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Intrauterine transfusion in Non-Immune hydrops fetalis with anemia

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Abstract

Hydrops fetalis is one of the fetal anemias that contributes for 10% - 27% case. Variety of causes in fetal anemia are bleeding, hemolysis, defective production of active red blood cells and abnormal hemoglobin production. Hydrops fetalis can be diagnosed with an ultrasound Doppler on middle cerebral artery-peak systolic velocity (MCA-PSV). MCA-PSV is a sensitive non-invasive method for determining degree of anemia, and the best ultrasound parameters, in reducing invasive procedures. Red blood cell transfusions are performed in hydrops fetalis are due to one of the following conditions such red blood cell alloimmunization, infection of parvovirus, bleeding of chronic fetomaternal, and congenital red blood cell disorders. The advantages of intrauterine transfusion: it is a safe procedure, low rate of complication and loss of perinatal.

Keywords: Intrauterine transfusion, Non-Immune hydrops fetalis, Anemia

Introduction

Hydrops fetalis defined as the pathological accumulation of excessive fluid in tissues or body cavities, such as the peritoneal cavity, pleural cavity, pericardial sac, and skin. There are two kind of hydrops fetalis, first Immune hydrops fetalis, and second is Non-Immune hydrops fetalis. Immune hydrops fetalis as known as fetal erythroblastosis, occurs in Hemolytic Disease of the Fetus and Newborn (HDFN), can cause severe anemia. Some etiologies such cardiac abnormalities, aneuploidy, hemoglobinopathies, lymphatic malformations, and congenital infections can cause nonimmune hydrops fetalis (Bellini et al., 2015; Bellini & Hennekam, 2012; Désilets et al., 2018).

The incidence of hydrops fetalis stable over several decades, estimated 1,500 to 3,800 births, although proportion of immune hydrops fetalis decrease after introduction of maternal RhD immunoglobulin therapy. Nonimmune hydrops fetalis is occurs in 1 in 1,700 to 3,000 pregnancies and only 1 in 4,000 live births due to of intrauterine fetal death incidence is high and termination of. (Bellini et al., 2015; Bellini & Hennekam, 2012).

Intrauterine transfusion plays a crucial role in treatment of hydrops fetalis in anemia of unknown etiology. Maternal or fetal can cause anemia, intrauterine transfusion can be a treatment option for anemic fetuses with an unknown diagnosis. Intrauterine transfusion is not a definitive therapy, but can reduce or eliminate morbidity and mortality associated with anemia and prolonged pregnancy, pregnancy continuation, and postpartum outcomes (Deka et al., 2016; Kamping et al., 2013; Mari, 2005).

The newborn may recover completely if anemia is secondary to isoimmunization of another rare blood group disease, and the cause (maternal antibodies) is eliminated after birth. Intrauterine transfusion can prevent complications, and effective treatment can be initiated after birth. Intrauterine transfusion is recommended if the hematocrit less than 30%. The hematocrit target in intrauterine transfusion between 40%-50%. Repeated intrauterine transfusions is needed, usually every 2 to 4 weeks,

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until 35 weeks gestation of fetus (Deka et al., 2016; Gynecologists, 2006; Pasman et al., 2015).

Case presentation

Mrs. I, 35, pregnant woman (gravida 2), para 1, and with 0 miscarriages, presented to the Obstetrics and Gynecology Clinic at the hospital at 23-24 weeks of gestation. She presented with her husband complaining of abdominal tightness. She was referred from the Cardiology Clinic for shortness of breath. An echocardiography examination was performed, which revealed dilated RA and RV, with normal RV and LV function. She was assessed for Primary Pulmonary Hypertension. She received Nitrocaf 2x2.5 mg. Subsequently, her shortness of breath subsided. Marital history: The patient married at age 28 and is in her seventh year. Menstrual history: patient's first period at age 12, with an average menstrual cycle of 7 days. Pregnancy history: The patient delivered a full-term vaginal delivery without complications with a midwife. Her first child, aged 13, is considered normal.

At the Obstetrics and Gynecology Clinic, a supporting examination, an ultrasound, was performed. The ultrasound revealed hydrops fetalis with a Multiple of Median of 1.6-1.8, indicating fetal anemia. Excess amniotic fluid (polyhydramnios) was found, with a Single Deepest Pocket (SDP) of 14.36 cm. The ultrasound also revealed subcutaneous edema. The clinician planned an Intrauterine Transfusion (IUT) for the patient.

