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.[4] 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. Air pollution data showed significantly lower levels of atmospheric $PM_{2.5}$, PM_{10} and SO_2 (but not NO_2) during the 2020 epoch.

This data suggests that shielding has been protective through the pandemic, leading to improved asthma control. The viral data may reflect the restricted movement of children, thereby limiting viral spread. Less air pollution is also likely a contributor to fewer exacerbations. Although there were greater airborne grass pollen levels in 2020, children may have been protected from outdoor exposure as a result of shielding indoors.

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, McElnay 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

Table 1: Key findings

Audit standard	Finding
Patients on warfarin should receive 15 IU/kg PCC if INR<4, 30IU/kg if INR>4	Baseline INR <4: average dose 16.4 IU/kg (24 patients) Baseline INR >4: average dose 29.5IU/kg (9 patients)
Patients on DOACs should receive 40IU/kg PCC	Average dose in patients on apixaban or rivoroxiban (8 patients) 35.6 IU/kg
Patients on warfarin should receive 5mg IV Vitamin K in addition to PCC	Number of patients who received Vitamin K - 38 Dose of Vitamin K administered: 1mg - 1/38 (3%) 5mg - 31/38 (82%) 10mg - 6/38 (16%) No vitamin K administered - 10/48
Patients on warfarin presenting with head injury should receive PCC prior to neuroimaging	Prior to neuroimaging - 1/14 (7%) After neuroimaging - 13/14 (93%)

summarise patients' baseline characteristics, PCC dosing, coagulation assay results and clinical outcomes.

Records were available for 62 of 98 eligible patients. Twenty-nine were female (47%). Ages ranged from 34-95 years, with a mean of 71 years. At time of PCC administration, 44 patients were receiving warfarin (71%), 8 apixaban (13%) and 6 rivaroxaban (10%). One patient was not receiving any anticoagulant (2%); information was unavailable for 3 patients (5%). Average dose of PCC was 1739 IU (range 714-4000 IU). Only 34/62 (55%) patients received doses involving use of whole (500IU) vials. Weight was recorded for 49 patients (79%) but prior to administration in only 18 cases (29%). 18/62 (29%) of weights were estimated rather than measured. Administration of PCC was associated with an average reduction in International Normalised Ratio (INR) of 2.13. The average INR after administration was 1.36. Twelve patients (28%) were deceased by 60 days after administration. Table 1 summarises other key findings.

Most PCC dosing adhered to guidance, although many patients were not weighed prior to administration. Other areas of shortfall were identified, however. In patients with suspected intracranial bleeding, PCC was frequently administered after, rather than prior to, neuroimaging. Vitamin K was often inappropriately omitted during reversal of warfarin. We also found that it was common practice to use incomplete vials of PCC. While not precluded by current guidance, this practice could lead to PCC, at a cost of up to £21,560 per year, being discarded that could potentially improve clinical response if administered. Targeted quality improvement work is now needed to ensure that patients are weighed appropriately, PCC is given prior to neuroimaging in patients with head injury, and vitamin K is co-administered when reversing warfarin. Guidance should be updated to recommend that PCC doses involve use of complete vials. These interventions have the potential to maximise the efficacy and cost-effectiveness of PCC in the treatment of life-threatening haemorrhage.

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REFERENCES

1. Rhoney DH, Chester KW, Darsey DA. Optimal dosage and administration practices for Vitamin K antagonist reversal with 4-Factor Prothrombin Complex Concentrate. *Clin Appl Thromb*. 2020;26:1-13. doi:10.1177/1076029620947474
2. Khorsand N, Kooistra HA, Van Hest RM, Veeger NJ, Meijer K. A systematic review of prothrombin complex concentrate dosing strategies to reverse vitamin K antagonist therapy. *Thromb Res*. 2015;135(1):9-19.
3. Makris M, Veen JJ, Tait CR, Mumford AD, Laffan M. British Committee for Standards in Haematology. Guideline on the management of bleeding in patients on antithrombotic agents. *Br J Haematol*. 2013;160(1): 35-46.
4. Belfast Health and Social Care Trust. Safety and quality learning letter: LL/SAI/2014/025 (AS): Head Injury in patients on Warfarin- treat as a medical emergency. Belfast: BHSCT, 2014.