

BRIEF REPORT

Indications and outcomes of exercise challenge tests performed in children before and during COVID-19 pandemic

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KEY WORDS

Children; COVID-19; exercise challenge test; exercise-induced asthma; Sars-Cov2.

ABSTRACT

COVID-19 pandemic has had a significant impact on general health. In fact, although barely affected by respiratory problems, children and adolescents undoubtedly suffered from the consequences of the pandemic, especially from a psychological standpoint. We aimed to evaluate whether the COVID-19 pandemic modified the indications and the results of Exercise Challenge Tests (ECTs) conducted in a pediatric pulmonology center. This was an observational retrospective monocenter study. We analyzed indications and results of all the ECTs performed between March 2021 and September 2022 (COVID-19 period) and, for comparison, those performed between September 2018 and March 2020 (pre-COVID-19 period). 62 ECTs were performed during the COVID-19 period and 64 during the pre-COVID-19 (proportion of positive test 19.3% and 18.7%, respectively). During the COVID-19 period there was a significant increase (18 vs 4) in the number of ECTs requested because of a mix of subjective respiratory symptoms and vague non-respiratory symptoms and all these tests resulted negative. During the pandemic era we observed an increased number of children and adolescents complaining mixed subjective exercise-related respiratory and non-respiratory symptoms. The ECTs conducted in these patients were all negative, suggesting a functional nature for the reported symptoms.

INTRODUCTION

Exercise challenge test (ECT) is a standardized test used to investigate exercise related respiratory symptoms allowing the differentiation between exercise-induced broncho-constriction (EIB) and other conditions (1, 2).

ECT, in fact, can trigger airway obstruction activating endogenous pathways involved in the pathophysiology of asthma (3). Moreover, the ECT can help differentiating EIB from other exercise related respiratory symptoms such as dysfunctional breathing or exercise-induced laryngeal obstruction (EILO), physical deconditioning and subjective sensation of breathlessness when reaching the personal physical limit (4).

COVID-19 pandemic had a significant impact on general health of children and teenagers.

Although children and adolescents have been less affected than adults from a medical perspective, showing milder respiratory symptoms, lower mortality (0-0.2%) and a better prognosis, they have been heavily affected by the psychological consequences of drastic routine disruption and lack of social interaction due to lockdown, distance teaching and sport interruption (5-7). During the pandemic, an increased number of emergency visits was reported for somatoform disorders, including disturbed sleep as well as respiratory and gastrointestinal issues (8, 9). The most frequently reported respiratory symptoms were shortness of breath and chest pain (8, 9). Moreover, dysfunctional breathing complaints because of hyperventilation during protective face mask wearing (10). These manifestations can mimic common respiratory disorders, like asthma, leading to further investigations to exclude a possible underlying pathologic condition.

We aimed to evaluate whether the COVID19 pandemic modified the indications and the results of ECTs conducted in a tertiary referral pediatric pulmonology center, having the ECTs conducted in the period before the pandemic as control.

METHODS

In this retrospective study we analyzed the indications and results of the ECTs performed at the Pediatric Allergology and Respiratory Medicine Unit of Women's and Children's Health Department of our Hospital.

Two different periods were considered: the first period, (pre-COVID-19 period) included the 18 months before the pandemic, from the 1st of September 2018 to the 1st of March 2020; the second period (COVID-19 period), coincided with the second part of the pandemic, from the 1st of March 2021 to the 1st of September 2022.

ECTs were scheduled in outpatients attending the Pediatric Allergy and Respiratory Medicine Unit who reported exercise related respiratory symptoms and who had a normal spirometry test at baseline and a negative bronchodilator reversibility test. ECTs were requested by the doctors who evaluated the patients. An independent pediatrician involved in the research project retrospectively analyzed all the ECT indications and classified them. ECTs were conducted according to American Thoracic Society and European Respiratory Society (ATS/ERS) guidelines and interpreted as positive in case of a post-exercise FEV1 decline of 12% or higher (1, 2).

