Excellent Prenatal Alloimmunization/HDFN Care Practices

The following constitutes a list of management, intervention and support practices which reflect the available peer-reviewed literature and expert opinion for the management of maternal red blood cell alloimmunization causing hemolytic disease of the fetus and newborn (HDFN). This list is meant to serve as a resource as patients are selecting a care provider, and as a criterion which members of the Allo Hope Foundation (AHF) use to recommend doctors among our patient base. Practices detailed herein reflect the most recent clinical practice guidelines for the management of alloimmunization in pregnancy.[1]

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Diagnosis and monitoring

- Offers paternal testing and cffDNA testing to avoid amniocentesis for fetal antigen determination if possible.
    - Facilitates cffDNA testing to patients with D, K, C, c, E and Duffy (Fya) antibodies when fetal antigen status is unknown. cffDNA NIPT testing is currently available in the U.S through BilliontoOne (Unity Screen) starting at 10wGA (100% sensitivity/specificity, 99.9% precision),[2,3] Natera (D only), Sanquin Laboratories in the Netherlands (can ship internationally), and through AU, UK, Canadian national laboratories.
    - Offers antigen phenotype (or genotype for RhD) testing for baby's father when possible
    - For fetal antigens not available for testing through cffDNA, offers serial maternal titers, and MCA doppler evaluations once a critical titer is noted. Amniocentesis after 15 weeks in patients with critical titers and unknown fetal antigen status may be indicated. In these cases, the placenta is avoided at time of amniocentesis to prevent further alloimmunization[4,5]
- Offers temporizing treatment options such as IVIG +/- plasmapheresis to patients with previous severely affected pregnancies (history of IUFD due to HDFN or fetal anemia <24w gestation) or extremely high titers (≥512 for D; ≥64 for K)[6,7]
- Checks antibody titers every 4 weeks until 24 weeks, then every 2 weeks thereafter or if titers are rising, until titers reach critical value[5,8]
- Weekly MCA Doppler scans for women with critical titers beginning at 16 weeks gestation or when titers become critical (critical titer is 4 for Kell, 16 for all other clinically significant antibodies; 4 IU/ml for anti-D in UK)[9]
- Receptive to starting MCA Doppler scans as early as 15 weeks for women with previously affected pregnancies or high titers or referral to a center with experience in doing so[10]
- MCA Doppler Peak Systolic Velocity (PSV) value in multiples of the median (MoM) nearing 1.5 results in prompt re-scan within 24-48hrs, followed by cordocentesis and IUT if levels remain or exceed 1.5 MoM[11]

- Avoids modifying clinical decision to conduct IUT if antenatal corticosteroids were administered in the last 48-72hrs due to its propensity to lower MCA MoM values[12,13]
- Institutes antenatal testing (non-stress test or biophysical profile) at least weekly from 32 weeks gestation until delivery in all alloimmunized pregnancies[14]

Intervention

Note that a clinician without extensive history in performing an IUT may still be an excellent provider for an alloimmunized patient and should remain highly recommended, given that they facilitate prompt referral to a more experienced center for IUTs should the need arise.

If the clinician does perform IUTs, such a clinician:

- Performs IUT within 24-48 hours after a MoM of 1.5 or higher after confirming anemia via cordocentesis, independent of the presence of hydrops[15]
- Has demonstrated competence in performing IUTs (previous research and Delphi expert consensus has indicated that initial competence is reached at 30-50 IUTs total and an average of 10 IUTs annually[16,17] or is supervised during procedure by an MFM who meets the aforementioned criteria for competence)
- Performs IUTs in an operating room or in a delivery room with immediate access to operating room (a joint decision with the patient)[18]
- Uses fetal paralytic medication during IUTs as indicated[18]
- Offers IV sedative to mother during IUTs[19]
- Does not bring starting hemoglobin/hematocrit up by more than three times the starting value during IUTs in patients < 24 weeks gestation.[19] In these cases, clinician repeats IUT in 48 – 72 hours to achieve normal fetal hematocrit
- Offers follow-up ultrasound the day after IUT[18,19]
- Once IUTs begin, they are continued at reasonable intervals with final IUT at approximately 35 weeks gestation[18,19]

Delivery and postpartum

- Delivers by 37 0/7-38 6/7 weeks in all alloimmunized pregnancies where the fetus is known to or may have antigen in question independent of antibody titer[7,20]
- Provides patients with a quick and accessible way to communicate with their care team during their pregnancy
- Has a method of ensuring appropriate follow-up care for newborn after birth; this may entail, for example, neonatal consultation, referral to pediatric hematology before discharge or sending printed instructions for the mother to deliver to their pediatrician

The Allo Hope Foundation provides this checklist as a resource to patients and as a transparent criterion by which AHF staff, board members and volunteers use to determine whether to recommend a clinician to a nearby patient. The Allo Hope Foundation and its staff, board members and volunteers are never incentivized financially or by any other means to recommend a clinician. AHF is not liable for any outcomes that result from the recommendation of a specific clinician.

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