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Vitamin K Deficiency Bleeding

Synonym: haemorrhagic disease of the newborn, vitamin K deficient bleeding in the newborn

Vitamin K deficiency bleeding (VKDB) is now the preferred term for haemorrhagic disease of the newborn (HDN). This is due to deficiency of clotting factors as a result of vitamin K deficiency. VKDB was first described over a hundred years ago but its relationship to vitamin K was not realised until 40 years later [1].

Vitamin K is required for the production of clotting factors II, VII, IX and X. It is involved in the normal clotting of blood, is present in some plants and is also synthesised by some *Escherichia coli* in the gut. All newborn infants have low levels of vitamin K and are at risk of developing VKDB. The body has very limited ability to store the vitamin.

- **Early VKDB** presents within 24 hours of birth.
- **Classic VKDB** presents between day 1 and day 7 of life.
- **Late VKDB** presents between week 2 and week 12 of life.

Late VKDB can result in significant morbidity and mortality due to intracranial haemorrhage and has resulted in most high-income countries having in place a protocol for giving supplemental vitamin K to all newborn babies.

Epidemiology [2]

- In the UK, VKDB is very rare with most cases occurring in breastfed babies whose parents have refused prophylaxis.
- The incidence internationally of early VKDB of at-risk neonates (see Risk factors, below) ranges from 6-12%.
- The incidence of the classic form is 0.01-0.44%.
- In developing countries most babies do not receive prophylaxis and VKDB is probably a common (but poorly documented) cause of death and handicap in the early months of life.
- Late VKDB occasionally occurs after intramuscular (IM) vitamin K prophylaxis [3]. One study quoted an incidence of 1/15.000-1/20.000 births [4].

Risk factors

- Early form - several drugs, such as isoniazid, rifampicin, anticoagulants and anticonvulsant agents, which have been taken by the mother, make the infant at risk of developing early VKDB.
- Classic form - often idiopathic but may be related to low placental transfer of vitamin K, low concentration in breast milk, lack of gastrointestinal flora in the newborn gut, and poor oral intake that commonly occurs in the newborn period at the start of breastfeeding.
- Late form - warm environmental temperatures predispose babies to developing late VKDB. Unsuspected liver disease, especially alpha-1-antitrypsin deficiency, increases the risk, as does malabsorption of fat-soluble vitamins, due to diarrhoea, coeliac disease or cystic fibrosis.

Presentation

Early VKDB

This is limited to babies whose mothers received various drugs during pregnancy (see 'Risk factors', above). It presents with bleeding at sites related to the trauma of birth, such as:

- Bleeding from the scalp monitor site.
- Cephalhaematoma, especially after ventouse delivery.
- Intracranial bleeding after a traumatic delivery, which may cause irritability and convulsions.
- Intrathoracic bleeding, which can produce blood-stained sputum, with or without respiratory distress.
- Intra-abdominal bleeding, which may present as melaena.
- Tachycardia due to exsanguination.

Classic VKDB

The bleeding in classic VKDB most often presents as bleeding from non-vital organs, such as:

- Gastrointestinal bleeding.
- Bleeding from the skin and mucous membranes - eg, the nose and gums.
- Prolonged bleeding following circumcision.
- Bleeding from the umbilical stump.

Late VKDB

- Late VKDB peaks at 3-8 weeks of age. It typically presents with intracranial haemorrhage and is often caused by undiagnosed cholestasis with resultant malabsorption of vitamin K[5].
- Late VKDB produces the greatest morbidity and mortality amongst the infants, due to sudden bleeding into the central nervous system.

History

If VKDB is suspected, it is important to go over certain aspects of history:

- Drugs taken in pregnancy.
- Gestation at delivery.
- Type and length of delivery.
- Feeding history, especially if breastfed or bottle-fed.

Differential diagnosis

- Haemophilia A, haemophilia B.
- Trauma.
- Accidental or non-accidental injury.
- Disseminated intravascular coagulopathy.
- Thrombocytopenia, including maternal isoimmune thrombocytopenia.
- Necrotising enterocolitis.
- Intussusception.

Investigations

- FBC.
- Clotting screen, including prothrombin time (prolonged), coagulation time and partial thromboplastin time.
- Other tests like estimation of PIVKA II (protein induced in vitamin K absence) level, and estimation of native prothrombin antigen using monoclonal antibody may be helpful[6].
- CXR or ultrasound scan may confirm intrathoracic bleed.
- CT or MRI scan if intracranial haemorrhage or other major haemorrhage is suspected.

Management

Immediate management

- When VKDB is suspected, vitamin K should be given as a supplement as soon as possible. This will result in a reduction in the bleeding time within a few hours. The injection should be subcutaneous:
    - An IM injection can produce a haematoma in a coagulation disorder.
    - The intravenous route can produce an anaphylactoid reaction.

- Infants of mothers taking drugs that inhibit vitamin K are at risk of early VKDB and should receive 1 mg IM as soon as possible after birth[7]. Classic VKDB is prevented by IM or oral administration of 1 mg vitamin K[8].
- Babies with severe bleeding or intracranial haemorrhage may require fresh frozen plasma (FFP) to be given in addition to vitamin K in order to arrest the bleeding as soon as possible[9].
- Babies who have lost a large amount of their circulating volume may require transfusions with whole blood[9].

Long-term management

In exclusively breastfed infants, single IM administration at birth is also effective in preventing (rare) late VKDB, but single oral administration is not. If given orally, prophylaxis should be continued. Regimes vary from unit to unit. One unit recommends 2 mg one week after birth, with an additional 2 mg at week four[7].

Babies with late VKDB who have suffered intracranial bleeds will require assessment from a specialised team to help minimise the long-term sequelae of the bleed. They will require early and continuing physiotherapy to minimise spasticity and retain function; they may require nutritional assistance if unable to swallow or suck, and they may require surgery or intracranial shunts to reduce intracranial pressure.

Complications

The complications of VKDB mainly relate to bleeds involving the central nervous system, and children who survive may have variable long-term neurological disability[10].

Prognosis

The prognosis is good for most affected babies. Intracranial haemorrhage and late VKDB account for the mortality associated with VKDB[11].

Prevention

All forms of VKDB are now far less common due to understanding of the aetiology. Routine antenatal screening of all mothers has allowed for the early identification of babies who may be at risk of early VKDB, and where possible therapeutic regimes are altered.

The greatest reduction has resulted from the routine administration of vitamin K in all newborn babies, usually at birth. This is given either in the form of an IM injection or a series of oral supplements and, as a consequence, VKDB is now rarely seen in the UK and other countries where this policy has been adopted. The IM route is preferred[6].

Classic VKDB is prevented by IM or oral administration of 1 mg vitamin K. In exclusively breastfed infants, single IM administration at birth is also effective in preventing late VKDB but single oral administration is not. If given orally, further doses should be given according to local protocol. The only infants not fully protected in this way are those with yet unrecognised liver disease[12].

Further reading & references

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