Fisher's exact test was used to compare proportions between groups, while the age was compared using t-Test for unpaired data. The study was approved by the Ethics Committee of our Hospital (328n/A0/23).

RESULTS

62 ECTs were performed during the COVID-19 period and 64 during the pre-COVID-19 period, with a similar proportion of positive tests (19.3% and 18.7%, respectively).

During the COVID-19 period, the 62 patients enrolled were 33 males and 29 females and had a mean age of 12.5 years (range 7.0-16.0) (see **Table 1**). During the pre-COVID-19 period, the 64 patients enrolled were 46 males and 18 females and had a mean age of 11.5 (range 7.4-19.5) (see **Table 1**).

16 (26%) patients tested during the COVID-19 period had a personal history of SARS-CoV2 infection before the ECT. In all these patients the disease presented with mild symptoms followed by complete recovery.

The proportion of positive ECT was similar in patients with and without a personal history of COVID-19 (18,7% vs 19,6%, $p = 0.9$).

According to ECT indications, patients of both periods were classified in the following 4 groups:

1. asthmatic patients who reported exercise-induced respiratory symptoms, despite regularly taking the maintenance therapy and having no symptoms apart from those related to physical activity;
2. patients with no previous diagnosis of asthma who reported respiratory symptoms only with exercise;
3. patients with no previous diagnosis of asthma who reported both exercise-related and at rest subjective respiratory symptoms;
4. patients with no previous diagnosis of asthma who reported exercise-related subjective respiratory symptoms (often described as short breath or inability to take a deep breath) together with vague non-respiratory symptoms (i.e. chest/abdominal pain, dizziness, hyperventilation with tremors, weakness and nausea).

Patient's demographic characteristics, classification according to indication and ECT results are reported in **Table 1**.

The number of ECTs belonging to group 4 significantly increased during pandemic ($p < 0.001$).

The distribution of positive and negative ECTs within each group in pre-COVID-19 and COVID-19 period is shown in **Figure 1**.

The number of positive ECTs in group 1 (asthmatic subjects with persistent exercise-related respiratory symptoms) was similar in the two periods analyzed (3 vs 5 pre- and during COVID-19 respectively) although the proportion was higher in the COVID-19 period (45% vs 14%). Comparison of positive ECTs

between the two periods resulted similar also in groups 2 (8 vs 7) and 3 (1 vs 0). No ECTs resulted positive in group 4 in both periods.

Patients with history of Sars-Cov2 infection (n = 16) were distributed among different groups as it follows: group 1 (n = 3), group 2 (n = 8) and group 4 (n = 5).

DISCUSSION

Our data show, during the COVID-19 pandemic, a significant increase in the number of patients who underwent an ECT because of mixed subjective exercise-related respiratory symptoms (often described as short breath or inability to take a deep breath) and vague non-respiratory symptoms (chest/abdominal pain, dizziness, hyperventilation with tremors, weakness and nausea) (group 4). The ECT was negative in all these patients and, therefore, the reported respiratory symptoms were interpreted as somatic.

These findings suggest that, in many cases, respiratory symptoms reported by children and adolescents during the COVID-19 pandemic had psychological roots. This hypothesis is in keeping with the increased anxiety, depression and psychological distress described by several papers in children and adolescents (11-14).

Factors contributing to the development of psychological issues in children and adolescents during the pandemic include concern of severe illness and fear of losing relatives, social isolation due to quarantine, routine life disturbance, exposure to parental stress and concern for family financial loss (5, 6, 15, 16). Pre-existing mental health problems has been described as a major risk factor (17). Also female gender has been reported as a risk factor, as girls seemed more exposed to COVID-19 psychological negative consequences (18, 19). Our data are in keeping with this, in fact we observed a significant increase in the request of ECTs in girls during pandemic ($p = 0.04$).

