Screening for Intracranial Haemorrhage Following Birth in Neonates with Severe Haemophilia

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Introduction

There is currently limited prospective data on the incidence and morbidity associated with intracranial haemorrhage (ICH) in neonates with inherited bleeding disorders. UK guidelines in 2012 recommend screening patients at birth with cranial ultrasound. MRI is only recommended in symptomatic neonates[1].

Clinical features of neurological impairment may be subtle or absent in neonates and ICH may remain undetected, having potentially significant effects. Alder Hey Childrens' Hospital, Liverpool, UK, has been undertaking screening utilizing cranial ultrasound within 24 hours of birth to detect early ICH and allow prompt treatment. MRI is then undertaken on day 3-4 following birth to allow detection of developing haemorrhage. Cranial ultrasound is widely available so can be performed in smaller district hospitals. MRI is recognized as a sensitive tool for detecting ICH and is becoming more readily available. Using Cranial Ultrasound and MRI imaging would potentially be an optimal and achievable way to screen for ICH in the perinatal period. We also present a general approach to the management of neonates with severe haemophilia. This includes full discussion with parents regarding use of factor at the earliest opportunity post birth. We offer recombinant factor therapy within a few hours of birth if an APTT is in the severe haemophilia range on cord blood. This strategy is achievable in hospitals where factor assays may not be done routinely or out of hours and has minimal risk associated.

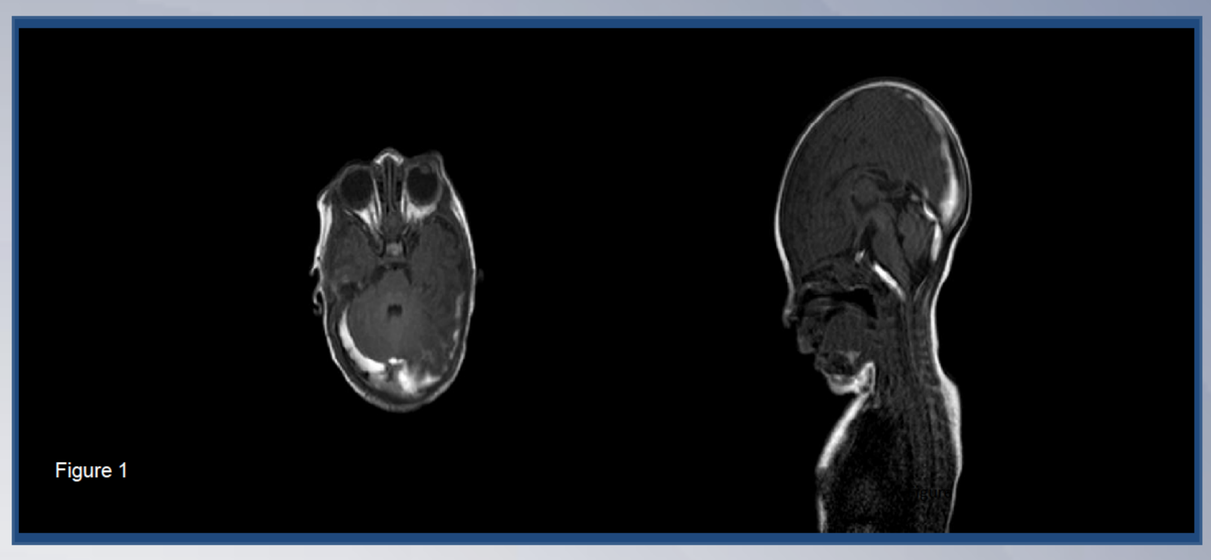

Figure 1

Antenatal

- Discussion with mother (If known carrier of severe haemophilia A or B) and her partner regarding …….
  - the way in which haemostasis centre in partnership with maternity unit manages the coagulation disorder
- the Cord blood test
  - The significance of a prolonged APTT
  - The rationale for a single dose of Factor therapy in the first hours after delivery
- **If they agree to the administration of replacement intravenous Factor this is documented**
- A delivery plan is documented- including the avoidance of forceps/ventouse and avoidance of invasive monitoring

Post Delivery

- The mother carries;
  - Citrated Coagulation Blood sampling bottles
- A single dose of Factor replacement therapy
- Cord blood is sent to check the APTT
- If significantly prolonged (i.e. around 80-90 sec or more) severe haemophilia is assumed very likely and factor is administered

Follow Up Imaging

- A cranial ultrasound is carried out in the 1st 24 hours after delivery
- An MRI head is arranged to be carried out on day 3 or 4 at central paediatric hospital
- Intracranial bleeds at any point were treated with further factor replacement and repeat imaging
- All patients had clinical review and follow up by the paediatric haematology team.

Results

Since 2005 all cases of expected haemophilia births (or those diagnosed shortly after birth) were offered post natal management as described. 5 neonatal cases with haemophilia A (factor levels <2%), were included. Uptake of prophylactic factor use post delivery was 100%. Of the cases included, 3 were spontaneous vaginal delivery, one via elective caesarian section and one via ventouse (diagnosis was only suspected shortly after delivery thus normal advice pre-delivery had not been given). All of the cases were at least 36 weeks gestation and had an eventual diagnosis of severe haemophilia A. 4 of the cases had normal cranial ultrasound scans within 24 hours of birth, 1 baby had a CT as initial imaging as they presented with cephalohaematoma. 2 cases had an intracranial haemorrhage (both "normal delivery") on MRI, one was a moderate bleed, and the other a very large one. Both of these patients had had a normal ultrasound. They were then treated with continuing factor replacement. There have been no further neurological concerns on follow up in any of the cases. Likewise there does not appear to be an increase in the development of inhibitors with early treatment[2]. The centre also had a further 7 babies born within the time period who were later diagnosed with severe haemophilia and were discovered to have a family history. This leaves potential for further possible cases being found prior to delivery with detailed antenatal history taking.

Patient	Ultrasound Scan	MRI Scan
1	Normal	Intracranial Haemorrhage- cerebellar bleed. Worsened on repeat scan (see fig 1)
2	Normal	No bleed
3	Normal	Right ventricular bleed
4	Normal	No bleed
5	Had CT- aponeurotic bleed	No intracranial haemorrhage

Conclusion

These cases suggest ICH can be large, asymptomatic, with normal cranial ultrasound scan and may be common following normal delivery. Combined MRI and Cranial ultrasound are very low risk and allow prompt detection and management of ICH. There is evidence that haemophilia patients' with intracranial haemorrhage have some difference in intellectual function and possibly specific learning difficulties when compared with controls, and that there is a role for early neuropsychological input in this group[3]. Therefore it may be of benefit, and is very unlikely to cause harm, to diagnose and manage intracranial haemorrhage as early as possible wherever possible. Prospective studies are needed to ascertain incidence and morbidity of ICH in this population, to further assess screening procedures and optimise management.

Method

This retrospective case review includes all patients following the screening process offered at a tertiary referral centre for paediatric bleeding disorders. It includes patients diagnosed with haemophilia prior to, or shortly after birth.

1) Chalmers, E et al. Guideline on the management of haemophilia in the fetus and neonate. A United Kingdom Haemophilia Centre Doctors' Organisation: Guideline approved by the British Committee for Standards in Haematology. Br J Haematology, 154, 208-215

2) Chalmers E et al. Paediatric working party of UKHCDO. Early Factor VIII exposure and subsequent inhibitor development in children with severe haemophilia A. Haemophilia ;13: 149-155

3) Miles B et al. Effect of intracranial bleeds on the neurocognitive, academic, behavioural and adaptive functioning of boys with haemophilia: Haemophilia 2012 18(2) 229-34

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