Prevalence of inducible laryngeal obstruction among patients diagnosed as bronchial asthma

Abstract

**Introduction:** Inducible laryngeal obstruction (ILO) is an important cause of a variety of respiratory symptoms and can mimic bronchial asthma (BA). This study was planned to measure the prevalence of ILO among patients diagnosed with BA and to detect its effect on BA control and severity.

**Material and methods:** Patients aged 18 years or older who were previously diagnosed with BA were enrolled. Laryngeal obstruction was induced using the patient’s specific trigger (e.g. exercise). Visualization of vocal folds was accomplished using a 70-degree rigid laryngoscope (Karl Storz). A visual grade score was utilized to determine the severity of laryngeal obstruction.

**Results:** Results showed that 38.3% (n = 46) of the patients had ILO with the majority being classified as grade 2 (80.4%) (n = 37). The most common subtype was glottic ILO (63%). Bronchial asthma duration, level of control, and severity were not associated with ILO (P values: 0.2, 0.3 and 0.8 respectively).

**Conclusion:** Asthma and ILO commonly co-exist. An accurate classification of patients is very important and must be considered in order to determine whether the symptoms are directly related to ILO or whether they are caused by BA. Ceasing inappropriate treatment may be necessary. Objective diagnostic modalities of ILO are essential.

**Key words:** inducible laryngeal obstruction; bronchial asthma; bronchial asthma control and severity

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Table 1. The 12-item vocal cord dysfunction questionnaire (VCDQ)

| Question                                                                 | Disagree | Disagree | Neither Agree nor Disagree | Agree | Agree Strongly | Score |
|-------------------------------------------------------------------------|----------|----------|----------------------------|-------|----------------|-------|
| 1. My symptoms are confined to my throat/upper chest                    |          |          |                            |       |                |       |
| 2. I feel like I can’t get breath past a certain point in my throat/    |          |          |                            |       |                |       |
| upper chest because of restriction                                      |          |          |                            |       |                |       |
| 3. My breathlessness is usually worse when breathing in                 |          |          |                            |       |                |       |
| 4. My attacks typically come on very suddenly                            |          |          |                            |       |                |       |
| 5. I feel that there is something in my throat that I can’t clear        |          |          |                            |       |                |       |
| 6. My attacks are associated with changes in my voice                    |          |          |                            |       |                |       |
| 7. My breathing can be noisy during attacks                               |          |          |                            |       |                |       |
| 8. I’m aware of other specific triggers that cause attacks               |          |          |                            |       |                |       |
| 9. My symptoms are associated with an ache or itch in my throat         |          |          |                            |       |                |       |
| 10. I am frustrated that my symptoms have not been understood correctly|          |          |                            |       |                |       |
| 11. I am unable to tolerate any light pressure around the neck,         |          |          |                            |       |                |       |
| e.g. tight clothes or bending the neck                                   |          |          |                            |       |                |       |
| 12. The attacks impact on my social life                                 |          |          |                            |       |                |       |
| Total                                                                   |          |          |                            |       |                | (12–60) |

Patients will replay on a 12-item questionnaire and their final score will be recorded. Total score ranges from 12 to 60; higher scores suggest VCD.

Material and methods

Study design: cross-sectional study. Patients enrolled in the study attended the outpatient clinic of the chest medicine department at Mansoura University Hospitals between May 2018 and December 2019. These patients were previously diagnosed with BA and were 18 years or older. Patients who refused to participate in the study, patients who were pregnant, patients with a known history of vocal fold immobility, patients with acute exacerbations of BA, and patients who were current smokers were excluded.

Enrolled patients were submitted to:
— thorough history taking and clinical examination;
— assessment of the level of BA control and severity according to GINA 2018;
— vocal cord dysfunction questionnaire (VCDQ, Table 1) [4]. Patients responded to a 12-item questionnaire and their final score was recorded. Total scores ranged from 12 to 60; higher scores suggest VCD [1];
— induction of laryngeal obstruction by the patient’s specific trigger (e.g. exercise) with visualization of vocal folds using 70-degree rigid laryngoscope (Karl Storz) interfaced with a camera (LEMKE MC 204). A visual grade score was utilized to determine the severity of the laryngeal obstruction [5]. This scoring system grades laryngeal closure at both the glottic and supraglottic levels; scores ranged between 0 (complete patency) and 3 (almost complete closure) [6].
— Fiberoptic-nasoendoscopy using Henke-Sass-Wolf type 10 was used in patients with high gag reflex.

