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Fetal Intravenous Immunoglobulin Therapy in Rh Hemolytic Disease

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Introduction: Immunoglobulins inhibit Fc receptors and so destruction of fetal anti-D coated erythrocytes is inhibited. Postnatal intravenous immunoglobulins (IVIG) have been found to improve the neonatal outcome. Fetal IVIG in cord blood during intrauterine transfusion (IUT) may also improve perinatal outcome of anemic fetuses.
Materials & Methods: IVIG was administered at the time of intrauterine transfusion (IUT) in cord blood in the dosage of 1 gm/kg of estimated fetal weight. Fetal anaemia, the need for repeated intrauterine transfusion and postnatal transfusion were assessed by serial ultrasound and fetal blood parameters.
Results:
Evaluation of five cases: All the 5 cases had haemoglobin in the range of 5-6 gm% and 2 fetuses had hydropic changes. Intrauterine transfusion started at 22, 26, 28, 29 & 34 weeks in these cases. Pre IVIG, transfusions were given in 3 cases where transfusions had to be given biweekly to weekly, but after IVIG, only 3 cases needed fortnightly transfusion and 2 cases did not need further transfusion. .Post natal transfusion was required only in one neonate with haematocrit of 23. Haematocrit in other neonates was 41, 45, 46 & 47 and they did not require any transfusion.
Conclusion: Fetal IVIG (1gm/kg) in cord blood at time of IUT delays the need of further intrauterine transfusions and reduces the need of postnatal transfusions.

Pregnancy Outcome After Repeat Chorion Villus Sampling in 27 Cases

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Objectives: The true risk of chorionic villus sampling (CVS) is poorly defined. CVS may be unsuccessful and repeat procedure may be sometimes required. The objective of this study was to review the pregnancy outcome of 27 patients where repeat CVS was required.
Methods: A total number of 27 patients were recruited in our comprehensive database from 1997 to 2005, who needed a repeat CVS. In the second sitting the placental location was identified by ultrasound once again and depending on placental location either transabdominal or transcervical CVS were performed by the single same operator. The mother was given bed rest for 7 days and followed up with regular antenatal visit till term. The maternal demographic profile, probable causes of failure of CVS, abortion rate, preterm delivery and delivery outcome were analyzed.
Results: Out of 27 patients which included two sets of twin pregnancy, in 22 patients transabdominal CVS and in 5 patients transcervical CVS were done. In 20 (74%) cases the indication of repeat sampling was inadequate sample. In 3 (11.1%) cases there were ambiguous results including one twin pregnancy, in 1 (3.7%) case there was mosacism and in rest 3 (11.1%) cases the indication was culture failure. The indication of CVS was as follows: 11 cases of thalassemia major in previous baby, to rule out Down's syndrome in 9 cases, hemophilia in 3 cases, cystic fibrosis in previous baby in 2 cases and spinamuscular atrophy in 2 cases. The mean gestation age was (12.4 ± 0.8) weeks, and 91.6% of the procedures were

performed between 11 and 13 weeks. In 18 (66.6%) cases placenta was situated posterior, in 6 cases placenta was fundal and in 3 cases it was located anteriorly. In 20 (74%) cases 2 punctures were attempted in the first sitting to get adequate sample. In all 27 cases successful sampling was done in the second sitting after 1 week. Genetic report was available within 14 days time in all patients. Fetus was affected with thalassemia major in 2 cases, Down's syndrome in 1 case and hemophilia in 1 case. The incidence of threatened abortion was 22% (6/27), procedure related fetal loss was 11.1% (3/27), and preterm labor 11.1% (3/27). The procedure related fetal loss was 11.1% in repeat CVS group and 5.2% (11/210) in other group in the study, a significant difference of 5.9% (CI-3.7 - 12). Seventeen patients reached upto term, there was no still birth and there was no fetus having IUGR. Fifteen patients (55.5%) had normal delivery and 5 (18.5%) patients had LSCS. The average baby Weight was 2520gms ± 242 gms. There was no major complications or procedure related problems in the neonates.
Conclusion:- Repeat CVS at 1 week interval may be necessary even in experienced hands. Inadequate sample was the major indication for repeat CVS. Trans abdominal procedure with particularly posterior located placenta had more failure to get adequate sample. There is increase incidence of procedure related fetal loss in repeat CVS. No major procedure related maternal or neonatal complication was seen.

