Kofinas Perinatal

Providing Care to the Unborn ®

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Low PAPP-A and small placenta size are risk factors for severe adverse pregnancy outcomes.

PAPP-A is short for pregnancy associated plasma protein A. It is a protein produced by the placenta during pregnancy very much the same way beta-human chorionic gonadotropin (beta-hCG). In recent years, PAPP-A was studied during the first trimester and was found to be low in pregnancies that subsequently delivered babies with Down syndrome and other chromosomal defects. Ever since, it has been incorporated in the nuchal translucency (NT) testing done in the first trimester of pregnancy for the detection of Down syndrome. When PAPP-A is low, the risk for Down syndrome is increased and when it is elevated, the risk is reduced. The use of PAPP-A along with beta-hCG, nuchal translucency and nasal bone measurements in combination can detect 95% of all fetuses with Down syndrome.

After a few years of use as a screening tool for chromosomal defects, it became apparent that pregnancies complicated by low PAPP-A but with chromosomally normal fetuses were at increased risk for adverse fetal and neonatal outcomes. Specifically, several studies have recently confirmed the increased risk of pregnancies with chromosomally normal babies but abnormally low PAPP-A. The normal value is 1 MOM or higher and the pathologic level is defined as a PAPP-A of <0.5 MOM. According to many recent retrospective and prospective studies, the followings risks are more likely to happen to pregnancies with low PAPP-A:

1. Miscarriage
2. Fetal demise (death) in utero
3. Intrauterine growth retardation (IUGR)
4. Preterm birth
5. Premature labor
6. Neonatal death
7. Cerebral palsy

All of the above are placenta failure related complications. We know that PAPP-A is produced by the chorionic villi of the fetus. Chorionic villi are the finger like projections of the fetal placenta into the intervillous space that contains the maternal blood. These chorionic villi contain specialized cells that regulate placental function and the production of many hormones essential for a healthy pregnancy. If they produce decreased amounts of PAPP-A then they are more likely to malfunction in other ways also and be associated with placenta malfunction and failure. Placenta failure is the cause of all of the above mentioned complications. So far, the studies that have been published only looked at the bad outcomes in relation to the blood test but never looked at the actual placental development. Recently, there was a study with 90 subjects that followed patients with a very low PAPP-A (<0.3 MOM) prospectively throughout pregnancy. The investigators noted that the outcomes were really poor. It is sad though that they observed babies die from severe placenta failure and prematurity and there was nothing they could have done. The main reason for this is the fact that most, if not all, obstetricians believe that there is

nothing one can do to help the placenta improve and prevent the poor outcomes. In this study the outcomes were really troublesome to put it politely. Below are the statistics:

1. 46% of women had premature babies; more than half of them were extremely premature. Extreme prematurity is prior to 32 weeks at which time many of the neonates suffer severe long term physical and developmental disabilities.
2. 22% of the babies suffered severe growth retardation (IUGR)
3. 15 babies (17%) died in utero and 3% more immediately after birth for a total death rate of 20%.

These outcomes are 10 to 20 times worse than the general population. Even high-risk pregnancies do not experience such severe rates of fetal demise and prematurity. This is very surprising to me because in similar patients we have not experienced any losses in the last 10 years. We have cared for more than 300 such patients at Kofinas Perinatal. According to the above statistics we should have lost approximately 60 babies. This would be a real tragedy. We have lost none of the babies we cared for. We have experienced a loss at 13 weeks on one patient who came to us for a second opinion after an abnormal genetic screen testing. Unfortunately, when she presented to us the placenta was so damaged that we could not do anything about it. Because we pay attention to placental development from the early stages of the pregnancy, most of the patients that we diagnose with low PAPP-A, we do so after we have already diagnosed the placental problems and started the treatment. However, even if we saw a patient after 12 weeks, we could still save the vast majority of the babies by treating them for the underlying coagulation disorder. All of these patients suffer from undiagnosed thrombophilic disorders and if treated properly can have a healthy pregnancy. It is sad that most obstetricians and perinatologists still believe that there is nothing one can do about helping the placenta heal and improve. Unless we all understand that, thousands of babies will be wasted every year here and abroad. However, let us not forget that for every baby that dies in utero, there are at least 5 more babies that suffer almost terminal insults but for some reason they survived. These babies are not the babies God meant them to be. They will suffer life-long consequences for no good reason other than pure ignorance on the part of their health care providers. It is time that we change that. Patients have the authority and the power to do so by learning to demand more from their obstetricians. If something does not make sense to you it is usually wrong. Do not accept any advice that does not make sense to you or for which you are denied an explanation. Demand explanations from your doctor for any recommendations, and if you do not get them, then get a new doctor. It is that simple. You have the absolute control and if you do not exercise this control, shame on you!

For practical purposes, if you are told that you have a low PAPP-A that increases your baby' s risk for Down syndrome and your baby turns out to be fine after the CVS, then you should ask your doctor to screen you for thrombophilia and treat you accordingly. Even in the absence of positive thrombophilia testing, with a 20% risk for fetal and neonatal death, treatment with anticoagulants is well justified even in the absence of clinical trials. It will take at least 15-20 years before "appropriate" studies are conducted to standardize such a treatment. At Kofinas Perinatal we cannot wait for such treatments. We develop them and use them while we save countless lives.