Management of Polycythemia in Neonates

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Abstract

Polycythemia is defined as a venous hematocrit above 65%. The hematocrit in a newborn peaks at 2 hours of age and decreases gradually after that. The relationship between hematocrit and viscosity is almost linear till 65% and exponential thereafter. Increased viscosity of blood is associated with symptoms of hypo-perfusion. Clinical features related to hyperviscosity may affect all organ systems. Neonates born small for gestational age (SGA) , born to diabetic mothers(IDM) ,multiple births are at risk for polycythemia . They should therefore undergo screening at 2, 12 , 24 hour of age. Polycythemia may be symptomatic or asymptomatic and guidelines for management of both types based on the current evidence are provided in the protocol.

Keywords: polycythemia, blood viscosity, newborn, therapy

Introduction

Polycythemia or an increased hematocrit is associated with hyperviscosity of blood. As the viscosity increases, there is an impairment of tissue oxygenation and perfusion and a tendency to form microthrombi. Significant damage may occur if these events occur in the cerebral cortex, kidneys and adrenal glands. Hence this condition requires urgent diagnosis and prompt management.

The viscosity of blood is directly proportional to the hematocrit and plasma viscosity and inversely proportional to the deformability of red blood cells. Symptoms of hypoperfusion correlate better with viscosity as compared to hematocrit. Viscosity is, however, difficult to measure at the bedside. Hyperviscocity is therefore suspected in the presence of an abnormally high hematocrit with or without suggestive symptoms. Relationship between viscosity and hematocrit is almost linear upto a hematocrit of 65% and exponential thereafter[1,2]. The polycythemia-hyperviscocity syndrome is thus usually confined to infants with hematocrits of more than 65%; it is very rare with hematocrits of <60%. **Definition**

A diagnosis of polycythemia is made in the presence of a venous hematocrit more than 65% or a venous hemoglobin concentration in excess of 22.0 gm/dl. Hyperviscosity is defined as a viscosity greater than 14.6 centipoise at a shear rate of 11. 5 per second[3].

Incidence

The incidence of polycythemia is 1.5-4% of all live births[4,5]. The incidence is higher among both small for gestational age (SGA) and large for gestational age (LGA) infants. The incidence of polycythemia is 15% among term SGA infants as compared to 2% in term appropriate for gestational age (AGA) infants[6]. Neonates born at high altitudes also

have a higher incidence of polycythemia[1]. Polycythemia is unlikely to occur in neonates born at less than 34 weeks gestation.

Physiological changes in postnatal life

Significant changes take place in the hematocrit from birth through the first 24 hours of life. The hematocrit peaks at 2 hours of age and values upto 71% may be normal at this age[7,8] It gradually declines to 68% by 6 hrs and usually stabilizes by 12 to 24 hours. The initial rise in hematocrit is related to a transudation of fluid out of the intravascular space.

Clinical features

Polycythemia can result in a wide range of symptoms involving several organ systems (Table 1). About 50% of neonates with polycythemia develop one or more symptoms. However, most of these symptoms are non-specific and may be related to the underlying conditions rather than due to polycythemia per se.

Screening for polycythemia

Screening should be done for polycythemia in certain high-risk groups (Table 2). We recommend screening in high-risk neonates at 2 hours of age. A normal value at 2 hours of age (hematocrit <65%) does not merit any further screening unless the infant is symptomatic. Hematocrit values >65% at 2 hours of age merit repeat screening at 12 and 24 hours. Any infant with clinical features suggestive of polycythemia should be investigated for the same.

Capillary vs. venous hematocrit

Capillary hematocrit measurements are unreliable and highly subject to variations in blood flow. Capillary hematocrits are significantly higher than venous hematocrits. This difference is even more apparent in infants receiving large placental transfusion[9]. Capillary samples may be used for screening, but all high values should be confirmed by a venous sample for the diagnosis of polycythemia.

Methods of hematocrit analysis

The two available methods are

Automated hematology analyzer: This calculates the hematocrit from a direct measurement of mean cell volume and the hemoglobin.

Micro-centrifuge: Blood is collected in heparinized micro-capillaries (110mm length and 1-2mm internal diameter) and centrifuged at 10,000-15,000 rounds per minute (rpm) for 3-5 minutes. Plasma separates and the packed cell volume is measured to give the hematocrit. An automated analyzer gives lower values as compared to hematocrits measured by the centrifugation method[10]. Most of the reported data on polycythemia is on centrifuged hematocrits.