Statistical analysis

Data was analyzed using SPSS V. 16. Categorical data were presented in the form of numbers (percent), while continuous data were presented either as mean (SD) or median (min-max) depending on the results of Shapiro-Wilk test which was used to test the assumption of normal distribution of data. The associations of different parameters with ILO were tested using the Chi² test or Fisher’s exact test in case of categorical data (with respect to the minimal expected values in the contingencies tables), Welch’s t-test in case of continuous data with normal distribution due to unequal variance of the groups, and the Mann-Whitney U test for continuous data with non-normal distribution. Paired data (pre/post treatment data of ILO cases) was compared using the paired t-test for continuous variables with normal distribution and the Wilcoxon Signed
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Ranks Test for ordinal variables (ILO grade: none, grade 1, grade 2, grade 3; severity of asthma: mild, moderate, severe; control of asthma: uncontrolled, partially controlled, well controlled). The correlation of asthma control with ILO control was tested using Spearman’s correlation. Significance level was set at 0.05.

Results

The study included 120 patients previously diagnosed with BA. 78.3% of them were females. Their mean age was 36 years (± 11). About a quarter of the patients had allergic rhinitis, and 60% of them had no comorbidities. More than half of the patients were partly controlled while 16.7% were uncontrolled as per BA (Table 2).

Prevalence of ILO among studied patients

Results showed that 38.3% (n = 46) of the patients had ILO, mostly grade 2 (80.4%) (n = 37) with the most common manifestation being glottic ILO (63%) (Table 3, Figure 1).

Many provocation techniques have been used to induce ILO for diagnosis. Most of our patients (about 100 patients) reported exercise as a trigger for their symptoms. However, GERD, uncontrolled allergic rhinitis with posterior nasal discharge and emotional stress were reported in other cases.

The association of ILO with different epidemiological characteristics of the patients

Table 4 shows that ILO increased with age with significant differences between age groups. For example, patients aged between 31 and 50 had significantly different results from those below 30 years of age (p = 0.023 and 0.038, respectively). However, there was no significant difference in people aged over 50 years of age. Also, being married was associated with a higher risk of ILO. Other parameters such as sex and occupation were not associated with ILO. Similarly, ILO was not associated with BMI of patients or with other comorbidities.

Table 2. Characteristics of the participants (n = 120)

| Characteristics                  | n   | [%]  |
|----------------------------------|-----|------|
| Age mean (SD)                    | 36  | (11) |
| Sex [n%]                         |     |      |
| Male                             | 26  | (21.7%) |
| Female                           | 94  | (78.3%) |
| Marital status [n%]              |     |      |
| Currently married                | 94  | (78.3%) |
| Not currently married            | 26  | (21.7%) |
| Occupation [n%]                  |     |      |
| Non-working                      | 77  | (64.2%) |
| Manual work                      | 17  | (14.2%) |
| Professional/administrative work | 26  | (21.7%) |
| BMI mean (SD)                    | 30.2| (7.2%) |
| Comorbidities* [n%]              |     |      |
| No                               | 72  | (60) |
| Allergic rhinitis                | 31  | (25.8) |
| Others                           | 17  | (14.2) |
| Asthma duration median (min–max) | 4   | (0.2–32) years |
| Asthma control [n%]              |     |      |
| Uncontrolled                     | 20  | (16.7%) |
| Partly controlled                | 69  | (57.5%) |
| Well controlled                  | 30  | (25%) |

*Classes are not mutually exclusive; Others: DM (4), HTN (7), Adenoid (2), peptic ulcer (2), GERD (6), OSA (1). BMI — body mass index

Table 3. Prevalence of ILO among studied patients

| Sites of ILO [n = 46] [n%]          | 8   | (17.4%) |
| Glottic                            | 29  | (63%) |
| Supraglottic and glottic           | 9   | (19.6%) |
| Severity of ILO [n = 46] [n%]      |     |      |
| Grade 1                            | 5   | (10.9%) |
| Grade 2                            | 37  | (80.4%) |
| Grade 3                            | 4   | (8.7%) |

ILO — inducible laryngeal obstruction

Figure 1. Grade 2 glottic inducible laryngeal obstruction

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The association of ILO with the vocal cord dysfunction questionnaire

Mean of VDCQ was 44 in ILO patients and 35.5 in non-ILO patients. These values had no clinical significance despite its statistical significance (P value < 0.001).

