are hypocapnia and respiratory alkalosis on the arterial blood gas. On the other hand, normality of Nijmegen score and arterial blood gas doesn't exclude the diagnosis of HVS. The hyperventilation test (HPVT) is required for HVS diagnosis. The aim of this study was to determine if dyspnea in patients with RLN palsy could be associated with HVS.

2. Material and methods

We conducted a preliminary observational prospective study over a 12-month period in consecutive patients who exhibited a definitive unilateral RLN palsy after thyroidectomy for benign disease and who complained of unexplained chronic dyspnea (i.e. cases of unilateral RLN palsy lasting longer than 6 months despite speech therapy). Dyspnea was considered as unexplained since lung function testing, electrocardiography, echocardiography were normal. We confirmed unilateral RLN palsy by videolaryngoscopy in all patients and the position of paralyzed vocal fold was systematically reported. The otolaryngologists screened all patients for the presence or absence of unilateral RLN palsy by laryngoscopy, both pre- and postoperatively. This study was approved by the local research ethics committee (IRB). Informed consent was obtained from all individual participants included in the study.

For each patient we performed the Nijmegen score, arterial blood gas and hyperventilation test. Hyperventilation test was positive according to already published criteria [6,7] (VMAX SensorMedics, SPECTRA 29 S). The Nijmegen questionnaire, comprising 16 items corresponding to the most frequent symptoms of HVS, can be used as a screening tool. Each item of the questionnaire is scored from 0 to 4 giving a maximum score of 64 and a score of > 23 is commonly used as a cut-off [5]. The diagnosis of HVS was defined if at least two criteria were present among: Nijmegen score > 23; reproduction of at least 2 usual symptoms during HVPT; an expirated pressure of CO2 (EpCO2) < 30 mmHg or < 90% of the initial EpCO2 after a 5 minutes recovery period following a 3 minutes voluntary hyperventilation [8].

3. Results

Three hundred and sixty-six thyroidectomies were performed during the study period. Twenty-three unilateral Recurrent Laryngeal Nerve (RLN) palsies occurred in this period (6.3%). No patient exhibited a bilateral RLN palsy. Eleven patients had a transient unilateral RLN palsy that lasted less than three months. In two patients, a permanent unilateral RLN palsy occurred but was not associated with dyspnea. Ten non-smokers patients (9 women and 1 man) were considered the study population (10%) i.e. including permanent unilateral RLN palsy (lasted more than six months) and dyspnea criteria. Mean (range) age of the patients was 59 years (44-76) (Table 1). None of them reported dyspnea before the surgery. The post-operative hormonal balance (thyroid stimulating hormone (TSH) and calcium and phosphorus homeostasis) was normal in all patients of the study population. The laryngeal examination showed a paramedian position of the vocal fold in six patients (60%) and an intermediate position in 4 patients (40%) (Table 2). No laryngeal oedema was described. An amyotrophy of the paralyzed vocal fold was reported in 5 patients (50%) with an induced sub-offset of the vocal fold in all cases. A glottic air leak was observed in 5 patients (50%) (Table 2). Spirometry was normal in all patients (Table 1). HVS was diagnosed in 8 patients (80%) (Table 1). The diagnosis of HVS was defined if at least two criteria were present among: Nijmegen score > 23; reproduction of at least 2 usual symptoms during HVPT; an expirated pressure of CO2 (EpCO2) < 30 mmHg or < 90% of the initial EpCO2 after a 5 minutes recovery period following a 3 minutes voluntary hyperventilation [8]. In our series, 5 patients have suggestive parameters for HVS on the arterial blood gas with hypocapnia (< 35 mmHg) and/or respiratory alkalosis (Ph > 7.42). Two patients presented a respiratory alkalosis on the arterial blood gas, but this criterion was insufficient to set the diagnosis of HVS (Table 1). Among the 5 patients with hypocapnia (PaCO2 < 35 mmHg), 3 were diagnosed with HVS. Out of 8 patients with confirmed diagnosis of HVS, 6 patients had positive Nijmegen score (75%). In Nijmegen, the main associated symptoms reported were feeling of anxiety (7/8 patients), feeling tense (6/8 patients), short of breath (8/8 patients). In 7/8 patients with confirmed HVS, HPVT was abnormal based on subjective criteria (reproduction of at least 2 usual symptoms) and on objective criteria (an expirated pressure of CO2 (EpCO2) < 30 mmHg after a 5 minutes recovery period following a 3 minutes voluntary hyperventilation). The last patient with confirmed HVS (the 6th patient in the Table 1) was a 49-year old woman with a medical history of arterial hypertension and a surgery of total thyroidectomy for benign multinodular disease. She had no dyspnea, no allergy, no cardiac dysfunction and no smoking habit before surgery. Pre-operative physical exam including indirect laryngoscopy showed normal vocal fold and symmetric arytenoid mobility. One day after surgery, a dysphonia without dyspnea was reported. Indirect laryngoscopy objectivized immobility of left arytenoid and a left vocal fold in intermediate position with no oedema. At one month follow-up, she complained about progressive breathing difficulties on exertion (shopping and climbing stairs) and shortness of breath. Clinical examination confirmed immobility of left arytenoid and a left vocal fold in intermediate position with no edema and a supraglottic compression during phonation. Pulmonary auscultation and chest radiograph were normal. She had voice therapy during 3 months. At 6 months follow-up, she complained about worsened dyspnea at rest, shortness of breath and anxiety. Physical exam showed no improvement of laryngeal mobility (with an amyotrophy of the left vocal fold) except improvement of the supraglottic compression. Nijmegen score was very high (39) and HVS was confirmed by an abnormal EpCO2 without reproduction of symptoms during HPVT.