Management

Before a diagnosis of polycythemia is considered, it is mandatory to exclude dehydration. If the birth weight is known, re-weighing the baby and looking for excessive weight loss would help in the diagnosis of dehydration. If this is present, it should be corrected by increasing fluid intake. The hematocrit should be measured again after correction of dehydration. Once a diagnosis of polycythemia is made, associated metabolic problems including hypoglycemia should be excluded.

Management of polycythemia is dependent upon two factors (Figure):

1. Presence of symptoms suggestive of polycythemia and/or
2. Absolute value of hematocrit

(a) **Symptomatic polycythemia**

The definitive treatment for polycythemia is to perform a partial exchange transfusion (PET). PET involves removing some of the blood volume and replacing it with fluids so as to decrease the hematocrit to a target packed cell volume of 55%. Following partial exchange transfusion, symptoms like jitteriness may persist for 1-2 days despite the hematocrit being lowered to physiological ranges.

The volume of blood to be exchanged is given by the formula shown in the box.

$$\text{Volume to be exchanged} = \text{Blood volume}^* \times \frac{(\text{Observed hematocrit} - \text{Desired hematocrit})}{\text{Observed hematocrit}}$$

**Blood volume is estimated to be 80-90 ml/kg in term babies and 90-100 ml/kg in preterm babies*

As a rough guide, the volume of blood to be exchanged is usually 20 ml/kg.

PET: peripheral vs. umbilical route

Partial exchange transfusion may be carried out via the peripheral route or the central route. In the former, blood is withdrawn from the peripheral arterial line and replaced simultaneously with saline via the venous line. In the central route, the umbilical venous catheter is used for withdrawing blood while the same amount of saline is replaced through a peripheral vein. Alternatively, the umbilical venous catheter may be used both for withdrawal of blood and replacement with saline. Two systematic reviews (including

a Cochrane review) have shown that the partial exchange transfusion through umbilical route may be associated with increased risk of necrotizing enterocolitis[11,12].

PET: fluids to be used

Crystalloids such as normal saline (NS) or ringer's lactate (RL) are preferred over colloids because they are less expensive and easily available, produce a similar reduction in hematocrit as colloids[13,14], and do not have the risk of transfusion associated infections. Moreover, adult plasma has been shown to increase the blood viscosity when mixed with fetal erythrocytes. *We use only normal saline for partial exchange transfusion.*

(b) Asymptomatic polycythemia:

The line of management in infants with asymptomatic polycythemia depends upon their hematocrit values.

i. *Hematocrit >75%:* These infants are usually managed a partial exchange transfusion.

ii. *Hematocrit between 70% and 75%:* Conservative management with hydration may be tried in infants with hematocrit of 70 to 75%. An extra fluid aliquot of 20 ml/kg may be added to the daily fluid requirements. The additional fluid may be ensured by either enteral (supervised feeding) or parenteral route (IV fluids). The rationale for this therapy is hemodilution and the resultant decrease in viscosity. However, liberal fluid therapy may be associated with problems especially in preterm neonates.

iii. *Hematocrit between 65% and 70%:* They only need monitoring for any symptoms of polycythemia and re-estimation of hematocrit. Further management depends upon the repeat hematocrit values.

Evidence for management of polycythemia

Partial exchange transfusion reverses the physiological abnormalities associated with the polycythemia–hyperviscocity syndrome. It improves capillary perfusion, cerebral blood flow and cardiac function. However, there is very little data to suggest that PET improves long term outcome in patients with polycythemia. The Cochrane review - published this year (2010) - concludes that "there are no proven clinically significant short or long-term benefits of PET in polycythemic newborn infants who are clinically well or who have minor symptoms related to hyperviscosity; PET may lead to an increase in the risk of NEC[12]." However, as the review authors pointed out, the data regarding developmental outcomes are extremely imprecise due to the large number of surviving infants who were not assessed and, therefore, the true risks and benefits of PET are unclear. It is possible that the underlying etiology of polycythemia is a more important determinant of ultimate outcome. Given the uncertainty regarding the long term outcomes, it is preferable to do partial exchange transfusion in symptomatic infants with hematocrit of >65% and in asymptomatic neonates with hematocrit of >75%.