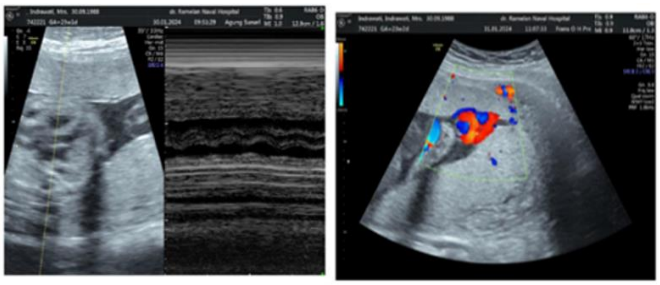

Figure 1. MCA-PSV Doppler ultrasonography obtained 1.6-1.8 MoM with Hydrops fetalis

Laboratory examinations revealed hemoglobin of 11.5 g/dL; erythrocytes of 5.39 million/µL; hematocrit of 38.90%; and erythrocyte indices including of mean corpuscular volume (MCV) is 87 fL, mean corpuscular hemoglobin (MCH) is 30 pg, mean corpuscular hemoglobin concentration (MCHC) is 35 g/dL. These results indicate the patient is anemic. The mother's blood type is O, Rh positive (Rh +), as is her husband's, blood type O, Rh positive (Rh +).

The patient was diagnosed with nonimmune hydrops fetalis with anemia. An intrauterine transfusion was planned. After explaining the procedure to the patient and her husband, and the informed consent form was signed. Patient was admitted to inpatient unit one day before the procedure. The clinician requested a 50 ml pediatric blood sample, leuco-depleted, blood type O, and Rh-negative (-). The intrauterine transfusion performed in the operating room under general anesthesia.

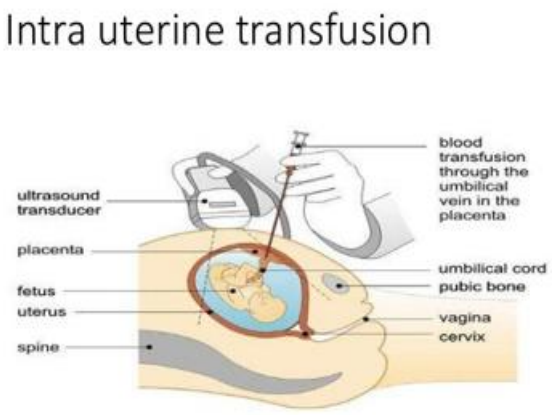

Figure 2. Intrauterine transfusion procedure
Source: (Texas Children's, n.d.)

Amniotic needle insertion was performed, blood was obtained as proof, 1 ml was extracted, and Hb was examined at 4.5 g/dL, Hematocrit 13.5%, and PRC O, Rh (-) blood was injected with 75% hematocrit, as much as 35 ml, after which it was flushed with 10 ml of NaCl. Hb after intrauterine transfusion was 11.2 g/dL. After the procedure, the patient was taken back to the inpatient room. Post-procedure observation was carried out. While in the room, the patient did not experience any complaints, and was able to mobilize. A Doppler ultrasound evaluation showed good fetal movement. The patient was scheduled to go home and be re-checked after 2 weeks for further evaluation, whether or not re-intrauterine transfusion was necessary. The clinician's Hb target is more than 14 g/dL to be born normally.

Table 1. Hb and Hematocrit results before and after intrauterine transfusion

Before intrauterine transfusion	After intrauterine transfusion
Hb: 4,5 g/dL	Hb: 11,2 g/dl
Hematocrit: 13,6 %	Hematocrit: 33,4 %

This case report was approved by Ethical Committee of Dr. Ramelan, Central Naval Hospital, with number 170/EC/KEP/2025. Informed consent was obtained from participant.

Result and Discussion

Four main mechanisms contributing to the development of hydrops fetalis: (1) increasing the pressure of capillary hydrostatic, (2) decreasing the pressure plasma oncotic, (3) obstructing flow of lymphatic, and (4) peripheral capillary damage. There are four etiologies can cause nonimmune hydrops fetalis: (1) cardiovascular (20.1%), (2) lymphatic dysplasia (15%), (3) hematologic (9.3%), and (4) chromosomal abnormalities (9%) (Bellini et al., 2015; Bellini & Hennekam, 2012).

