Original Article

CLINICAL PRESENTATION OF LATE HAEMORRHAGIC DISEASE OF NEWBORN

Rehana Majeed[1], Yasmeen Memon[2], Farrukh Majeed[3]

ABSTRACT

Objectives: To observe the clinical presentation of late haemorrhagic disease of the newborn (LHDNB), and clinical improvement after the administration of vitamin K_1.

Methodology: This is a prospective descriptive study. All the children older than seven days who presented with bleeding were admitted in pediatrics ward of Isra University Hyderabad from April 2006 to April 2007 were included. Data collection was done by means of detailed proforma. Analysis was done on SPSS version 11.

Results: Thirty five cases were included. Commonest site of bleeding was subcutaneous followed by oral and injection site. Mean age of late haemorrhagic disease of newborn was 109 days and minimum age of presentation was 28 days. Common clinical presentations were irritability, convulsions, poor reflexes and poor feeding. Mostly recovery was within 24 hours after vit K.

Conclusion: Late HDN results in severe hemorrhage especially hemorrhage in the central nervous system. Administration of Vitamin K (1mg, IM) at birth can present these severe complications.

KEY WORDS: Vitamin K deficiency bleeding (VKDB), Late haemorrhagic disease of newborn (LHDN), Intraventriculer haemorrhage, Vit K, Prothrombin Time (PT), Activated partial thromboplastin time (aPTT).

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INTRODUCTION

Vitamin K is a fat-soluble vitamin that can be absorbed from the gastro intestinal tract in the presence of bile salts. Vit. K is required for the production of coagulation factors II, VII, IX, and X in the liver. Because of the short half-life of these factors, and the small amounts of vitamin K that can be stored in the body, inadequate intake of vitamin K can result in deficiency in a short period of time. PIVKA, inactive precursor proteins induced in vitamin K's absence, are measurable and can be used as an indicator of vitamin K deficiency. The more appropriate term for haemorrhagic disease of newborn is vitamin K deficiency bleeding (VKDB).[1] Historically, all bleeding disorders in the newborn were grouped together under the diagnosis of haemorrhagic disease of the newborn (HDN). With methods available today for the accurate diagnosis of other factor deficiency states and immune thrombocytopenia, VKDB can be distinguished from other disorders by exclusion and appropriate analysis of these other factors involved in coagulation.[2]

Haemorrhagic disease of the newborn (HDN) is one of the commonest causes of acquired haemostatic disorder in early infancy.[3] Incidence of Late-HDN in the eastern world is 25-80/100,000 births which is higher than that in the western world (4-25/100,000 births).[4] VKDB can occur in three general time frames.[1]

1. Dr. Rehana Majeed, FCPS
Assistant Professor,
Pediatric Department,
Isra University, Hyderabad, Pakistan.
2. Dr. Yasmeen Memon, FCPS
Pediatric Department,
Liaquat University of Medical and Health Science,
3. Dr. Farrukh Majeed,
Department of Physiology,
Dow University Karachi, KARACHI.

Correspondence

Dr. Rehana Majeed
E- Mail: drrehanamajeed@yahoo.com

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Early onset, at less than 24 hours after birth, rarely occurs and is almost always associated with maternal medications that interfere with vitamin K, such as anticonvulsants, anticoagulants, and antibiotics. Postnatal administration of vitamin K has no effect in preventing early-onset disease. Maternal vitamin K supplementation that is administered parentally may prevent this form of VKDB.[2] The classic onset of VKDB is 2-7 days after birth in breastfed infants.[3] Late-onset VKDB occurs after1-2 weeks of life. In addition to breastfeeding, risk factors include diarrhea, hepatitis, cystic fibrosis (CF), celiac disease and alpha1-antitrypin deficiency or absence of prophylaxis in otherwise healthy infants. Late-onset VKDB tends to be more severe than early-onset or classic disease and has a high frequency of intracranial haemorrhage (ICH). Late HDN usually occurs between 2-8 weeks but can occur anytime in the first year.

