



Asthma Control and Attacks in Children with Severe Asthma on Biologics during the COVID-19 Pandemic

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Introduction

The COVID-19 pandemic caused by SARS-COV-2 virus affects fewer children than adults and there are no reports of children with asthma developing severe COVID-19 disease [1]. However, the COVID-19 pandemic has caused a devastating impact on health care delivery and resources [2]. Children with severe asthma suffer from significant morbidity and mortality [3]. Health professionals caring for children and adolescents with se-

vere asthma have impelled drastic changes to the way the care is delivered to this vulnerable group [4]. Emerging data suggests significant reduction in children presenting to the emergency department with asthma attacks [5,6]. However, the impact of lockdown on asthma control and attacks in children and adolescents with severe asthma, especially those on biologic therapy, is unknown. Prior to the COVID-19 pandemic, we routinely ad-



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ministered biologics in a hospital setting and performed the assessment of asthma control by questionnaires, spirometry and Fractional Exhaled Nitric Oxide (FeNO) during each visit. The COVID-19 pandemic resulted in biologics being administered at home in suitable children with assessment of asthma control by virtual administration of asthma control questionnaires and review of symptoms every four weeks. We describe asthma control in children with severe asthma on biologic therapy during the first 4 months of the COVID-19 pandemic cared for at two regional paediatric severe asthma centres in the UK.

Methods

Children aged 6 to 16 year receiving add on biologic (Omalizumab and Mepolizumab) therapy for severe asthma cared for at Birmingham Women's and Children's Hospital and King's College Hospital, UK were included in the study. The study was registered with the audit departments of the respective hospitals. All the children on biologic therapy fulfil the criteria for severe asthma in children [7]. Children were phenotyped by multidisciplinary assessment and biologics were prescribed as add on therapy after an attempt made to correct any modifiable factors. All children satisfy the National Institute for Health and Care Excellence (NICE) criteria for prescribing Omalizumab and Mepolizumab [8] in children with refractory severe allergic/eosinophilic asthma.

Social distancing measures undertaken by our patients were in line with UK government advice as part of a "national lockdown". Schools were closed and households were advised against all but essential travel. Those "shielding" were advised not to leave their dwelling even for exercise, encouraged to have groceries delivered and advised not to have any social contact outside their household group.

The prospectively collected data was acquired from the electronic database maintained in both the units. Demographic data including age, sex, medications and type of biologic was analysed. Asthma control was assessed every four weeks as part of the clinical pathway for children on biologics using the Asthma Control Test (ACT-maximum score of 25, score ≤ 19 suggest inadequate asthma control, score ≥ 20 indicates adequate asthma control). Childhood Asthma Control Test (c-ACT) was used in children < 11 yr. Asthma attacks were defined by administration of a short course of systemic steroids either in primary care or in the hospital. COVID-19 symptoms reported by the patients and carers were also reviewed. The data was analysed in two groups, pre COVID-19 (November 2019 to February 2020) and COVID-19 (March 2020 to June 2020) using GraphPad Prism v5 (GraphPad Software, La Jolla, CA, USA). The Wilcoxon matched pair test and Wilcoxon signed rank test were used to compare the paired data. Where applicable, data are shown as median and Interquartile Range (IQR).

Results

34 children were on biologic therapy for severe asthma. The median age was 13 yr (IQR 15-11.5 yr), 25/34 (73.5%) were male and 15/34 (44.1%) were Caucasian. Of the 34 children, 16 (47%) were on Omalizumab add on therapy and 18/34 (53%) on Mepolizumab. The median 4 weekly ACT score 4 months prior to the COVID-19 pandemic was 17.5 (IQR 20.5-13.5) which improved to 19.5 (IQR 22-19) during the pandemic $p = 0.007$ (Wilcoxon paired match test). Fifteen children (44.1%) had median 4 weekly ACT scores of less than 19 pre COVID with a median score of 15.6 (IQR 17-12.6) which improved to 20 (IQR 22-16),

$p = 0.009$ during the COVID-19 period (Figure 1a).

Nineteen patients (55.8%) had at least one asthma attack during 4 months pre COVID-19. The median asthma attack was 1 (IQR 2-1) which improved to 0 (IQR 1-0), $p = 0.01$ during the 4 months COVID-19 (Wilcoxon sign rank test). Thirteen of these 19 patients (68.4%) had no asthma attacks during the COVID-19 period. Three patients (8.8%) had more asthma attacks during COVID-19. None of the 34 patients reported COVID-19 symptoms.

