The Royal College of Pathologists
Pathology: the science behind the cure

Patient Safety Bulletin

Hyperammonaemia – it's not always spurious

What happened and what were the issues/implications?

Ammonia measurement was requested on an unwell neonate, along with other investigations. The sample was haemolysed, no numerical result was reported to the ward staff (as per laboratory protocol and manufacturer's instructions) and a repeat sample was requested by telephone. A repeat sample was received in the laboratory 4 hours later with a result of >1000 µmol/L. Clinical suspicion of an inborn error of metabolism (IEM) was low at this stage and the accuracy of the result was queried by clinical staff. In light of this, another repeat sample was analysed and the elevated result was confirmed. Collectively, several short delays meant that action was not taken until 10 hours after receipt of the initial sample.

At this stage, a paediatric metabolic consultant was involved and the patient was transferred to a tertiary centre where they were treated with haemofiltration, ventilation, IV glucose, arginine and nitrogen-scavenging drugs. A diagnosis of a urea cycle disorder was confirmed. The patient suffered adverse neurological effects from prolonged hyperammonaemia and the treating metabolic paediatrician felt that the delay in initiating treatment significantly contributed to this. Subsequently, the patient's metabolic disorder was relatively easy to manage, indicating that the underlying metabolic defect was not severe. The permanent neurological damage sustained by this child could have largely been avoided with earlier initiation of treatment during their first episode of decompensation.

This case highlights the need for prompt measurement of ammonia and action in the event of hyperammonaemia. This is particularly important in neonates and young children where the cause of symptoms may be difficult to determine and an IEM may not be high on the differential diagnosis.

What actions were taken?

Several actions were taken in light of this adverse incident. Practice was changed to report all ammonia results, even in the presence of haemolysis. These results are now reported with a comment stating that the sample was haemolysed and the true ammonia result may be lower, along with a recommendation for an urgent repeat sample if the concentration is elevated. While this is against manufacturer's protocol, it is felt that it is clinically justified to do this. Practice was also changed so that raised ammonia results in paediatric samples should be phoned to the on call paediatric or neonatal consultant, instead of phoning to the ward, to help ensure the urgency of the result is understood and acted upon – compliance with this is currently being audited. While investigating, it was also noted that where a single sample was received for full blood count (FBC) and ammonia measurement, the FBC was prioritised; this practice was changed in collaboration with the haematology and neonatal departments, to prioritise the ammonia measurement.

What did you learn?

In this situation, it is safer to report a result on a poor-quality sample which may be an overestimate of plasma ammonia, along with an appropriate comment and requesting an urgent repeat, instead of not providing a result. An elevated result is likely to generate a repeat to be sent more promptly and any false elevation (e.g. due to haemolysis) should be excluded with a repeat sample. It is also important for laboratory staff to recognise that repeat samples may not be a priority on a busy ward, and those that are particularly urgent should be clearly communicated to a senior clinician.

In addition, mild haemolysis is likely to result in a modest elevation of ammonia concentration (up to 10–20%). If a child has an extremely elevated ammonia concentration after taking this into account, it would be appropriate for the clinical team to seek advice from a metabolic paediatrician alongside arranging a repeat sample. The impact of gross haemolysis is less predictable and can generate completely spurious results.

How was the learning shared?

The case was discussed between laboratory and clinical colleagues, and a joint statement was issued to relevant staff. An update to the laboratory computer system to enable reporting of ammonia results on haemolysed samples was implemented and communicated to relevant staff. Discussion took place with colleagues in tertiary referral centres and practices were compared. Recommendations were formed and circulated to relevant referral hospitals as well as the tertiary centres. Re-audit of practice and the impact of these changes will take place in due course.

Read more patient safety bulletins at: rcpath.org/patient-safety-bulletins