Discussion:

Methimazole (active metabolite of carbimazole) has been associated with transient, asymptomatic elevations in serum aminotransferase levels, typically during the first 3 months after starting high dose, induction therapy.¹

It can also cause a clinically apparent, idiosyncratic liver injury. Onset is usually within 2 to 12 weeks of starting therapy and typically causes a cholestatic or mixed pattern of enzyme elevations, without evidence of hepatic necrosis on liver biopsy.² Most patients recover on drug discontinuation. There are, however, occasional reports of severe and fatal cases. The proposed mechanism of carbimazole-induced cholestasis is not fully understood.¹

This patient developed severe hyperbilirubinemia 1 year after starting treatment with carbimazole. His bilirubin level peaked at 518, significantly higher than reported levels in the literature to date. It then began to slowly settle over a period of 4 weeks. Although hepatotoxicity is a rare side effect of antithyroid medication, it can be a significant one. It is important to remember to consider it as a cause of jaundice, with the potential to occur many months after starting treatment. Patient awareness is very important and they should be counselled about the potential side effect and to consult a doctor if they notice jaundice developing. This patient waited for 6 weeks before seeking medical attention, without realising that his medication could be causing this problem.

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REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). LiverTox: clinical and research information on drug-induced liver injury. Bethesda: NIDDK; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547852/. Last accessed May 2021.

2. Kota SK, Meher LK, Kota SK, Jammula S, Modi KD. Carbimazole-induced cholestatic hepatitis in Graves’ disease. Indian Journal of Endocrinol Metabol. 2013; 17(2): 326-8

FACTORS ASSOCIATED WITH IMPROVED CLINICAL CONTROL IN A DIFFICULT-TO-TREAT PAEDIATRIC ASTHMA COHORT THROUGH THE COVID-19 PANDEMIC LOCKDOWN PERIOD

It is recognised that fewer children attended Emergency Departments (ED) with asthma exacerbations during the COVID-19 pandemic.¹² However, it is unclear why. The common triggers of asthma attacks include viral infections, high pollen counts and air pollution. It would seem likely that significant changes in one of more of these would impact on asthma control. There have been no reports, to our knowledge, examining asthma control and medication adherence in a paediatric difficult to treat (DTA) asthma cohort over this period, and comparing it with air pollution and respiratory viral data. The clinical course of, and external influences upon, the Northern Irish paediatric DTA cohort through the pandemic can inform this discussion. The UK

Table 1: Comparison of factors associated with asthma control for the Northern Irish paediatric DTA cohort between corresponding epochs in 2019 and 2020. Air pollution and pollen levels refer to daily levels measured in Belfast over the specified epoch

| Statistic | 1st Feb-31st May 2019 | 1st Feb-31st May 2020 | p-value |
|-----------|------------------------|------------------------|---------|
| PM₁₀(μg/m³) | 16.4 (10.6) | 13 (9-6) | <0.01 |
| PM₂.₅(μg/m³) | 52.5 (24) | 31.1 (12.9) | <0.01 |
| SO₂(μg/m³) | 43 (2.2) | 1.3 (0.6) | <0.01 |
| NO₂(μg/m³) | 11 (4.9) | 10.9 (7.8) | 0.9 |
| Plane tree pollen (grains/m³) | 0.4 (1.5) | 0.05 (0.1) | 0.01 |
| Hazel tree pollen (grains/m³) | 1.1 (2.2) | 0.4 (1) | <0.01 |
| Ash tree pollen (grains/m³) | 2.2 (4.6) | 10 (23.3) | <0.01 |
| Grass pollen (grains/m³) | 0.4 (1.4) | 2.3 (6.8) | 0.04 |
| Unscheduled care attendances/patient* | 0 (0.1) | 0 (0.0) | 0.01 |
| ACT score (out of 25) * | 17 (12.19) | 20 (15.24) | <0.01 |
| Number of courses of oral corticosteroids/patient* | 0 (0.1) | 0 (0.0) | 0.01 |
| Adherence (% of collections of ICS prescriptions)* | 100 (60,100) | 100 (50,100) | 0.6 |

Data are presented as Mean (SD) unless indicated.

* Median (IQR). Statistical tests used: Student t-tests and Wilcoxon rank-sum tests for non-parametric data. A p-value <0.05 indicated statistical significance.

ICS: Inhaled corticosteroids; ACT: Asthma Control Test; NO₂: Nitrogen dioxide; PM₁₀: Particulate matter less than 10 μm in diameter; PM₂.₅: Particulate matter less than 2.5 μm in diameter; SO₂: Sulphur Dioxide.