While determination of exact incidence of HDN is possible only in an elaborate population based study, the morbidity and mortality can be indirectly gauged from referral centers considering the alarming nature of clinical manifestations necessitating admission in most cases. There are few case reports available on this aspect from the region. The present hospital based study was carried out to assess the clinical profile, and outcome of patients with late HDN.

PATIENTS AND METHODS

All infants above the age of 7 days admitted in pediatric ward of Isra University Hospital, with bleeding from April 2006 to April 2007 were evaluated.

A child fulfilling the following criteria was defined as having late HDN:

* Bleeding in an infant after 7 days of life.
* No thrombocytopenia (platelet counts >1.5 lac/cumm).
* Normal peripheral blood smear examination.
* Prolonged prothrombin time and prolonged aPTT (index (PTI) (INR >1.8)
* Rapid correction of PTI or cessation of bleeding after vitamin K administration.

Protein induced in vitamin K absence (PIVKA) and serum fibrinogen levels were not available and were not considered essential in the case definition. Vitamin K 2mg intravenous was given to all the patients and investigations were repeated after 24 hours. Infants fulfilling the criteria were evaluated with regard to following aspects: place of birth, vitamin K administration, feeding history, history of prolonged diarrhea, use of antibiotics, clinical signs. Other investigations done with particular reference like CT scan head where indicated.

Exclusion criteria:

1. Infants with presence of icterus, significant hepatomegaly and/or derangement of liver enzymes.
2. Failure of PT to return to normal after a single dose of vitamin K were considered to have liver disease.
3. Children who received Vitamin K before hospitalizations.
4. Children in whom coagulation tests were not performed before, during and after therapy.

RESULTS

Thrity five infants were diagnosed to have late HDN. It included 24 boys and 11 girls. Ten (28.5%) were born in the hospital of which 6(19%) received vitamin K. The rest were delivered at home or maternity home and did not receive any vitamin K prophylaxis. None of the mothers were on medications during pregnancy, which could alter the coagulation status of these infants. All 35 infants were breastfed. Mean age of presentation was109 days,earliest presentation on day 28 and longest duration were 280 days. These infants did not have any underlying illness; like liver disease or malabsorbtion syndrome. Mild to moderate fever was reported in 50% of the cases. Table-II Pallor was seen in all infants (100%). Anterior fontanel was tense and bulging in three (8.5%) infants. CT scan showed intracranial haemorrhage in four (11.4%) cases Two infants did not have CT scan but presented with clinical features suggestive of intracranial bleed. Only one (2%) infant had a blood in

Table-I: Bleeding sites in late hemorrhagic disease of newborn

Bleeding sites eeding	*No. (Total=35)*	*%*
Skin Bruises	25	71
Intracranial	4	11.4
Rectal bleeding	12	34
Blood in stool	17	48
Nasal bleeding	14	40
Injection site	7	20
Blood in urine	1	2

urine.All babies were born at term. Twenty eight babies were born by normal vaginal delivery and seven by cesarean section, indication of being nonprogression of labour. The place of delivery was home in 25(71%) while 10 were born in private nursing homes.

The sites of bleeding on admission are shown in Table-I. The clinical manifestations are shown in Table-II. Majority of the infants (71%) presented with skin bleeds which were noted by the parents. In physical examination; there was bulging or full fontanel in three patients (8.5%), diminished or absent neonatal reflexes in nine patients (24%) and ecchymosis in 25 patients (71%). Rectal bleeding 12(34%) and oral bleeding findings were found in 11 (73%). Table-III shows response of Vit K on PT and aPTT both of which were corrected by it within 24 hours.