Children's vulnerability to the pandemic negative psychological effects has been highlighted by various cross-sectional studies and systematic reviews, which indeed focused especially on anxiety symptoms, while somatoform disorders have been less explored (8, 12, 16, 20). Somatization is a common phenomenon encountered in pediatrics, characterized by presentation of symptoms that are

inconsistent with history, physical examination, and investigative findings (21). When symptoms cause distress and affect patient's everyday functioning, somatization becomes a medical illness, defined by DMS-5 "somatic symptom disorder" (SSD) (15).

Children's most frequent somatization include pain manifestations such as abdominal pain and headache, and respiratory issues (e.g. dysfunctional breathing, hyperventilation, sighing dyspnea, psychogenic cough) (22).

R. Turco *et al.* recently reported, in children, a significant increase in emergency department admission rate because of somatic symptom disorder during pandemic compared to pre-pandemic year (8). In this retrospective study, the symptoms reported more frequently in pandemic compared to pre-pandemic era were chest pain, trouble breathing, anxiety, insomnia, general discomfort, anorexia, dysphagia and tachycardia, with children under 12 being apparently more affected than adolescents (8).

In a cross-sectional survey focused on behavioral consequences and coping strategies related to the COVID-19 pandemic, interviewed parents reported behavioral changes and somatoform disorders in 64.3% and 72.5% of children under 6 and 6-18 years, respectively (9). Somatization was the major behavioral change observed in the 6-18 years old group, being shortness of breath the most frequently reported symptom, while children under 6 years of age were mostly affected by behavioral changes (irritability and sleeping disorders, in particular) (9).

Interestingly, our study did not reveal an increased number of ECT-based asthma diagnosis during the pandemic. In fact, the number of positive ECTs (FEV1 fall higher than 12%) was the same in the two periods analyzed (n = 12 in each period), with almost all the children with a positive ECT belonging to group 1 (which included asthmatic children) and group 2 (which included children with respiratory symptoms only during physical activity).

Moreover, we found no significant association between the ECT result and the previous SARS CoV2 infection since the proportion of positive ECTs was similar in children with and without a personal history of COVID-19.

These data suggest, one more time, that the differences described between the preCOVID-19 period and the COVID-19 period are not ascribable to a lung dysfunction induced by the viral infection but they are likely due to the psychological distress suffered during pandemic by children and adolescents.

We acknowledge that our results have to be interpreted with caution considering study limitations. Being a retrospective study, we might have missed useful information regarding, first of all, psychological background, that could provide a better characterization of somatic aspects in our patients.

Furthermore, it could be argued that for children and adolescents belonging to group 4 the medical history and the type of symptoms reported were already indicative of a possible functional disorder. Indeed, it is difficult to exclude an underlying respiratory condition by considering only the medical history. In addition, proving that the exercise test causes no significant symptoms nor airway obstruction can reassure the patient (and family), making the child or adolescent confident in going back to his/her regular activities, including sport training.

In conclusion, during the pandemic era we observed an increased number of children and adolescents complaining mixed subjective respiratory and non-respiratory symptoms. The ECTs conducted in these patients were all negative, demonstrating no exercise-induced bronchial obstruction or respiratory symptoms. Our findings suggest a functional nature for these symptoms and are in line with the pandemic-related increase in somatoform disorders in children and adolescents previously described by other authors.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests

xxx

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The authors have no relevant financial or non-financial interests to disclose.

Authorship

xxx.

Author contributions

Study conception: SC and SZ; clinical data: GDB and VF; data analysis: SC; first draft of the manuscript: GDB. All the authors critically revised the manuscript and approved its final version.

Ethical approval

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and it was approved by the Ethics Committee for Clinical Research of Padova (Comitato Etico per la Sperimentazione Clinica della provincia di Padova) (328n/AO/23).

Human studies and subjects

N/A.

Animal studies

N/A.

Data sharing and data accessibility

N/A.

Publication ethics

Plagiarism

N/A.

Data falsification and fabrication

N/A.

Manipulation of images

N/A.