4. Discussion

Breathing problems are not usually described in unilateral RLN palsy but in clinical practice, several patients complain of dyspnea. In a series of 63 patients with unilateral RLN palsy, 75% of them reported breathing problems in everyday life, half of them with considerable to severe problems [1]. One limitation of our study is the selection of a group on basis of dyspnea. This criterion is subjective but no dyspnea was reported before surgery. An organic etiology must be firstly explored in case of dyspnea with RLN palsy: a cardiorespiratory insufficiency or a hypopharyngeal and laryngeal local cause. In an uncommon reported case of dyspnea with unilateral vocal fold paralysis in a patient with acromegaly, the etiology of dyspnea was due to hypopharyngeal and laryngeal soft tissue swelling [9]. Nasofibroscopy revealed a global and major oedema of the glottis and supraglottis and also a paralysis of the left vocal fold. In our series, no cardiac or lung dysfunction was found to explain dyspnea in our patient and no oedema was reported in nasofibroscopy. Another cause of dyspnea after surgery after thyroidectomy could be hypothyroidism [10]. Although hypothyroidism has an insidious onset and relatively asymptomatic, exertional dyspnea and fatigue can be the presenting complaints [10]. In a recent article about pulmonary consequences of hypothyroidism DLCO and exercise testing parameters were significantly reduced (Even with the presence of normal chest X-ray, arterial blood gases, and spirometry) in 42 patients with hypothyroidism versus 12 control subjects [10]. In our series, all patients with dyspnea and UVFP had normal value of thyroid

Table 1
Characteristics of patients and results of tests.

Patient	Sex	Age (years)	Body mass index (kg/m^2)	Vocal fold position	PaCO2[b] (mmHg)	pH	FEV1 (%pred)	FVC (% pred)	FEV1/FVC	Nijmegen score[c]	Hyperventilation Test				HVS diagnosis
											Basal EpCO2 (mmHg)	EpCO2 after 3 minutes of hyperventilation (mmHg)	EpCO2 after 5 minutes recovery (mmHg)[d]	Reproduction of at least 2 symptoms	
1	F	67	25	Paramedian	45.2	7.4	126	121	86.15	25[a]	25.1	12.3	25.8[a]	Yes[a]	Positive[a]
2	F	44	23	Paramedian	32.3[a]	7.47[a]	108	115	81.2	15	33.7	19.5	34	no	Negative
3	F	76	30	Paramedian	39.2	7.46[a]	90	92	81	3	39.9	18.1	28[a]	Yes[a]	Positive[a]
4	M	72	29	Intermediate	30[a]	7.39	104	104	76	13	26.7	12	26[a]	Yes[a]	Positive[a]
5	F	62	19	Intermediate	21.6[a]	7.57[a]	91	NA	NA	30[a]	22.7	14.6	16.5[a]	Yes[a]	Positive[a]
6	F	49	23	Intermediate	41	7.42	95	NA	NA	39[a]	29	16.7	25.4[a]	no	Positive[a]
7	F	76	26	Paramedian	37	7.4	105	120	70	34[a]	37	17	25[a]	Yes[a]	Positive[a]
8	F	66	26	Paramedian	34.8[a]	7.44[a]	81	85	80	14	37.3	25.9	33.7	no	Negative
9	F	25	28	Paramedian	33[a]	7.4	89	99	93	34[a]	27.9	15.6	25[a]	Yes[a]	Positive[a]
10	F	53	24	Intermediate	41	7.4	85	90	88	45[a]	35	19.5	24[a]	Yes[a]	Positive[a]

Abbreviations: F: female; M: Male; pred: predicted; FEV1: forced expiratory volume after one second; FVC: forced vital capacity; EpCO2: expirated pressure of CO2.

[a] abnormal values contributing to establish the diagnosis of HVS.

[b] Normal values of PaCO2: between 35 à 45 mmHg.

