

Kofinas Perinatal

Providing Care to the Unborn ®

Alexander D. Kofinas, MD

Director, Kofinas Perinatal

Associate Professor, Clinical Obstetrics and Gynecology

Cornell University, College of Medicine

Protocol for the management of pregnancies conceived by ART

Introduction:

Infertility affects 10% of couples. Although there are many causes for infertility, the vast majority relate to maternal problems regarding ovulation and implantation. As many as 50% of infertile couples do not suffer from inability to conceive but after conception, the embryo fails to implant due to maternal problems. These problems are usually vascular in nature and relate to the quality of the endometrial vasculature that is instrumental for the placental formation. The most common condition that affects the quality of placental vasculature formation is thrombophilia. Thrombophilia is both genetic and autoimmune in origin. Approximately 98% of patients with very early pregnancy loss and infertility suffer from one or both types of thrombophilia and with proper treatment achieve successful pregnancies. However, infertility and recurrent pregnancy loss is one of the manifestations of such patients. Even after successful early pregnancy, patients who suffer from thrombophilia and conceived with ART are subject to serious pregnancy complications because of deficient placental formation. These complications are a continuum of the infertility/ recurrent early pregnancy loss syndrome and they are manifest in the form of second trimester fetal demise, third trimester fetal demise, fetal growth failure (IUGR), preterm labor, preterm delivery from either preterm labor or incompetent cervix. The common denominator of the above complications is a poor placental formation due to disturbed coagulation mechanism (excessive clotting and/or hypofibrinolysis). Such disturbances interfere with the process of trophoblastic conversion of the uterine endometrial spiral arterioles. Poor conversion leads to a deficient placenta formation that then causes the above complications as well as many of the hypertensive disorders of pregnancy (PIH and HELLP syndrome). At Kofinas Perinatal, we have been treating such pregnancies since 1994 when our intramural

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research revealed increased incidence of adverse outcomes of such patients along with increased incidence of placental thrombosis. Most recently several studies from American and European institutions have confirmed our findings and demonstrated the increased risk for adverse perinatal outcomes in such patients. At Kofinas Perinatal, we were able to reduce the prematurity of such patients from as high as 30% to less than 5% by implementing the following protocol.

Management of ART pregnancies

All patients with ART pregnancies are seen for the first visit at 5-6 weeks for careful assessment of the early placental development and to R/O chorionic tissue degeneration/subchorionic clot formation. Next visit is in 7-12 days depending on the presence or absence of fetal heartbeat. Since most of these patients are already treated for thrombophilia, assessment of appropriate anti-Xa activity is documented. If levels are not therapeutic or if the placenta does not respond, the dosage and/or the frequency of injections is increased. Starting dosage is 40 mg SC qd and it may increase to as much as 60 mg BID if indicated. Any treatment adjustments are correlated with maternal anti-Xa levels as well as placental quality. Placental pathology in the presence of acceptable anti-Xa levels indicates reduced Lovenox **bioavailability** and the dosage is adjusted upwards until the placental condition is improved.

Subsequent visits are every two weeks. Wider intervals between follow up visits may be associated with extensive and irreparable placental damage.

The visits involve the following:

1. Placental assessment of major fetal and maternal placental vessels with color and PW Doppler.
2. Assessment of fetal chorionic villi and the intervillous space with high resolution high magnifying power grey scale imaging combined with high definition power color angio. (This imaging identifies evidence of fetal chorionic damage at the earliest possible stage and when it is still treatable).
3. Fetal anatomical and growth assessment.

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- a. Decline in fetal growth rate is treated with upward adjustment of the antithrombotic treatment as indicated.
4. Assessment of maternal uteroplacental arterial compliance with progressing gestational age.
5. Cervical assessment for evidence of shortening, inclusion cysts that may compromise cervical integrity, and for funneling.
6. Assessment of lower uterine segment for premature labor signs:
 - a. Contractility
 - b. Lower uterine segment ballooning

Any changes on the cervix and/or the lower uterine segment are treated with education, reduced activity and or complete bed rest. If cervical length continues to decline despite bed rest, treatment according to our preterm labor management protocol is instituted. Such management has for the most part eliminated the complications of such pregnancies with minimal episodes of IUGR, preterm delivery secondary to preterm labor, abruptio, and pre-eclampsia.