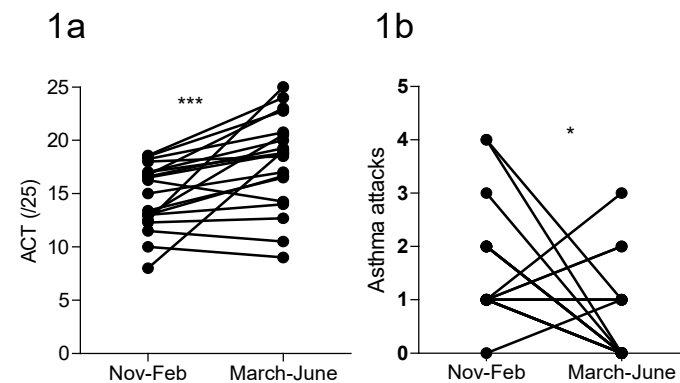


Figure 1: Asthma control test (ACT) and asthma attacks in patients on add on biologic therapies 4 months pre COVID-19 (November 2019 - February 2020) and during 4 months (March 2020 - June 2020) of the COVID-19 pandemic. **(1a):** Changes in the ACT in all the 34 children during the study period. ACT improved in 10/34 children by more than 3 points.

(1b): Changes in asthma attack in children with at least one attack during the study period ($n = 19$). Asthma attacks reduce in 16/19 children during the COVID period. Wilcoxon paired test and Wilcoxon signed rank test used to analyse the paired data. *** $p < 0.0001$, * $p < 0.05$.

Discussion

This report is the first to describe improved asthma control in children with severe asthma on biologic therapy during the first 4 months of the COVID-19 pandemic in the UK. Improved asthma control was demonstrated in 2 domains measured by Asthma Control Test and numbers of asthma attacks. Our study showed no symptoms of COVID-19 infection in the cohort of severe asthmatic children. The strength of our study is the data from two geographically distinct centres in the UK. All the children in the study cohort had detailed disease phenotyping by a multidisciplinary team and initiated biologics after an attempt was made to correct modifiable factors.

Our study provides further evidence the reduction in asthma attacks during the pandemic is also notable in children with severe disease. We analysed data on the short course oral steroids prescribed in primary care as reported by the patients which has not been captured in the recent reports on reduced emergency visits for asthma in children. Improved asthma control during the pandemic could be related to shielding advised by the UK government, reduced exposure to viral infections, improved adherence to prescribed asthma therapies, and reduced outdoor pollution [9]. Although the Asthma Control Test (ACT) has been validated for longitudinal use and demonstrated to be responsive to changes in asthma control over time through correlation with specialist assessment and spirometry [10], the minimum clinically important difference in ACT is 3 points [11]. We acknowledge that this is greater than the improvement

seen in our patient group. However, a corresponding improvement is also demonstrated in the domain of asthma attacks and the study has relatively low patient numbers. We did not monitor spirometry or Fractional Exhaled Nitric Oxide (FeNO) as additional measures of asthma control due to infection control measures during the pandemic. These tests were performed routinely as part of clinical care in the pre COVID-19 period. The measures of asthma control were obtained by the validated questionnaires completed by the children and the carers.

As shielding was suggested for our whole patient group, we were unable to compare administration of biologic treatments at home with a continuation of usual practice. Therefore, we compared pre-pandemic data to post pandemic data for our cohort of patients. We acknowledge that data were compared at different times of the year which means that different weather patterns and seasonal exposure to viruses are potential confounders since risk factors for asthma exacerbation vary by season [12]. The emergency department syndromic surveillance system published by Public Health England [13] shows that the rate of viral infection in the community was significantly lower during the COVID-19 period (March 2020- June 2020) compared to November 2019 to February 2020. Decreased exposure to transmissible community viruses due to shielding measures is therefore likely to be a significant explanation for the demonstrated improvement in asthma control. Treatment with biologics may also have contributed however, since there is evidence that the use of omalizumab reduces the frequency of seasonal asthma exacerbations as well as having antiviral properties in terms of illness and viral shedding [14,15]. In summary, we report improved asthma control and no reported COVID-19 symptoms in children with severe/refractory asthma on biologic therapy.

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