The Iowa Perinatal Letter

Obstetric Perinatal Mortality Review

From January 2002 through June 2003, the obstetric half of the perinatal team collected information on stillbirths (fetal deaths) and neonatal deaths at the time of hospital visitations across the state. All levels of care were represented. The purpose of this communication is to review the causes of fetal/neonatal death identified and to comment on cases which were potentially preventable or which reflected suboptimal care. It must be emphasized that the reviewers had the benefit of hindsight, brought their individual attitudes as to what constitutes appropriate care, and do not know with certainty that, if care had been modified, the outcome would have been any different. Nevertheless, large numbers of deaths were reviewed and some assessment can be made as to areas of potential preventability and to areas of obstetric care which can be improved.

Three hundred forty-four perinatal deaths were studied. Two-thirds of these were fetal deaths and one-third neonatal deaths. Singleton pregnancies represented 84 percent of the deaths with products of multiple gestation accounting for 16 percent. Since products of multiple gestation constitute approximately 3 percent of Iowa live births, one can see the disproportionate risk of perinatal loss associated with multiples.

Multiple Gestation

Fifty-six deaths occurred in multiple gestation pregnancies. The significance of early preterm delivery is highlighted by the fact that 63 percent of the mortality occurred under 24 weeks' gestation. Early preterm labor and functional cervical incompetence are the most significant problems in multiple gestation pregnancies.

Fourteen, or one-quarter, of the deaths occurred in the third trimester. Twin-twin transfusion, cord accidents including those in monoamniotic twins, intrauterine growth restriction and congenital malformations were represented.

Singleton Pregnancies

There were 288 perinatal deaths in singleton pregnancies, 210 of these represented fetal deaths, and 78 were neonatal deaths.

Fetal deaths

Of the 210 fetal deaths reviewed, 22 percent occurred at less than 24 weeks' gestation. Some of these occurred prior to labor and others as a result of the stress of the preterm labor. The most common cause of fetal death at or after 24 weeks' gestation was "unknown". This unknown category comprised 41 percent of the 164 deaths. Many deaths wound up in the unknown category, because no evaluation of the stillbirth was undertaken. Others remained without explanation despite extension evaluation. A protocol for the evaluation of fetal deaths was published in *The Iowa Perinatal Letter*, volume XXIII, #2, April/May/June 2002. Cord or placental factors were implicated in 22 percent of the deaths at or after 24 weeks' gestation, intrauterine growth restriction in 12 percent, congenital malformations in 11 percent, and an "other" category in 14 percent.

The "other" category included non-immune hydrops, diabetes, fetomaternal hemorrhage, and preeclampsia.

Neonatal deaths

Seventy-eight neonatal deaths occurred in singleton pregnancies. More than one-third of these were delivered at less than 24 weeks' gestation. Thirty-six of the neonatal deaths occurred in pregnancies which ended in the third trimester. Twenty neonates were anomalous and 10 newborns suffered from fetal distress/birth asphyxia (non-immune hydrops, placental abruption, maternal death, and diabetes were represented).

Suboptimal Care

The physician and nurse reviewer identified suboptimal care in 8.4% of the 344 perinatal deaths reviewed. Eight instances of "preventability" were ascribed to the patient. No prenatal care and drug abuse were common. There were 21 cases in which suboptimal care was ascribed to the physician or nurse. These will now be considered.

Poorly controlled diabetes – N=4

The hallmark of managing diabetes in pregnancy is good blood glucose control. It is desirable to have fasting sugars less than 95, two-hour postprandial sugars less than 120, and one-hour postprandial sugars less than 140. This is true for both gestational and pre-gestational diabetics. If a woman with diabetes requires more than diet for blood sugar control, tests of fetal well-being should be employed in late pregnancy. Even if this testing is normal, and the blood sugar control is good, these patients should probably be delivered prior to their due dates. Two of these four deaths occurred after the EDD. Poor

blood sugar control and/or abnormal fetal well-being testing would indicate an earlier delivery.

No cervical surveillance in twins – N=4

Women with multiple gestation pregnancies are at risk for delivery in mid-gestation. Our recommended practice in this situation is to follow the cervix with transvaginal determinations of cervical length biweekly from 16-24 weeks' gestation. If cervical shortening is identified (lengths less than 20-25 mm), intervention is called for. Activity restriction, tocolytic therapy, cervical cerclage, or transfer to a perinatal center might be considered depending on individual circumstances.

Inappropriate reaction to non-reactive non-stress test at term – N=4

As stressed in *The Iowa Perinatal Letter*, volume XXIV, #4 – October/November/December 2003, a non-reactive non-stress test at term, not explained by congenital malformation or maternal medication, generally means that delivery should be effected. The urgency of delivery is determined in part by other features of the tracing (baseline variability, presence of decelerations). If the tracing is worrisome, move quickly.

Slow response to fetal distress in labor – N=3

Physicians and nurses both should be able to identify distress patterns on the monitor and to respond appropriately.

