RESEARCH ARTICLE

ANALYTICAL STUDY OF CAUSATIVE FACTORS OF NEONATAL LIMB GANGRENE.

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Manuscript Info

Abstract

Aim and objectives: To analyze the various etiological factors involved in development of neonatal limb gangrene.

Duration of study – Two years (Aug 2015 to Aug 2017).

Study design – Retrospective and Prospective.

Inclusion criteria: Neonates present with limb gangrene within 28 days.

Exclusion criteria: Neonates present with limb gangrene after 28 days.

Conclusion: Preterm and low birth weight with malformation babies with sepsis, and maternal risk factors like diabetes and birth trauma and repeated venous cannulation and drug extravasation play a major role in development of neonatal limb gangrene.

Introduction:
Peripheral limb ischemia and gangrene occurring in the first month of life is an uncommon condition. Only few cases are in literature. Many etiologic factors are postulated but none is proven. Birth asphyxia, rhesus disease, respiratory distress, severe congenital anomalies, infection and sepsis, dehydration, maternal diabetes, direct pressure from the maternal pelvis, arterial thrombosis, emboli, leukocytoclastic vasculitis, vein puncture, umbilical catheterization trauma, contraction bands, polycythemia and coagulopathies are possible causes. The treatment is symptomatic, allowing the ischemic area to demarcate along with specific interventions with respect to the cause.
## Analysis of Etiological Factors

| S. No | Day of Presentation | Term/Preterm | Birthweight | ANS/CMF | Rh | D M | H T | DVT/Thromboprophylaxis | CTD/Vascular | Abruptio Placentae | Birth Trauma | Birth A/R/D | Hb/PCV/PL count | IV Can | Blood C/S | Kawasaki Disease | Conclusion |
|-------|---------------------|--------------|-------------|---------|----|-----|-----|------------------------|--------------|------------------|-------------|-------------|-----------------|--------|-----------|------------------|------------|
| 1     | 1st Day             | Preterm      | 1.1 kg      | NLAB    |    |    |    |                        |              |                  |             |             | Yes             |        |           |                  |            |
|       |                     |              |             | PDA+     |    |    |    |                        |              |                  |             |             | 13.5 gm PCV 48, Pi -2.75 L |        |           |                  | Preterm with LBW |
| 2     | 2nd Day             | Term         | 2.7 kg      | NLAB    |    |    |    |                        |              |                  |             |             | 14 gm PCV 51, Pi 3.1 L |        |           |                  | Sepsis     |
| 3     | 3rd Day             | Preterm      | 9.0 kg      | NLAB    |    |    |    |                        |              |                  |             |             | Yes             |        |           |                  | Preterm with LBW |
|       |                     |              |             | PDA+     |    |    |    |                        |              |                  |             |             | 12.5 gm PCV 52, Pi -3 L |        |           |                  |            |
| 4     | 2nd Day             | Term         | 3.6 kg      | NLAB    | Yes|    |    |                        | Yes (forceps Delivery) |                  |             |             | Hb 14 gm PCV 53, Pi 8.5 L |        |           |                  | Birth Trauma |
| 5     | 10th Day            | Term         | 3 kg        | NLAB    |    |    |    |                        |              |                  |             |             | 15 gm PCV 52, Pi 4.8 L |        |           |                  | Pneumococcal Sepsis |