Detection of Fetomaternal Hemorrhage Following Chorionic Villus Sampling by Kleihauer Betke Test and Rise in Maternal Serum Alpha Feto Protein

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Background and Objectives: Prospective study was conducted to assess the incidence and volume of fetomaternal hemorrhage (FMH) occurring after CVS by Kleihauer Betke test (KBT) and rise in maternal serum alpha feto protein (MSAFP).
Methods: Total of 61 cases who required transabdominal CVS were recruited in the study. Blood samples were drawn before and after CVS. MSAFP was estimated using the ELISA technique. Fetal cells were counted using the acid elution technique of Kleihauer and Betke. Volume of FMH with both techniques was calculated using standard formulae.
Results: Of the 61 cases studied, 60 (98.36%) cases showed FMH by MSAFP while 61 (100%) showed FMH by KBT. The mean volume of the FMH detected by MSAFP was 0.1+0.1424 (range 0.00ml – 0.104ml) and by KBT was 0.58ml+0.637ml (range 0.001 – 0.348ml). Significant FMH up to 0.1 ml was found in 20 (32.8%) and 45 (60.6%) by MSAFP and KBT respectively.
Conclusion: Both MSAFP and KBT are sensitive methods to detect the incidence of FMH after CVS. Concordance between the two tests is poor, and KBT has been found to overestimate FMH. 50µgm of anti D is sufficient to cover the FMH occurring after CVS.

Outcome of Rh Isoimmunised Babies Who Received Intrauterine Transfusion: AIIMS Experience

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Objective: To evaluate the perinatal and neonatal outcome of Rh isoimmunised babies who received intrauterine transfusion (IUT).
Methods: *Design:* Retrospective evaluation of 18 babies who received red cell IUTs in the last one and half year period. *Setting:* Division of Neonatology, All India Institute of Medical Sciences. *Subjects:*

18 Rh isoimmunised babies who had fetal hydrops and/or evidence of severe hemolysis thus needing an IUT; 8 fetuses had received single IUT, while 10 had received multiple IUTs. 15 mothers had been given antenatal IVIG. *Duration:* January 2004 to June 2005. *Methods:* Maternal and neonatal records were reviewed and the following data obtained: number of IUTs, perinatal outcome, cord PCV & bilirubin, number of babies with hydrops, hyperbilirubinemia requiring phototherapy and/or exchange transfusion, anemia requiring partial exchange, respiratory distress needing ventilator support, and incidence of sepsis. The data was analyzed using Microsoft Excel 2002 & EpiInfo 2000.
Results: There was 1 still birth and 2 neonatal deaths (due to hydrops / pulmonary hypoplasia) and the rest 15 survived (83.3%). While 9 fetuses had evidence of hydrops, only 6 had hydrops at birth. Cord blood hematocrit was < 30% in 7, while bilirubin was > 4.5mg% in 2 babies. DCT was negative in 5 babies, while 9 babies were Rh negative at birth. Those who received multiple IUTs were more likely to be Rh –ve (9/10, P<0.05). 5 babies had severe anemia requiring partial exchange transfusion. All babies received IVIG. 14 (82.3%) and 12 (70.5%) babies required phototherapy and exchange transfusion respectively. While 5 babies had serum bilirubin > 15mg%, only one baby had > 20mg%; none of the babies had evidence of kernicterus. 6 babies (33.3%) had clinical sepsis while 9 (50%) babies had respiratory distress requiring ventilatory support. No significant association was found between the ICT titers, number of IUTs, gestation at first IUT and the outcome (deaths / hydrops / hyperbilirubinemia).
Conclusion: Severely Rh isoimmunised babies who received IUTs and IVIG have a good survival rate (>80%) with a lower incidence of significant hyperbilirubinemia requiring exchange transfusion.