Recording maternal, not fetal heart rate – N=2

It is important for nurses, when providing care in the labor room, to be certain that indeed it is the fetal heart rate that is being represented on the monitor. In these two

cases, the monitor looked "fine", but very depressed babies were delivered. In retrospect, the fetal heart rate was not what was being recorded.

Failure to identify intrauterine growth restriction – N=2

Conscientiously determine fundal heights at each visit. In the woman of normal size, if fundal heights do not seem appropriate, order an ultrasound to try to identify growth restriction. In the obese patient fundal heights are of limited value. In the obese patient with significant hypertension, get an ultrasound for growth to be certain that growth restriction is not missed.

Failure to deliver the woman with pre-eclampsia at term –N=1

Although patients with gestational hypertension at term can be treated expectantly with close follow-up, patients with genuine pre-eclampsia at term generally should be delivered.

Doptone response to decreased fetal movement –N=1

If a woman complains of decreased fetal movement from the time when the fetus is potentially viable, (23-24 weeks' gestation), the response to the complaint should be to order a non-stress test. Doptone evaluation can identify that the fetus is alive, but not necessarily that the fetus is healthy.

Conclusion

Periodically, obstetric perinatal mortality reviews have been reported in *The Iowa Perinatal Letter* for the past quarter century. Over the years clear improvements in obstetric care have been noted. As indicated in the preceding paragraphs, however, we can and should do better.

 - Frank J. Zlatnik, M.D.-Kathryn R. Papke, R.N.

Neonatal Polycythemia/Hyperviscosity Syndrome

Neonatal polycythemia is a significant potential source of morbidity and an issue confronting every clinician providing newborn care. Historical descriptions of plethoric infants abound, heralding back to biblical times with the description of what some suspect detail Isaac and Rebekah's monochorionic twin pregnancy with "red" Esau born followed by Jacob who arrives holding onto his brother's heel. Case reports and publications surfaced in the 1950s describing infants with convulsions, cyanosis, respiratory distress, and cardiovascular strain associated with plethora and high hematocrits. Most of these infants were treated with observation and supportive care while some underwent therapeutic phlebotomy. The medical management of polycythemic infants with subsequent trials of intervention created the foundation for our current evidence-based practice. The purpose of this brief article is to review neonatal polycythemia with respect to the physiologic basis and risk factors, symptoms and diagnostic criteria, potential morbidities, and finally, treatment.

The definition of neonatal polycythemia often seems elusive as it may include infants with and without symptoms having hematocrits ranging from 60 percent to greater than 70 percent. The reported incidence of polycythemia ranges from 0.4 to 12 percent in newborns, making it a likely candidate in every newborn nursery. Considering the potential sequelae of polycythemia, which include pulmonary hypertension, congestive heart failure, hypoxemia, myocardial strain, thromboses, gangrene, and stroke – it should not be overlooked.

Fetal red blood cells (RBC) have a larger mean cell volume and are less deformable than more mature cells, leading to increased viscosity. The relatively

hypoxic in utero environment induces RBC production leading to an increased RBC mass at birth and thus a relatively polycythemic state. It is the combination of these two scenarios that led to the descriptive term of polycythemia/hyperviscosity syndrome. It is the effects of the hyperviscosity that can ultimately be most devastating.

The initial research done in neonatal polycythemia utilized a viscometer to measure how easily blood could flow. These studies displayed a fairly linear relationship between viscosity and RBC mass with hematocrits less than 60-65 percent. Once the hematocrit exceeded 60-65 percent, viscosity increased exponentially. Thus, the only marker in current use today (hematocrit) may under-represent the degree of hyperviscosity for many polycythemic infants. Interestingly, the initial studies also identified a significant correlation between an umbilical cord hematocrit above 56 percent and an infant hematocrit greater than 70 percent at two hours of age.

As laboratory equipment such as centrifuges became readily available in the office and nursery setting, spun hematocrits replaced determination of viscosity for diagnosis of polycythemia and thus, by inference, of hyperviscosity. Newer technology has now replaced the spun hematocrit in many nurseries, providing an automated determination of hematocrit by calculating the mean RBC volume and hemoglobin. This current method provides lower values for hematocrit when compared to the centrifugation method and thus may under-represent the frequency of clinically important polycythemia.

Polycythemia may occur in a number of clinical scenarios. Infants of diabetic mothers or those who experienced placental insufficiency in utero (i.e., preeclampsia, maternal smoking, maternal heart disease or maternal use of propranolol, SGA/LGA

infants) may be polycythemic at birth in response to chronic hypoxia. The incidence of polycythemia ranges from 22-29 percent in infants of poorly controlled diabetic mothers. Twin-twin transfusion and genetic syndromes (such as the trisomies 13, 18, and 21 and Beckwith-Wiedemann) as well as neonatal thyrotoxicosis, congenital adrenal hyperplasia, and hypothyroidism are also associated with neonatal polycythemia. Certainly, no specific underlying cause or predisposition can be identified in many cases.