| 6     | 7th Day             | Term         | 2.9 kg      | NLAB    | Yes|    |    |                        |              |                  |             |             | Hb 12.8 gm PCV 55, Pi 37 L |        |           |                  | Maternal DM |
| 7     | 1st Day             | Term         | 2 kg        | ASD, VSD |    |    |    |                        |              |                  |             |             | Hb 16 gm PCV 52, Pi 3.6 L |        |           |                  | Congenital Malformation |
| 8     | 12th Day            | Term         | 2.5 kg      | NLAB    |    |    |    |                        |              |                  |             |             | 14.5 gm PCV 50, Pi -3.75 L |        | Yes       |                  | IV Cannulation |
| 9     | 2nd Day             | Preterm      | 1.4 kg      | NLAB    |    |    |    |                        |              |                  |             |             | 14.5 gm PCV 50, Pi -2.25 L |        |           |                  | Preterm with LBW |
| S. No | Day of Presentation | Term/ Preterm | Birth weight | ANS/ CMF | Rhesus IC | DM | HT | DVT/ Hypercoagulable | CTD/ Vasculitis | Birth Trauma | Abruptio Placenta | Birth ARDS | Hb/ PCV/ PL count | IV Can | Blood C/S | Kawasaki Disease | Conclusion |
|-------|---------------------|--------------|--------------|----------|-----------|----|----|---------------------|----------------|--------------|------------------|-------------|------------------|--------|-----------|------------------|------------|
| 10    | 5th Day             | Term         | 3.8 kg       | NL AB    | Yes       | -  | -  | -                   | -              | -            | -                | -           | Hb 16gm PCV 50 PL 5L | -      | -         | -                | Birth Trauma |
| 11    | 17th Day            | Term         | 3.1 kg       | NL AB    | -         | -  | -  | -                   | -              | -            | -                | -           | Hb 15.5gm PCV 55 PL 2.1L | E. coli Pseudomonas | -         | -                | Sepsis |
| 12    | 21st Day            | Term         | 3 kg         | NL AB    | Yes       | -  | -  | -                   | -              | -            | -                | -           | Hb 16gm PCV 55 PL 4.7L | -      | -         | -                | Maternal DM |
| 13    | 24th Day            | Term         | 2.8 kg       | NL AB    | -         | -  | -  | -                   | -              | -            | -                | -           | Hb 12.5gm PCV 52 PL 3 L | Yes     | -         | -                | IV Cannulation |
| 14    | 5th Day             | Preterm      | 1 Kg         | NL AB, PDA+ | -       | -  | -  | -                   | -              | -            | -                | -           | Hb 15.5gm PCV 46 PL 4 L | -      | -         | -                | Preterm with LBW |
| 15    | 8th Day             | Term         | 3.5 kg       | NL AB    | -         | -  | -  | -                   | -              | -            | -                | -           | Hb 14.8gm PCV 58 PL 4.38L | -      | -         | -                | Birth Trauma |
| 16    | 3rd Day             | Term         | 2.25 kg      | TOF      | -         | -  | -  | -                   | -              | -            | -                | -           | Hb 12.5gm PCV 52 PL 3 L | -      | -         | -                | Congenital Malformation |
| 17    | 18th Day            | Term         | 3 kg         | NL AB    | -         | -  | -  | -                   | -              | -            | -                | -           | Hb 16gm PCV 52 PL 3.6L | Staph. aureus | -         | -                | Sepsis |
| 18    | 4th Day             | Preterm      | 1.25 kg      | NL AB, PDA+ | -       | -  | -  | -                   | -              | -            | -                | -           | Hb 14.5gm PCV 50 PL 3.75L | -      | -         | -                | Preterm with LBW |