[c] Nijmegen score: abnormal value > 23.

[d] EpCO2 after 5 minutes recovery (mmHg): Abnormal value of < 30 mmHg.

Table 2
Description of laryngeal examination in the study population $n = 10$.

Patient	Vocal fold position	Side of VF paralysis	Laryngeal axis	VF aspect	Laryngeal oedema	Sub-offset of vocal fold	Glottic air leak	Supraglottic compression
1	Paramedian	Right	Normal	Normal	No	No	No	Yes
2	Paramedian	Left	Normal	Normal	No	No	No	No
3	Paramedian	Left	Normal	Normal	No	No	Yes	Yes
4	Intermediate	Left	Deviation	Amyotrophy	No	Yes	Yes	Yes
5	Intermediate	Left	Normal	Amyotrophy	No	Yes	Yes	No
6	Intermediate	Left	Normal	Amyotrophy	No	Yes	Yes	Yes
7	Paramedian	Right	Normal	Normal	No	No	No	No
8	Paramedian	Right	Normal	Amyotrophy	No	Yes	No	Yes
9	Paramedian	Left	Normal	Normal	No	No	No	No
10	Intermediate	Right	Normal	Amyotrophy	No	Yes	Yes	Yes

Abbreviations: VF: vocal fold.

stimulating hormone (TSH). Dyspnea caused by UVFP is generally not highlighted in the literature. Several hypotheses have been proposed in literature to explain the pathophysiology of dyspnea in RLN palsy. In a recent series of 10 patients with dyspnea and UVFP with no significant cardiorespiratory insufficiency, the etiology of dyspnea is variable according to the author: in six patients the glottic opening was insufficient for effortless breathing. In four cases, the respiratory insufficiency was more a manifestation of limits on exertion relative to their very active lifestyle (e.g., hunting or sport activity) [11]. However, our results tend to confirm an absence of correlation between the position of the paralyzed vocal fold and the severity of the dyspnea in adults. In the series of Brunner et Al., no correlation between grade of dyspnea and position of the paralyzed vocal fold or reduced glottic space was observed [1]. In the same way, in a series of thirteen patients with benign glottic or subglottic stenosis, there was no correlation between glottic resistance values and dyspnea score [12].

For Laccourreye et al. [2], dyspnea could be explained by synkinesis that reflects a process of aberrant re-innervation of paralyzed laryngeal muscles (nerve fibers to re-innervate adductor laryngeal muscles whose function is abductor and vice-versa) [2]. For Brunner et al. [1], dyspnea could be explained by neurosensorial deficits of the laryngeal mucosa or by discrepancy between effort and output of breathing.

The HVS is a psychosomatic stress-related disorder. On a psychopathological level, the HVS begins with an initial stress that creates increasing ventilation leading to a sensation of dyspnea due to an inappropriate muscular effort. Then a vicious circle appears since dyspnea becomes an anxious stimulus that maintains a chronic hyperventilation. In unilateral RLN palsy, the intense emotional stress due to the surgical complication and the resulting dyspnea could initiate the process of HVS. According to this theory, we showed in our series that all patients complained dyspnea and short of breath and an anxiety was reported in almost patients (7/8 patients). According to Boulding et al., dyspnea is unlikely to be caused solely by inadequate or inefficient ventilation either due to hyperventilation or an abnormal breathing pattern and additional factors, such as poor subjective awareness of breathing by patients, are thought to play a role. HVS could occur after surgery because of a change in breathing sensation or breathlessness [13]. Many patients after thyroidectomy complain of tightness and pressure and a sensation of constriction which may be a contributory factor to HVS. In a recent study, frustration, isolation, fear, and altered self-identity were primary themes reporting by patients with RLN [14]. Moreover, HVS could explain the decreased quality of life and general health status and the negative impact on social functions of patients with RLN palsy [15,16].

In order to prove a causal relationship between unilateral RLN palsy and HVS, a prospective study is necessary to compare the pre- and post- thyroidectomy values in patients with and without palsy (i.e. a control group without palsy).

5. Conclusion

In summary, this preliminary study is a proof of concept that HVS might explain chronic dyspnea among patients with unilateral RLN palsy. Thus a global clinical evaluation, combining ENT exam, Nijmegen score and HPVT needs to be considered in the diagnostic and therapy strategies in patients with unilateral RLN palsy and dyspnea. Further data are required to determine the incidence of respiratory impairment and HVS among patients with unilateral RLN palsy. In case of HSV diagnosis, a specific rehabilitation therapy (i.e. hypoventilation therapy) can be proposed in order to improve symptoms and quality of life of patients with unilateral RLN palsy.

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All authors have read and agree with the paper's content. No authors have competing interests. Neither the work nor any part of its essential substance, tables or figures have been or will be published or submitted to another scientific journal or are being considered for publication elsewhere.

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