Pregnancy Outcome in Balanced Translocation Our Experience

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Introduction: Recurrent Spontaneous abortion is one of the common cause of referral to Obstetrics & Genetics clinic. There are various causes of recurrent spontaneous abortion. Carrier of balanced translocation accounts to about 4-10% fertile couple with 3 or > consecutive first trimester abortion
Case Report: We present our experience in four cases of carrier of balanced translocation. Three mother were carrier of balanced translocation (Carrier of Robertsonian Translocation 45XX der t (13;14)(q10q10), Carrier of balanced translocation.Chr (1:3), Carrier of Balanced Translocation 46 XXt(6:19) (p25q12). A father was carrier of Robertsonian Translocation 46XY(13:14). All the couples presented with the history of recurrent spontaneous abortions in first trimester. Counselling was done for risk of having an unbalanced fetus and option of fetal karyotype by invasive sampling was given.Three couples opted for Amniocentesis and one Cordocentesis. Out of 4 fetuses two were normal two were carrier of balanced translocation. All babies were clinically normal at birth.
Discussion: Balanced Translocation is a structural chromosomal abnormality in which two different chromosomes break and exchange material with no apparent loss or gain of genetic material, and the carrier is phenotypically normal. Translocation account to about 6% of first trimester loss due to chromosomal abnormality. Incidence 1 in 1000 . Risk of carrier of balanced translocation having abnormal child is 5-10%
Half of structural abnormalities may be inherited from parent carrying balanced chromosomal translocation. Parental carriership is found in about 4-6% of couples with recurrent miscarriage. In a case of parental carriership of balanced structural chromosomal abnormality next pregnancy may result in a child with unbalanced structural chromosomal abnormality, multiple congenital malformation or mental handicap. So Prenatal Diagnosis therefore recommended.
Conclusion: In couples who are carrier of balanced translocation, structural chromosomal rearrangements, proper genetic counselling, family screening and prenatal diagnosis (Amniocentesis, Cordocentesis) should be offered.

Perinatal Outcome Following Antenatal Therapy for Fetal Primary Pleural Effusions

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Objective: To study the impact of foetal thoracoamniotic shunting (TAS) on the perinatal outcome of fetal primary pleural effusion.
Study design: Retrospective review of 59 fetuses undergoing TAS.
Results: 89 fetuses with pleural effusion were referred to our centre. The comprehensive work up was negative in 59/89 (62.5%) fetuses (primary pleural effusion). 30(33.7%) had antenatal pleural drainage as a first procedure. In 39/59 (66.1%) fetuses TAS was the first procedure. The shunt between the pleural effusions and the amniotic cavity consisted of a double pigtail silastic catheter (Rocket catheter, London, UK) inserted through a metal cannula with a trocar (external diameter of 3 mm and 15 cm long).The mean GA at TAS insertion was 27.3 weeks (range 19-35). The mean GA at delivery for the shunted fetuses was 33.9 weeks (range 27-42) and mean birth weight was 2514 gm (840-4640 gm). 53/59(89.8%) were alive at delivery and 40/59(67.8%) survived neonatal period. Of all survivors of shunts 4-24 months of follow up is available. Six have severe and one has mild morbidity leading to 56% intact survival..
Conclusion: Carefully selected cases of primary fetal pleural effusion benefit from antenatal TAS, prolonging pregnancy and improving neonatal survival.

"Prenatal Diagnostic Procedures: Our Experience"

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Introduction: Prenatal diagnosis has increasingly proven to be beneficial for couples with increased risk of having children with chromosomal abnormalities and genetic disorders. Since majority of these diseases do not have a cure, prenatal diagnosis provides reassurance to the parents, in those cases where the test results are normal and avoids suffering for the child and the family in those cases where the test results reveal an affected fetus.
Data Analysis: We hereby present our analysis of Prenatal Diagnostic Procedures undertaken over the last one year. The data is analysed on the basis of indications, the geatational age, the type of procedure, the methodology, the benefits and side-effects, the patient acceptance etc
Period of study: Dec 2004 to Dec 2005.
No of prenatal diagnostic procedures: 52 (Amniocentesis, Chorion Villous Sampling, Cordocentesis, Others)
Place of study: Jehangir Hospital, Sahyadri Hospital and Sasoon Hospitals, Pune.
Gestational age at which procedures were done: As per the RCOG guidelines ie. CVS (11 to 14 wks) amniocentesis (15 wks onwards) and cordocentesis (the gestational ages were 22 wks onwards).
The **indications** were varied and included Prenatal screen positive patieints, major or minor anomalies or mulitple soft markers on USG, h/o of previous affected child or carriers of genetic disorders.
Complications: 1 patient had PPROM and preterm delivery at 28 wks. 2 culture failures (in one there was delay in the sample reaching the laboratory by >48 hrs and therefore fungal contamination)
Results: Amongst those who underwent prenatal diagnosis for molecular diagnosis and enzymatic analysis (Duchenne's muscular dystrophy, Tay Sach's disease, Galactosemia), the results ruled out the disorder and the patients continued the pregnancy.
Amongst those with previous child having Translocation Trisomy 21, the results revealed the same abnormality and therefore the pregnancy was terminated.