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	Pre-COVID19 period		COVID19 period		p value
Number of ECTs	64		62		
Males/Females	46/18		33/29		0.04
Age (mean, range)	11.5 (7.4-19.5)		12.5 (7.0-16.0)		0.21
Group 1					
	21 (33%)		11 (18%)		0.065
	<i>Positive ECT</i> 3 (14%)	<i>Negative ECT</i> 18 (86%)	<i>Positive ECT</i> 5 (45%)	<i>Negative ECT</i> 6 (55%)	
Group 2					
	36 (56%)		26 (42%)		0.11
	<i>Positive ECT</i> 8 (22%)	<i>Negative ECT</i> 28 (78%)	<i>Positive ECT</i> 7 (27%)	<i>Negative ECT</i> 19 (73%)	
Group 3					
	3 (5%)		7 (11%)		0.20
	<i>Positive ECT</i> 1 (33%)	<i>Negative ECT</i> 2 (67%)	<i>Positive ECT</i> 0 (0%)	<i>Negative ECT</i> 7 (100%)	
Group 4					
	4 (6%)		18 (29%)		<0.001
	<i>Positive ECT</i> 0 (0%)	<i>Negative ECT</i> 4 (100%)	<i>Positive ECT</i> 0 (0%)	<i>Negative ECT</i> 18 (100%)	

Table 1. Patient's demographic characteristics and group distribution according to exercise challenge test (ECT) indications and ECT results.

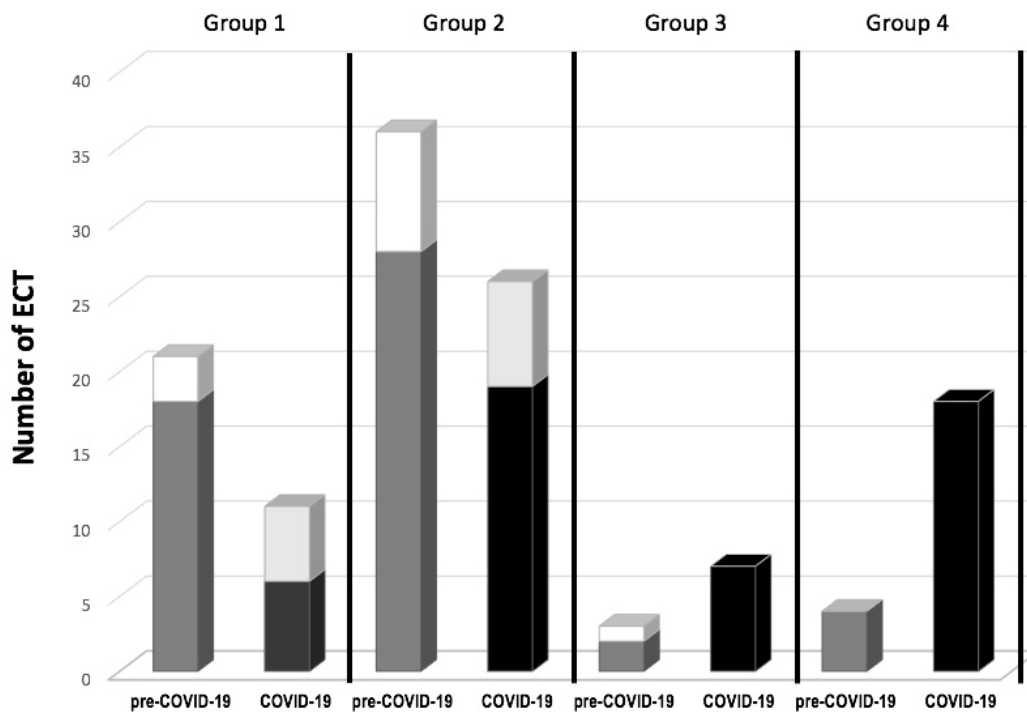


Figure 1. Exercise challenge test (ECT) indications and results during pre-COVID19 and COVID19 period. For each group negative tests are represented in dark gray (pre-COVID19 period) or black (COVID19 period), while positive tests are represented in white and light gray respectively.