The association of ILO with BA duration, severity and control

Bronchial asthma duration, level of control and severity were not associated with ILO (P values = 0.2, 0.3 and 0.8 respectively; Table 5).

Discussion

Inducible laryngeal obstruction (ILO), an induced, inappropriate adduction of the vocal cords, can coexist with bronchial asthma. Accurate differentiation has been challenging because of overlapping symptoms and the absence of sensitive diagnostic criteria for either condition. Although challenging, an accurate diagnosis of patients is very important due to the differing treatment modalities for asthma and ILO [7].

This study included 120 patients previously diagnosed with bronchial asthma and receiving asthma medications for many years. About 38.3% of them were diagnosed with ILO for the first time [80.4% were grade 2 with the most common presentation being glottic ILO (63%)]. The diagnostic difficulty in this study is demonstrated by a mean delay of about 4 years before reaching an ILO diagnosis. Accurate classification of patients is very important to differentiate if symptoms are directly related to ILO or to BA. Ceasing inappropriate treatment may be needed.

The presence of comorbidities, abnormal vocal cord dysfunction questionnaire results, bronchial asthma duration, level of bronchial asthma control, and level of bronchial asthma severity could not aid in the diagnosis of ILO in studied patients. Therefore, objective diagnostic modalities are essential. Lee et al. also concluded that clinical assessment, questionnaire scores, and presence of comorbidities were not sufficient enough to diagnose ILO [7].

Table 4. The association of ILO with different epidemiological and clinical parameters of the patients (n = 120)

| Parameter                  | ILO absent n = 74 | ILO present n = 46 | Significance |
|----------------------------|------------------|-------------------|--------------|
| Age ≤ 30                   | 29 (74.4)        | 10 (25.6)         | \( \chi^2 = 5.18, p = 0.023^* \) |
|                            | 10 (25.6)        | 22 (50)           | \( \chi^2 = 4.2, p = 0.038^* \) |
| 31–40                      | 22 (50)          | 22 (50)           | P = 0.734**  |
| 41–50                      | 10 (47.6)        | 11 (52.4)         |              |
| ≥ 50                       | 13 (81.2)        | 3 (18.8)          |              |
| Sex [n%]                   |                  |                   |              |
| Male                       | 15 (57.7)        | 11 (42.3)         | \( \chi^2 = 5.12, p = 0.02^* \) |
| Female                     | 59 (62.8)        | 35 (37.2)         |              |
| Marital status [n%]        |                  |                   |              |
| Currently not married      | 21(80.8)         | 5(19.2)           | \( \chi^2 = 0.86, p = 0.649^* \) |
| Currently married          | 53 (56.4)        | 41 (43.6)         |              |
| Occupation [n%]             |                  |                   |              |
| Non-working                | 49(63.6)         | 28(36.4)          | \( \chi^2 = 0.86, p = 0.649^* \) |
| Manual work                | 11(64.7)         | 6(35.3)           |              |
| Professional/administrative work | 14(53.8)   | 12 (46.2)         |              |
| BMI mean (SD)              | 29.7 (5)         | 31 (5.9)          | T = -1.23, p = 0.219*** |
| Comorbidities [n%]         |                  |                   |              |
| No                         | 43 (59.7)        | 29 (40.3)         | \( \chi^2 = 1.79, p = 0.407^* \) |
| Allergic rhinitis          | 22 (71)          | 9 (29)            |              |
| Others                     | 9 (52.9)         | 8 (47.1)          |              |

Chi² test; * Fisher’s exact test; ** Welch’s t-test.

BMI — body mass index; ILO — inducible laryngeal obstruction; r — reference
Conclusion

Asthma and ILO commonly co-exist. Accurate classification of patients is very important in order to determine whether symptoms are directly related to ILO or to BA. Ceasing inappropriate treatment may be necessary.

The presence of comorbidities, abnormal vocal cord dysfunction questionnaire results, BA duration, and its BA level of control/severity could not aid in diagnosing ILO in studied patients. Therefore, objective diagnostic modalities are essential.

Conflict of interest

None declared.

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