There was a mosaic trisomy in one and a marker chromosome in 2 and structural abnormalities in two more.
Conclusion:The final results have proven the usefulness of Prenatal Diagnosis in couples who are at risk of carrying an affected fetus. However, we could not help few of the couples where there was no definite diagnosis in the previous child either because of the non-availability of molecular diagnosis or lack of awareness of genetic disorders and further investigations could not be undertaken because the previous child was deceased. We also present the lessons learnt and the steps to be undertaken to avoid the above.

Successful Fetal Therapy for Arrhythmia and Heart Failure in Two Cases of Different Etiology

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Fetal arrhythmia and heart failure is one of the major preventable causes of fetal mortality. Fetal arrhythmia when seen on echocardiography can be managed by fetal transplacental therapy. Here we present two cases of fetal arrhythmia, one without any cardiac defect and the other with a rare structural cardiac defect, which were managed conservatively by transplacental therapy and resulted in good outcome.
Case one was a patient with non immune hydrops fetalis detected at 32 weeks of gestation. Fetal heart rate was 300 beats per minute. Ultrasound and fetal Doppler echocardiography showed it to be due to supraventricular tachycardia. Following failed maternal therapy with digoxin alone amiodarone with digoxin was used. Conversion to sinus rhythm and resolution of hydrops followed this treatment. In the second case, routine ulstrasonography at 28 weeks showed abnormal four-chamber view with arrhythmia, echocardiography showed isolated congenital left ventricular diverticulum, the patient was followed up. The fetus subsequently developed pericardial effusion with ventricular ectopy. Maternal digoxin therapy was started and restoration of fetal sinus rhythm was achieved within 48 hours. Serial fetal echocardiograms were performed every week, followed by a normal vaginal delivery at term. There are only few cases of prenatal diagnosis of ventricular diverticulum diagnosed till date. Thus, fetal arrhythmia after diagnosis by echocardiography can be treated and regular follow up can lead to successful outcome.

Genetic Screening of Infertile Males Opting for ART

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Ten to twenty five percent couples encounter difficulty to procreate. Microdeletion of the long arm of the Y chromosome, are associated with spermatogenic failure and have been used to define three regions on Yq (AZFa, AZFb and AZFc) which are critical for spermatogenesis. These 3 loci act at different stages of germ cell development and deletion of each loci result in a characteristic phenotype. Deletion of AZFa, AZFb, AZFc results in Sertoli Cell Only syndrome (SCO), maturation arrest and hypospermatogenesis respectively.
One hundred and ninty five infertile males with idiopathic oligozoospermia and azoospermia were included in this study. Cytogenetic and semen analysis was done in each case. Testicular Fine Needle aspiration Cytology was collected whenever possible. Of the 195 cases, 22 were identified as Klinefelter Syndrome (KFS), 14 cases were mosaic KF and 6 cases were variant Klinefelter, 4 cases had other cytogenetic abnormalities. In cytogenetically normal cases (n=136) microdeletion analysis was done using STS-PCR approach using primers sY84, sY86 (AZFa); sY127, sY134 (AZFb); sY254, sY255

(AZFc). The STS was considered as absent after 3 amplification failures. Twelve of the 136 cases showed deletion of at least one of the AZF loci. Six cases had AZFc deletion, five cases had AZFa and AZFb deletion and one case showed AZFb deletion alone. Two cases with AZFa and AZFb had SCO Type 1 syndrome and 2 cases of AZFc deletion showed hypospermatogenesis and 1 case showed maturation arrest. The FSH and LH levels were elevated in these cases. Variation in testicular phenotype in cases with AZFc deletion is due to multiple copies of the gene presence of autosomal genes. Thus various factors genetic, epigenetic and environmental modulate the effect of these genes. Cases with AZFc microdeletion show a progressive decline in semen quality thus these cases are counselled to go in for semen cryoconservation at the earliest age should they opt for ICSI at a later date. In a large number of cases with AZFc microdeletion there is a population of germ cells with XO cell line and these cases are counseled prior to going in for ART about the risk of male offspring being born with sexual ambiguity, turner phenotype in addition to being infertile. Deletion on Y chromosome make the Y chromsome more prone to secondary larger deletions resulting in worsening of testicular phenotype. Thus in a large number of idiopathic cases of male infertility there is a genetic basis. Therefore detection of Yq microdeletions encompassing the AZF loci determines the prognosis and management of these infertile cases.