Part of the postnatal adjustment following delivery involves shifts in intra- and extracellular fluid leading to a peak in the hematocrit between two and six hours of age. It is always appropriate to obtain a capillary hematocrit in the ruddy, high-risk, or symptomatic infant to screen for neonatal polycythemia. This method may overestimate the central hematocrit by 5-15 percent as sludging or sampling from a suboptimally perfused extremity may yield falsely elevated values. Thus, a capillary hematocrit value above 65 percent warrants repeating by venipuncture. If the venous sample has a value between 65-70 percent, the clinician must decide on further intervention based on the presence or absence of associated symptoms; treating if symptoms exist. Symptoms of polycythemia include respiratory distress, tachypnea, hypoglycemia, tremulousness, lethargy, irritability, apnea, seizures, jitteriness, poor feeding, weak suck, and cyanosis.

Clinical studies and observations have provided us with guidelines for the treatment of infants with neonatal polycythemia. The symptomatic infant with a venous hematocrit greater than 65 percent or arterial value greater than 63 percent warrants intervention. (Some suggest that the symptomatic infant with a venous hematocrit greater than 60 percent likewise warrants intervention – this must be decided on a case-by-case basis.) The asymptomatic infant with a venous hematocrit value of 70 percent or

greater needs intervention. Thus, serum glucose, blood gas, pulse oximetry, serum platelet count, and calcium should be obtained to screen for hypoglycemia, hypoventilation or hypoxemia, thrombocytopenia, and hypocalcemia, all of which can be associated with polycythemia, and these conditions must be addressed if present. If the infant is between the age of 24-48 hours and dehydration is suspected, serum sodium, blood urea nitrogen, and urine specific gravity may aid in the diagnosis. Serum bilirubin should also be monitored closely as polycythemic infants are likely to have increased turnover of red blood cells leading to increased production and accumulation of bilirubin.

If the venous hematocrit is less than 65 percent in an asymptomatic infant who is already six hours old, no further evaluation is needed. A repeat venous hematocrit should be obtained in infants of less than six hours to avoid false reassurance prior to the time of peak hematocrit values. If dehydration is diagnosed in the first few days of life, a trial of rehydration may be attempted for 6-8 hours. The hematocrit should be followed during this period and assessed every 4-6 hours. If the venous hematocrit is 65-70 percent in the asymptomatic infant, observation and serial assessment of the hematocrit with adequate hydration is appropriate.

For the infant with symptoms consistent with polycythemia or with a central hematocrit greater than 70 percent, a partial exchange transfusion is indicated. Historically, many fluids have been used in the partial exchange, including normal saline, 5 percent albumin, and fresh frozen plasma. Because the use of blood products has not been demonstrated to offer significant benefit and because there is risk of infection from a donated human product, we use normal saline for the partial exchange transfusion. The

amount of blood to exchange for normal saline is calculated to each a final central

hematocrit of 50-55 percent, using an estimated blood volume of 80 cc/kg.

$$\text{Vol exchanged (mL)} = \frac{[\text{Weight (kg) x blood vol}] \times [\text{Hct of patient} - \text{desired Hct}]}{\text{Hct of patient}}$$

Thus, a 4 kg infant with a central hematocrit of 70 percent would need 69-90 cc of

saline exchanged for removed blood to achieve a post-procedure central hematocrit of 50-

55 percent. We recommend drawing a hematocrit form the umbilical catheter prior to the

exchange and basing calculations on this value if it is significantly different from the

peripheral venous sample. We typically withdraw blood slowly from a low-lying

umbilical venous catheter (inserted to 4 cm or where good blood return is first obtained)

and simultaneously infuse normal saline through a 24 or 22 gauge peripheral IV. We

discourage the "push-pull" technique of withdrawing aliquots of blood and then infusing

through the same umbilical catheter, as this has been associated with an increased

incidence of post-procedure necrotizing enterocolitis. We provide maintenance hydration

needs with an intravenous dextrose solution and delay feeding for 4-6 hours after the

exchange to allow normalization of gastrointestinal blood flow.

The partial exchange transfusion, though potentially lifesaving, is not without risk

and requires intensive monitoring during and following the procedure. Laboratory

studies such as calcium, glucose, hematocrit, and platelet count would be obtained before

and after the exchange. If the infant displays symptoms suggestive of sepsis, coverage

with ampicillin and gentamicin is warranted. Post-procedure antibiotic prophylaxis is

controversial as infection is uncommon, however, it is the most frequent complication of

the procedure. Other complications include necrotizing enterocolitis, coagulopathies (from thrombocytopenia or diminished coagulation factors), hypoglycemia, and hypocalcemia. In settings where support personnel may be less familiar with the procedure and necessary monitoring, it is important to consider the initiation of adequate intravenous hydration and to arrange transport of the infant to a center with neonatologists and the nursing support required for medical intervention.

In summary, high-risk and symptomatic infants should be screened for polycythemia. If neonatal polycythemia is confirmed on venous sampling, treatment must be initiated or transport arranged to a treating facility.

-Nicole Schmidt, M.D.

Neonatologist in Private Practice

Portland, Oregon