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## Octaplas<sup>®</sup> is not equivalent to fresh frozen plasma in the treatment of acute angioedema

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### EDITOR:

In the UK, when an anaesthetist prescribes the blood product ‘fresh frozen plasma’ (FFP), the current National Blood Service practice is to supply single-donor-unit plasma unless otherwise specified. However, since 2002 in the Republic of Ireland, the policy of the Irish Blood Transfusion Service (IBTS) has been to dispense the commercial product Octaplas<sup>®</sup> (Octapharma Ltd, Coventry, UK) in place of FFP whenever that is prescribed. Octaplas<sup>®</sup> is a solvent/detergent-treated pooled-donor plasma, which has been shown to be as effective as FFP in the replacement of clotting factors [1] and to lack the potential antigenicity found in single-donor FFP [2]. However, prior to its widespread introduction, concerns had already been expressed regarding the relative therapeutic equivalence of these two plasma products in certain clinical contexts [3]. IBTS routinely supplies Octaplas<sup>®</sup> rather than FFP when the latter is prescribed; because of this ‘at source’ substitution, most clinicians are unaware of the difference between the two products. We recently encountered one critically ill patient to whom both Octaplas<sup>®</sup> and FFP were administered and whose case highlights further limitations to Octaplas<sup>®</sup> use.

A 19-yr-old female was brought by ambulance to our Accident and Emergency Department with sudden onset of lip and tongue swelling, associated with progressive dyspnoea and stridor. Subcutaneous epinephrine had been administered without improvement. Ongoing stridor suggested imminent airway compromise and, following rapid sequence

induction, the patient’s trachea was intubated. At direct laryngoscopy, glottic structures were noted to be swollen. She was subsequently transferred to the ICU for further management.

Information from the patient’s mother suggested a possible history of type III hereditary angioedema, a rare oestrogen-dependent X-linked dominant disease with a reported prevalence between 1 in 10 000 and 1 in 50 000 [4]. This diagnosis had been reached in another hospital near the patient’s home (150 km away), to which she had previously presented with recurrent episodes of generalized abdominal pain associated with acute lip and tongue swelling. She had never required intubation before. Although a diagnosis of hereditary angioedema was initially suspected, the patient’s serum C3, C4, C1-esterase inhibitor and CH100 levels were either supra-normal or within normal limits on testing, and more detailed enquiry into her family history revealed similarly affected male relatives. This informed a revised diagnosis of idiopathic relapsing angioedema, further supported by the predominance of airway structure involvement and resistance to standard treatments. Specifically, previous episodes had not responded to epinephrine, antihistamine or corticosteroids, but had resolved after intravenous infusion of FFP; accordingly, FFP was now prescribed. However, 2 U of Octaplas<sup>®</sup> were received from the Blood Bank, and were infused by ICU nursing staff. In contrast to previous episodes treated with FFP, Octaplas<sup>®</sup> produced no improvement in her condition.

Subsequent contact with the hospital where prior acute episodes had been managed provided the information that episodes do not respond to Octaplas<sup>®</sup> and require 2–4 units of single-donor FFP. This triggered concerns regarding the therapeutic equivalence of Octaplas<sup>®</sup> and FFP in this context.

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Enquiries were made of the IBTS and 6U of single-donor FFP were then made available to the patient.

By the fifth day following her admission, airway swelling had begun to subside and the patient was transferred to a tertiary hospital near her home. She was discharged well 2 days later.

Octaplas<sup>®</sup> has been approved by the United States Food and Drug Administration since 1998 as a virally inactivated alternative to FFP for the replacement of coagulation factors and the reversal of the effect of warfarin. This product is prepared from the pooled plasma of a large number of donors, which is heated to 31°C for 4 h in the presence of the detergents tri(*n*-butyl)phosphate and Triton-X-100. The final product is filtered through a 0.2 µm filter to remove particulate foreign matter [5]. While this method is highly effective in virally inactivating the plasma, thus rendering it safer for transfusion, it also presents some biochemical shortcomings. It has been shown that heat and/or detergents induce irreversible conformational changes in the structure of serine protease inhibitor proteins in Octaplas<sup>®</sup>, thus inactivating them [3]. This family of proteins represents the largest class of proteinase inhibitors in plasma representing all of the major proteolytic cascades, including antitrypsin, antiplasmin, vonWillebrand factor, C1-inhibitor and heparin cofactor II.

Therefore, Octaplas<sup>®</sup> is not suitable for use in situations of low plasma antiplasmin activity such as that seen during the anhepatic phase of liver transplantation, where the acquired fibrinolytic state and subsequent intraoperative bleeding may necessitate massive transfusion [3]. In Ireland, liver transplantation is the single exception to the 'compulsory' use of Octaplas<sup>®</sup> and a separate stock of FFP is maintained by the IBTS for supply to the National Liver Transplantation Unit. All other hospitals and departments, however, receive Octaplas<sup>®</sup>.

In light of our experience, it seems likely that inhibitors of the complement cascade, themselves serine proteases, may be inactivated in the manufacture of Octaplas<sup>®</sup>, possibly rendering it unsuitable for use in the management of acute attacks of angioedema. While licensed indications for Octaplas<sup>®</sup> are identical to those for FFP [6], we feel that further direct clinical comparison of the two products is now warranted in order to inform guidelines governing their use, and we would therefore suggest that Octaplas<sup>®</sup> is not an equivalent or appropriate substitute for FFP in all circumstances.

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## Foreign body occlusion of syringe driver mechanism

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### EDITOR:

We would like to report a 'near-miss' incident that occurred in our hospital recently.

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A 14-yr-old male was receiving an intravenous (i.v.) remifentanyl infusion for intraoperative analgesia during a Laparoscopic Cholecystectomy. The procedure had been uneventful with the remifentanyl infusing at 21 mL h<sup>-1</sup> (0.2 µg kg<sup>-1</sup> min<sup>-1</sup>) from a Monoject<sup>\*</sup> 50-mL syringe (Tyco Healthcare, Gosport, UK) mounted on an IVAC<sup>®</sup> P3000 syringe driver (Alaris<sup>™</sup> Medical Systems, Basingstoke,