Aim: To describe the use of nitazoxanide in the treatment of human parainfluenza-3 (HPIV-3) in a critically ill patient.

Clinical features: Patient JH, a 60 year old female of Korean background, was admitted to a large teaching hospital with a HPIV-3 induced exacerbation of asthma. Past medical history included hypertension, type 2 diabetes and obesity (BMI = 29). After development of respiratory failure, she deteriorated rapidly, requiring admission into the intensive care unit (ICU) for intubation and mechanical ventilation. Continuous veno-venous haemodialysis filtration (CVVHDF) was started on Day 9 of ICU admission as the patient’s renal function declined.

Diagnostics: Computed tomography (CT) scans showed tracheobronchitis and tracheomalacia, and consecutive bronchoalveolar lavage (BAL) tests were positive for HPIV-3. After three weeks in ICU receiving maximal respiratory support and antimicrobial therapy, she remained HPIV-3 positive, thus a collaborative decision was made between the infectious diseases team, the ICU team and ICU pharmacist to target the underlying cause of HPIV-3 with a trial of nitazoxanide therapy.

Nitazoxanide is a drug originally developed in the 1970’s and is currently approved for use for Cryptosporidium and Giardia. It acts on anaerobic bacteria and protozoa by inhibiting pyruvate:ferredoxin oxidoreductase (PFOR) enzyme dependent electron transfer reactions that are essential to anaerobic energy metabolism.1 It is thought to work in viruses by blocking the maturation of viral haemagglutinin, which is responsible for viral binding to host cells, at the post-translational stage. It does not affect neuraminidase or the M2 protein, targets for existing influenza antivirals on the market.2

Evidence for use: A randomized, double-blinded, placebo-controlled phase 2b/3 trial conducted by Haffizula et al (2014) recruited patients between 12-65 years old, with symptoms of fever and at least one respiratory (eg cough, sneezing) and constitutional symptom (eg headache, chills), as well as confirmation of influenza by local laboratory testing. Patients were allocated to receive either placebo, nitazoxanide 300mg orally (PO) twice a day (BD) or nitazoxanide 600mg PO BD. Nitazoxanide was shown to reduce the average length of symptoms from 117 hours (placebo) to 96 hours (nitazoxanide 600mg BD). Median time to cessation of viral shedding was also reduced, from 91.3 hours (placebo) compared to 71.8 hours (nitazoxanide 600mg BD).2

Treatment: Based on this evidence, nitazoxanide 600mg BD via nasogastric tube for 5 days was trialed to treat the primary viral cause of the patient’s condition. A powder for suspension was procured to facilitate nasogastric administration, via the Special Access Scheme. Pharmacokinetic information noting small amounts of active metabolite excreted in urine suggested no dose adjustments were required in CVVHDF.

Results: Upon immediate completion of the 5 day course, a repeat aspirate sample did not detect any HPIV-3. A repeat CT scan showed partial improvements in tracheobronchial inflammation.

Conclusion: This case report demonstrates, to our knowledge, the first documented use of nitazoxanide in Australia for treatment of human parainfluenza-3. This example supports the potential use of a 5 day course of nitazoxanide in treating human parainfluenza-3, however, further research is warranted to support efficacy.

References: