Maternal Serum Interleukin-6 as A Predictor of Preterm Labor

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By

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The interluikin-6 shows mild elevation in all non-infected preterm labors with 13.35 as a cut off point, and shows also higher elevation in infected preterm labor with 50.5 as cut off point, so it can be used as an excellent predictor of infection induced preterm labor.

Recommedations

From the practical point of view, the use of interleukin-6 as a predictor of preterm labor for each case is costly effectiveand the examiner shold collect 96 cases to start using the kit, as the kit available to measure the IL-6 in 96 cases collectively for onley one use as u cannot open the kit to examine only one case and this is not practicle.

Introduction

Preterm labor remains a major unresolved problem in perinatal medicine. It's strongly related to increased perinatal mortality and morbidity ***(Hagberg, 2001)***.

Preterm labor is sometimes due to obstetric conditions such as sever intrauterine growth retardation, pre-eclampsia, multiple pregnancies or to the presence of fetal malformations.

Preterm labor may occur spontaneously either with intact membranes or following preterm prelabor rupture of membranes ***(Gomez et al., 2005)*.**

Alarge subset of cases of preterm labor and premature rupture of the membranes is believed to be secondary to intrauterine infection ***(Minkoff et al., 1983).*** The infection organisms are thought to originate in the vagina, ascend through the cervix, and infected decidua, fetal membranes, placenta and fetus. The organisms associated with preterm labor and premature rupture of membranes include the pathogenic bacteria *Neisseria gonorrhea, and Chlamydia trachomatis*, as well as the organisms associated with bacterial vaginosis, and even normal flora. Bacterial vaginosis is a condition marked by a relative overgrowth of vaginal anaerobes as *gardenerella vaginalis* and an abnormally low concentration of lactobacilli.

Bacterial vaginosis is associated with a 4 fold increase in the risk of preterm labor ***(Gravett et al., 1986)*** and 3 fold increased risk of premature rupture of membrane ***(Manikoff et al., 1984).***

One hypothesis regarding the pathogenesis of bacterial vaginosis is that bacterial vaginosis causes the release of prostaglandins, agents known to be involved in the mechanisms of both term and preterm labor. Phospholipase A2 and phospholipase C, two enzymes that catalyze the release of arachidonic acid, the initial step in prostaglandin production, have been found to be elevated in the lower genital tract of patients with bacterial vaginosis ***(McGregor et al, 1991).***

Investigations have determined that up to 26% of patients with preterm labor and intact amniotic membranes have a subclinical intra amniotic infection ***(Lencki et al., 1994).***

The frequency of preterm labor which is 8%-10% has not changed over the last 30 years despite the use of tocolytic drugs ***(Lettieri et al., 1993)***

Some diagnostic tools have been developed such as transvaginal ultrasound or fetal fibronectin in cervical secretions in order to find a marker to predict preterm labor ***(Goldenberg et al., 1998)***.

The cytokines are important immune-cell mediators that control inflammations and the host response to infection.

Numerous studies have detected the inflammatory cytokines:

1. Interleukin-1α.
2. Interleukin-1β.
3. Interleukin-6.
4. Tumor necrosis factor-α.

In the amniotic fluid of women in preterm labor, and these cytokines are thought to be part of the maternal or fetal immune response to intrauterine infections ***(Greig et al., 1993).*** Several authors have suggested that the presence of cytokines in the lower genital tract may predict preterm labor ***(Lockwood et al., 1994)***.

The production of prostaglandins are increased by cytokines such as interleukin-6 leading to cervical ripening and uterine contractions ***(Mitcheli et al., 1990)***.

Interleukin-6 is a pro-inflammatory cytokine that can be induced by other cytokines such as interleukin-1 or tumor necrosis factor and in response to bacterial products such as lipopolysaccharides in the presence of an infection ***(Furtunato, et al., 1996).***

Several studies have shown a positive correlation between interleukin-6 in amniotic fluid ***(El-bastawissi et al., 2000)*** and cervical fluid ***(Jun et al., 2000)*** and subsequent preterm labor**.**

Interleukins may act to set the delivery process in motion by promoting the synthesis of prostaglandins and archidonic acid by the myometrial and decidual cells which give rise to uterine contractions ***(Rath et al., 1998).***

Chapter 1

Preterm labor

Preterm labor is the most common cause of perinatal mortality and morbidity in the developing countries and the single most important complication of pregnancy in the absence of congenital abnormalities. This complication continues to be a major health care problem throughout the world ***(Arias et al., 1996).***

In 1935, the American collage of pediatrics defined prematurity as a live-born infant weighting 2500 grams or less ***(Cone et al., 1985).*** These criteria were used widely until it became apparent that there were discrepancies between gestational age and birth-weight because of restricted fetal growth. The world health organization in 1961 added gestational age as a criteria for premature infants, defined as those born at 37 weeks or less. A distinction was made between low birth weight (2500 grams or less) and prematurity (37 weeks or less than 259 days since the first day of the last menstrual period).

Others have suggested that preterm birth be defined as those infants delivered prior to the completion of 37 weeks ***(American Collage of Obstetricians and Gynecologist et al., 1995).***

Gestational age at birth, together with birth weight, is recognized as a reference standard related to the outcome and prognosis of the preterm infant ***(Moutquin et al., 2003).***

Incidence:

Preterm birth results from three clinical conditions; medically indicated preterm birth (8.7%-35.2%), preterm premature rupture of membranes (PPROM) (7.1 %-51.2%) and spontaneous (idiopathic) preterm birth (23.2%-64.1%) ***(Moutqain et al., 2003).***

Villar et al., 1994 has estimated that approximately 13 million infants are born preterm each year worldwide. In several countries, the incidence of preterm birth has been reported to be between 5% and 10% of all births, and this rate has been stable over the past two decades but varies between different populations ***(Lumley, 1993).***

Preterm birth and perinatal mortality:

Perinatal mortality compromises neonatal mortality (death of any live borne in the first 28 days after birth), plus death in the last trimester (still birth). It was found that no infants less than 22 weeks gestation survived, but survival rates increased sharply to about 77% at 28 weeks, 96% at 32 weeks, and > 99% at 36 weeks.

Gestational age -specific neonatal mortality rates for 3386 live-born infants between 1982 and 1986, decreased from 100% at 23 weeks to about 10% at 29 weeks, with little additional improvement through 34 weeks. Also the probability of neonatal death before 26 weeks exceeds 75 % ***(Copper et al., 1995).***

The chance of survival increase appreciably at or above 1000 grams birth weight ***(Fanltroff et al., 1995).*** It is also reported that survival is possible for infants weighting 500-750 grams. Many of these extremely low birth weight infants; however were growth restricted and therefore of more advanced maturity. For example: survival of a 380 grams infant has been reported, but the gestational age was confirmed to be 25 weeks. Clearly, expectations for neonatal survival are primarily influenced by gestational age and maturity rather than bil1h weight alone ***(Ginsberg et al., 1990).***

The major danger of the preterm infant are due to organ immaturity. Their incidence and severity are inversely related to gestational age (***Robertson et al., 1992).***

Whyte et al., 1993 followed for a minimum of 2 years 321 infants borne at their hospital between 23 and 26 weeks. There were no survivors among infants delivered at 23 weeks, and only 6% of the survivors at 24 weeks did not sustain major

long-term morbidity. Approximately half of infants delivered at 25 and 26 weeks were intact at a minimum of 2 years of age.

Preterm birth and perinatal morbidity:

I- Respiratory Distress Syndrome (RDS)

The major and most frequent cause of morbidity in preterm neonates is hyaline membrane disease (HMD), caused by lack of surfactant formation in distal bronchioles and alveoli**.** They also found that the incidence of HMD at 34 weeks to be (14.9%), the incidence of HMD was very low between 35 and 36 weeks of gestation ***(Robertson et al., 1992).***

Antepartum fetal asphyxia account for at least 34% of the fetal asphyxia in the pregnancies that were delivered preterm. The 50 % incidence of moderate to sever asphyxia in the antepartum preterm pregnancy compares with 15 % in term pregnancies. Moderate to sever asphyxia occurred with equal frequency with early and delayed intervention. So, fetal asphyxia in pregnancies those were delivered preterm is present frequently before onset of labor and this increased frequency implies a great likelyhood of long term morbidity or death (***Robertson et al., 1992).*** Abnormal fetal assessment tests are valuable predictors of antepartum fetal asphyxia.

The important preventive therapy is the administration of exogenous surfactant and antenatal corticostcroids which are responsible for much decrease of hyaline membrane disease as a cause of neonatal death, and were used as prophylaxis of preterm infants at risk of RDS ***(Long et al., 1995).***

II- Necrotizing Enterocolitis (NEC):

This condition has now become recognized as an important cause of serious illness and death in infants requiring intensive care. Most affected babies are preterm and it seems probable that ischemia of the bowel wall is the underlying pathology with asphyxia and catheterization of the umbilical vessels as predisposing factors ***(Neligan et al., 1979).***

III- Intra-ventricular hemorrhage (IVH):

The incidence of ventricular hemorrhage depends on gestational age at birth. The incidence increased in preterm babies, about 50 % of neonates born before 34 weeks will have some evidence of some hemorahage, while this incidence decreases to 4% at term. Low birth weight infants have the earliest onset of hemorrhage and greatest likelihood of progression into the parenchymal tissue thus highest mortatity rate. Most hemorrhages develop within 72 hours of birth but they may be observed as late is 24 days ***(Perloman and Volpe .,***