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Table 1. Clinical features ascribed to polycythemia and hyperviscosity

Central nervous system

Early: Hypotonia and sleepiness, irritability, jitteriness , seizures and infarcts
Late: motor deficits, lower achievement and IQ scores

Metabolism

Hypoglycemia
Jaundice
Hypocalcemia

Heart and lungs

Tachycardia, tachypnea, respiratory distress
Cyanosis, plethora
Chest radiography: cardiomegaly, pulmonary plethora
Echocardiography: increased pulmonary resistance, decreased cardiac output

Gastrointestinal tract

Poor suck, vomiting
Feed intolerance – abdominal distenstion
Necrotizing enterocolitis

Kidneys

Oliguria (depending on blood volume)
Transient hypertension
Renal vein thrombosis

Hematology

Mild thrombocytopenia
Thrombosis (rare)

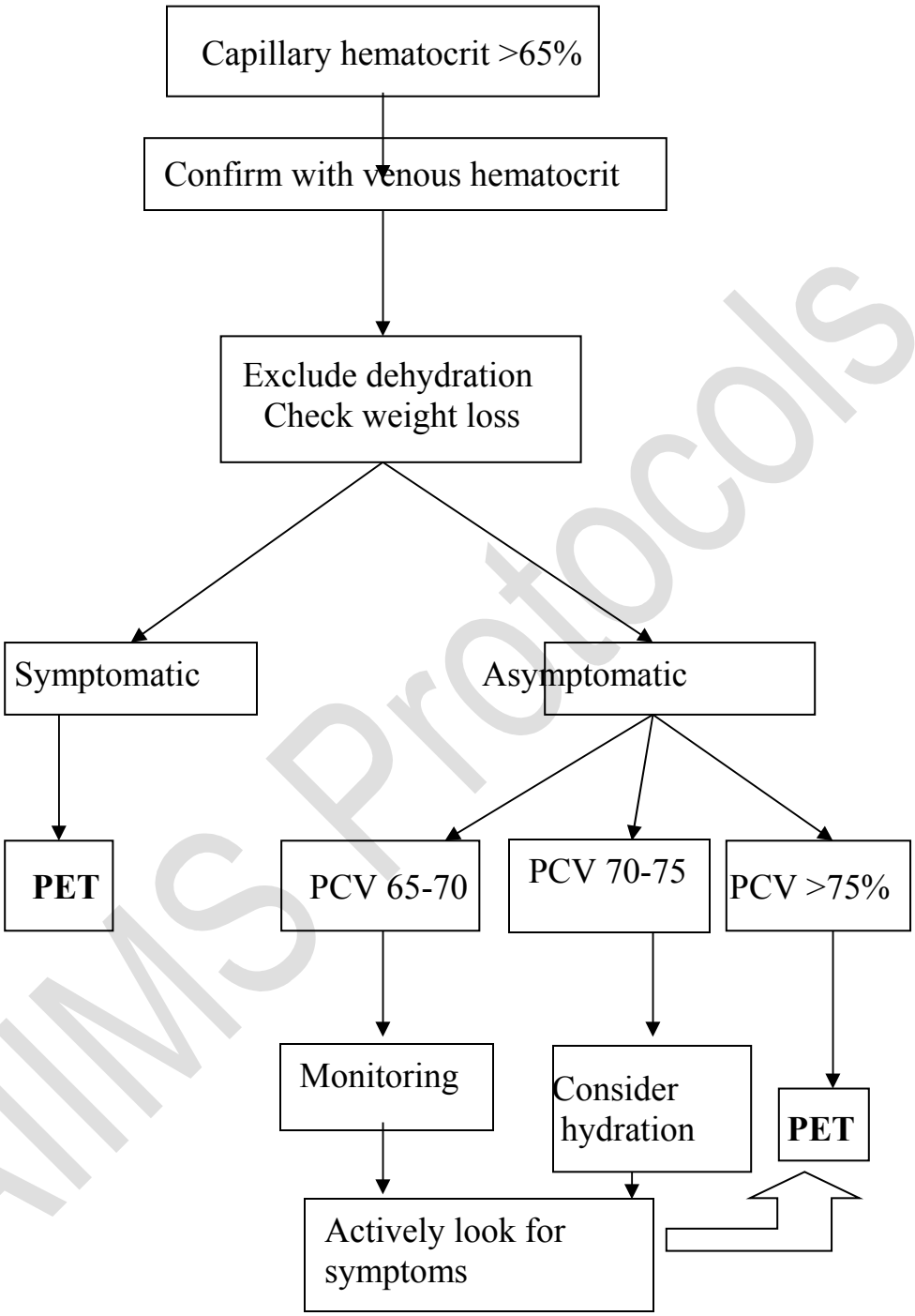
Miscellaneous

Peripheral gangrene,
Priapism,
Testicular infarction

Table 2. Screening for polycythemia

Screening is recommended for the following:
(a) Small for gestational age (SGA) infants (b) Infants of diabetic mothers (IDM) (c) Large for gestational age (LGA) infants (d) Monochorionic twins especially the larger twin (e) Morphological features of growth retardation.

Figure: Algorithm for management of polycythemia



PET: partial exchange transfusion