DISCUSSION

Our data confirms that late hemorrhagic disease of newborn remains a cause of serious morbidity and mortality in our part. In developed countries LHDN is now a rare life threatening disease due to the widespread use of effective prophylaxis with vitamin K at birth.[3] Most reports of late HDN have been seen in babies born at home.[5] In the present study, deliveries were conducted mainly at home and private clinics, where the practice of routine vitamin K administration does not exist. Admission to the pediatrics department after early neo-natal life, indicate that late-HDN is not an insignificant problem. The low concentration of vitamin K in human breast milk and the predisposition to vitamin K deficiency bleeding following exclusive breast feeding is emerging as a matter of concern especially in developing countries where exclusive breast feeding is vigorously advocated to promote optimal health in the infant.Two thirds of babies were in the age group of 4-8 weeks. Vitamin K (menaquinones) is absent in newborn liver, but gradually accumulates after birth. This, together with low concentration of vitamin K in human breast milk (1.5µg/dL)as compared to 6µg/dL in cow's milk) may explain the peak frequency of late HDN at this age.[3,6] Almost all the infants of late HDN in studies received breast feeding and very few receive vitamin K prophylaxis at birth.[7] In the present study also, majority of the babies were on breast milk exclusively and had not received vitamin K at birth.

Table-II: Clinical Presentation

Clinical symptoms	*No. (total=35)*	*%*
pallor	35	100
Poor feeding	7	20
Irritable	8	22.8
Convulsion	4	11.4
Bulging fontanel	3	8.5
Discoloration of skin	25	71.4
Vomiting	8	22.8
Poor reflexes	9	24

Table-III: Response of vit K on PT & aPTT.

	Before administration	*After administration*
P.T	70±40.5s	15±1.6s
aPTT	110±60s	32±1.0s

The common manifestations of late HDN reported earlier are evidence of intracranial haemorrhage, deep ecchymosis, bleeding from GI tract and/or bleeding from mucus membrane, skin punctures or surgical incisions.[7] This is also indicated by our study. In the present study ICH was the presenting feature in 10% of cases. The remaining had skin haemorrhage and rectal bleeding. Subdural hemorrhage has been the commonest type of ICH reported, followed by subarachnoid haemorrhage.[5] In other studies ICH was found to be 70% of cases.[8] In the present study, most of the patients i.e., 75% had haemorrhages at multiple sites, which is not frequently

described.ICH has been seen in 50-80% of affected babies in various studies and causes death or severe handicap in 50-70% of these babies.[4] An overall mortality of 14% to 50% has been reported.[4,9] The low mortality of 5% in this study may be because study group is small.Late HDN may mimic findings of nonaccidental head injury and may lead to mistaken diagnosis of child abuse.[10] Occasionally, baby may present with respiratory distress due to thymic haemorrhage or hemothorax.[11,12] Babies may rarely present with secondary hydrocephalus.[13] In the present study vitamin K was not administered to all at birth but only 6(19%) received it. A few case reports are available of late HDN in babies even after receiving injection vitamin K.[14] An epidemiological study from Germany by von Kries[15] showed a failure rate (occurrence of late HDN) of 0.25 per 100,000 infants after IM administration compared with 1.4 per 10,000 in countries where oral vitamin K is given.There are reports of preterm babies who had received intravenous injections of vitamin K at birth presenting with late HDN;[16] this is because IM route has longer duration of effect than IV as a result of depot preparations. Intravenous route is less effective for long-term prophylaxis for preventing HDN.[16] Oral route is economical, effective, practical and more acceptable to the parent. But many studies have shown that oral Vitamin K is less effective in preventing late HDN.

CONCLUSION

It may be difficult to administer vitamin K injection to all newborn babies especially those born at home, which form the bulk of total deliveries in a country like Pakistan. However, it is clear that concept of vitamin K administration at birth is not familiar to health care providers; more than 20% of babies admitted in this series were delivered at nursing homes and yet did not receive vitamin K. The recommendation is to give vitamin K1 to all newborns as a single intramuscular dose of 0.5 to 1mg. Since breast fed infants are at highest risk of late HDN, it is imperative that vitamin K prophylaxis be promoted. Warning bleeds like umbilical bleed (which may precede intracranial bleeds), epistaxis or skin bleeds should be taken seriously in any breast-fed infant. Our study highlights the morbidity and mortality associated with a potentially preventable condition. Vitamin K prophylaxis should be offered to all newborns who are exclusively breast-fed. The occurrence of a significant hemorrhage like ICH leading to death or life-long neurological deficit is enough justification for routine administration of vitamin K at birth.

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