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 severe 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-
ministered biologics in a hospital setting and performed the as-
essment 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 re-
view of symptoms every four weeks. We describe asthma con-
trol 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 (Omaliz-
uzumab and Mepolizumab) therapy for severe asthma cared for
at Birmingham Women’s and Children’s Hospital and King’s Col-
lege Hospital, UK were included in the study. The study was reg-
istered 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 multidis-
ciplinary assessment and biologics were prescribed as add on
therapy after an attempt made to correct any modifiable fac-
tors. 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/ee-
sinophilic 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 con-
tact outside their household group.

The prospectively collected data was acquired from the elec-
tronic database maintained in both the units. Demographic data
including age, sex, medications and type of biologic was anal-
ysed. 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 in-
adequate 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
(March-June) was 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 symp-
toms.

<table>
<thead>
<tr>
<th>Month</th>
<th>Asthma attacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov-Feb</td>
<td>4</td>
</tr>
<tr>
<td>March-June</td>
<td>0</td>
</tr>
</tbody>
</table>

**Figure 1**: Asthma control test (ACT) and asthma attacks
in patients on add on biologic therapies 4 months pre COV-
ID-19 (November 2019 - February 2020) and during 4 months

**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 chil-
dren 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 se-
vvere 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 emer-
gency 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, im-
proved 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.

References

8. NICE. Omalizumab for treating severe persistent allergic asthma. 2013.