ANS - Antenatal Screening, CMF - Congenital Malformation, DM - Diabetes, HT - Hypertension, NLAB - No Limb Abnormalities, PDA - Patent Ductus Arteriosus, ASD - Atrial Septal Defect, Rh IC - Rh Incompatibility, LBW - Low Birth Weight, VSD - Ventricular Septal Defect, CTD - Connective Tissue Disorder, ARDS - Acute Respiratory Distress Syndrome, Hb - Hemoglobin, PCV - Packed Cell Volume, PL - Platelet Count, IV - Intravenous, Blood C/S - Blood Culture Sensitivity.
ETIOLOGICAL FACTOR

Pictures shows gangrene of right hand and forearm
Pictures shows gangrene of left heel and foot
Discussion:-
The causes of thrombosis in the neonatal period is often uncertain but some key factors bear special mention, it is mainly sick children who are affected. In one early series 80% of cases were associated with infection. Embolic source from heart secondary to fibrillation and anomalous valves.

Some maternal factors are important. Both venous thrombosis and peripheral gangrene have been reported in the infant of diabetic mothers, venous emboli may pass through the foramen ovale to enter the arterial circulation. Thrombus formation in the placental vein is unusual in a normal pregnancy, but occurs quite often in maternal hypertension. Chorionic thrombi may embolise to fetal vessels and have been linked to the presence of pulmonary and portal venous emboli. In cases of initial twin pregnancy with subsequent fetus papyraceous of one, fragments of
thromboplastic material may pass through vascular shunts to the circulation of the live fetus to present as local ischemic damage due to thrombosis. It is estimated that 32% of pregnancies which are twin at 10 weeks lead to single deliveries. Thrombi may also form within patent duct us, particularly when there is an aneurysmal dilatation and resulting emboli can cause peripheral vessel occlusion.

**Abnormalities of the vessel wall:**
If during birth a limb is trapped between the fetal head and the maternal pelvis, damage to the intima of a major vessels sufficient to precipitate thrombosis may occur. Birth trauma may explain some cases of limb ischemia but thrombosis has also been after caesarean section in association for example with amniotic constrition bands and entrapment by the umbilical cord.

External pressure on the vessel wall due to compartment syndrome has been reported to causes vessel obstruction and digital ischemia fasciotomy was beneficial. Even drugs extravagated into the subcutaneous tissues during emergency neonatal reconstruction can obstruct the venous return of an upper limb, and removal of the offending material by aspiration using blunt cannulae can restore the circulation.

**Flow:**
Hyper viscosity of the blood is reported in 1-5% of neonates. In newborn a venous packed cell volume greater than 65 is considered to be indicative of hyper viscosity. A small rise in packed cell volume above 70 result in a considerable increase in blood viscosity.

Delayed cord clamping can increase packed cell volume by permitting extra placental blood to be transferred to the infant. Hyper viscosity is also related to the deformability and agreeability of the red blood cells those of a newborn infant are larger and less deformable than in older children and are associated with increased platelet adhesion. Increased blood viscosity is noted in the infant of smokers and diabetic mothers where sluggish maternal circulation may cause compensatory polycythemia in the fetal blood. Small for dates babies are also prone to polycythemia and in them this may be a response to chronic hypoxia as a result of placental insufficiency.

**Coagulation:**
It is currently thought that damage to the vessel wall and disturbances of the flow are more directly implicated in neonatal thrombosis than the peculiarities of neonatal hemostasis and fibrinolysis. In a healthy infant both the coagulation and fibrinolysis systems are immature but in balance. Inherited deficiencies of antithrombin 3 and protein c have been reported in neonates and were associated with fatal thrombosis.

**Treatment:**
**Heparin:**
The newborn infant appears to require a proportionally larger amount of heparin than an adult to achieve an adequate therapeutic effect and as the half life is short, continuous infusion is the best method of treatment. A 100 units/kg bolus followed by 20 units/kg/hour has been shown to resolve femoral artery thrombosis after cardiac catheterization in 43% to 80% of cases.

**Thrombolysis:**
Thrombolytic treatment has been shown to be effective and safe in a pediatric population. Thrombolytic agents urokinase and rtPA are widely used to activate plasminogen which is converted to photolytic enzyme plasmin, capable of dissolving fibrin clots. Administered systemically these drugs can treat both arterial and venous thrombosis but there is a risk of haemorrhage especially in preterm babies who already have a high risk of intracranial haemorrhage. Clots less than five days old are more susceptible to thrombolysis. Local administration at the site of blockage using a catheter permit lower doses and reduce the systemic complications.

**Surgery:**
Thrombectomy in very young infants is prone to re thrombosis but inspite of this, useful limb salvage is often achieved. The passage of a Fogarty catheter down a small vessel may fissure the intima and even mobilizing a vessel has been reported to cause thrombosis in this age group. Flannigan et al noted that very small 2 or 3 French Fogarty catheters could not enter the femoral arteries of a neonate. Clots can be removed by aspiration using a small plastic catheter with a blunt end length.
Conclusions:-
Peripheral limb ischemia and gangrene in neonates is a rare and unexplored entity in the vascular surgeons practice. Preterm and low birth weight with malformation babies with sepsis, and maternal risk factors like diabetes and birth trauma and repeated vein cannulations and drug extravasation are plays a major role in development of neonatal limb gangrene. Proper screening by sonologist, gynecologist, neonatologist and cardiologist and early referral can reduce the incidence. Symptomatic treatment and anticoagulation remains the main stay of therapy, surgical thrombectomy and thrombolysis are alternative treatment.

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