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Government recommended that children with severe asthma should ‘shield’ from COVID-19 infection. 3 To determine if there was evidence of a significant difference from the previous year, the clinical course of the DTA cohort of 51 patients through the epoch February-May 2020 was compared with the corresponding epoch in 2019. Unscheduled care attendances, courses of rescue oral corticosteroids (OCS), a marker of medication adherence (repeat prescriptions), and Asthma Control Test (ACT) scores for the DTA cohort were compared (Table 1). Levels of airborne aeroallergens, air pollution data and prevailing respiratory viruses over the two epochs were also compared.

Unscheduled care attendance data suggested that the cohort presented significantly less to emergency services and received fewer courses of rescue OCS during the pandemic than in 2019. ACT data was better for the 2020 epoch, suggesting that these differences may be on the basis of improved asthma control. No difference in inhaler adherence was observed. This may represent a ‘ceiling effect’, as sub-optimal adherence is improved and reinforced with remote monitoring at our DTA clinic. 5 Respiratory viral data showed that the number of samples of secretions positive for rhinovirus in 2020, as a percentage of the total number of positive samples, was less than half of that for 2019 [total positive samples: 9940 in 2019 and 12645 in 2020 - and rhinovirus positive samples: 428 (4·3%) v 234 (1·9%)]. There was no consistent pattern for tree pollen levels but there were greater levels of grass pollen in 2020, children may thereby limiting viral spread. Less air pollution is also likely resulting in greater exposure to respiratory viruses. However, schools have tried to implement measures to maintain social distancing and attenuate viral spread. It remains extremely important to optimise adherence, inhaler technique and the use of asthma plans over this period of uncertainty to help to minimise asthma morbidity.

Once shielding stopped, children were mixing much more, resulting in greater exposure to respiratory viruses. However, schools have tried to implement measures to maintain social distancing and attenuate viral spread. It remains extremely important to optimise adherence, inhaler technique and the use of asthma plans over this period of uncertainty to help to minimise asthma morbidity.

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External data sources
Pollution data: The World Air Quality Index Project
Pollen data: The UK Meteorological office
Respiratory viral data- The Regional Virology Laboratory, Belfast

REFERENCES
1. Kenyon CC, Hill DA, Henrickson SE, Bryant-Stephens TC, Zorc JJ. Initial effects of the COVID-19 pandemic on pediatric asthma emergency department utilization. J Allergy Clin Immunol Pract. 2020;8(8):2774-6. e1. doi: 10.1016/j.jaip.2020.05.045
2. Krivec U, Kofol Seliger A, Tursic J. COVID-19 lockdown dropped the rate of paediatric asthma admissions. Arch Dis Child. 2020;105(8):809-10.
3. British Pediatric Respiratory Society. Updated BPRS COVID-19 guidance, 11th January 2021. Southampton: BPRS; 2021
4. Shields MD, ALQahtani F, Rivey MP, McNlny JC. Mobile direct observation of therapy (MDOT) - A rapid systematic review and pilot study in children with asthma. PLoS One. 2018; 13(2):e0190031. doi: 10.1371/journal.pone.0190031.

PROTHROMBIN COMPLEX CONCENTRATE USE IN BELFAST HEALTH AND SOCIAL CARE TRUST

Dear Editor,

Prothrombin factor concentrate (PCC; Octaplex®), a combination of human coagulation factors II, VII, IX and X, protein C and protein S, is a potent reversal agent for vitamin K antagonists. Along with Vitamin K, it is used in emergency management of bleeding associated with warfarin and direct oral anticoagulants (DOACs). 1 Despite widespread use, there is a lack of consensus about optimal dosing, 2 with current guidelines specifying large ranges for dosing or, in the case of DOACs, no dosing recommendations at all. 3 Lack of clarity complicates development of clear local protocols, making accurate and timely administration more difficult, as highlighted by a serious adverse incident in which delayed administration led to a poor clinical outcome. 4

This service evaluation aimed to assess current use of PCC in Belfast Health and Social Care Trust (BHSCT), to identify areas for improvement and improve alignment between local guidance and practice on-the-ground.

Two current BHSCT guidelines on management of bleeding while receiving anticoagulants provided audit standards. We sought records of all patients who received PCC within BHSCT between January and June 2016. We designed, piloted and adapted a pro-forma which was then used by Haemovigilance Specialist Nurses. Data were collated in Microsoft Excel and analysed using descriptive statistics to