Hydrops fetalis can be detected through ultrasonography (USG), which fluid accumulation reveals at least one compartment (peritoneal, pleural, or pericardial) with edema and polyhydramnion, or without edema. Another common finding is placental thickening. In this case, subcutaneous edema and placental thickening are present. Ultrasound also reveals polyhydramnios with a BMI of 14.36 cm. Doppler ultrasonography used to measure blood flow through the Middle Cerebral Artery (MCA) helps diagnose fetal anemia (Moise Jr, 2008; Oepkes et al., 2006).

Perform Doppler ultrasonography on the Middle Cerebral Artery-Peak Systolic Velocity (MCA-PSV) shows hepatomegaly, placentamegaly, and cardiomegaly. There are late signs of severe fetal anemia due to heart failure in hydrops fetalis such ascites, pleural or pericardial effusion, and scalp edema, MCA-PSV measurement is a sensitive, non-invasive method to determining the anemia, an indication the degree of anemia, and the best parameter, in reducing invasive procedures (Mari, 2005; Moise Jr, 2008; Sallout et al., 2004).

Increasing cerebral artery blood flow velocity in fetuses with anemia, indicating that flow of blood velocity in circulatory sites, such the brain, shows fetus with anemia due to increased cardiac output and decreased blood viscosity. Furthermore, peak systolic velocity in the middle cerebral artery is decrease and fetal hematocrit is increase, suggest a relationship between hemoglobin concentration and cerebral blood flow velocity. The risk of anemia in fetuses if peak systolic velocities more than 1.50 Multiple of the Median (MoM). Fetus with peak systolic velocities below 1.50 MoM (Multiple of the Median) are either anemic or only mildly anemic, while moderate or severe anemia should be performed cordocentesis and require intrauterine transfusion (Moise Jr, 2008; Zimmermann et al., 2002).

Prenatal therapy depends on the etiology of non-immune hydrops fetalis. Fetal intrauterine transfusion indicated in severe anemia (e.g., Rh alloimmunization, parvovirus, congenital anemia, maternal hemorrhage). Peak systolic cerebral artery velocities were monitored. The umbilical vein is also monitored, site for intrauterine transfusion is the umbilical cord. Another alternatives is umbilical artery but associated with risk of complications or intraperitoneal transfusion if the umbilical vessel cannot be achieved (e.g., less than 18 weeks of gestational age) or there is technical difficulties related to position of fetal or location of the umbilical cord and placenta (Deka et al., 2016; Kamping et al., 2013; Tongsong et al., 2006; Zimmermann et al., 2002).

Intrauterine transfusion can be performed performed periodically up to 35 weeks' gestation. The choice of intrauterine transfusion depends on the age of gestational fetus, complications, laboratory findings, and anesthesia. Once the fetus reaches for viability, corticosteroids should be administered to promote fetal lung maturity, and the intrauterine procedure should be in the operating room (I. T. Lindenburg et al., 2012; I. T. M. Lindenburg et al., 2014; Pasman et al., 2015).

Fetal IUT is an outpatient procedure, but hospitalization and overnight observation are generally recommended. If the patient is on anticoagulant therapy, it should be discontinued two

days prior. Blood transfused should be O-negative, leuco-depleted double-packed. Recommendation for the donor's hematocrit is closed to 80% to minimize the volume of blood transfused to prevent fetal cardiac overload (Clarke et al., 2020; Villeneuve et al., 2021).

At the beginning of the procedure, the maternal blood sample is checked for hemoglobin, hematocrit, complete blood count, blood type, and Rh group. The blood volume to be transfused is calculated using the formula, depends on the fetus and donor hematocrit (Santiago et al., 2010):

$$\text{Transfusion volume: } \frac{(\text{Hb Target} - \text{Hb Fetal}) \times \text{Fetal blood volume}}{(\text{Hb Donor} - \text{Hb Target})}$$

$$\text{Fetal blood volume: } 1.046 \times \text{Fetal weight (g)} \times 0.14$$

Rate of intrauterine transfusion is performed at 3-5 mL/minute using a syringe pump. The goal of intrauterine transfusion is hematocrit until 40%-45% in the end of transfusion. Fetal blood sample is measured to determine the final hematocrit and help the timing of the next transfusion. Hb and Hct measurements are performed bedside at the operating table using a POCT device. The role of Clinical Pathology here is as a consultant during the intrauterine transfusion phase, from blood sampling and calculating the transfused blood volume, to the final Hb and Hct examination, and to determine whether the transfused blood volume is sufficient or excessive, which could increase the fetal heart load (Banerjee & Aladangady, 2014; Clarke et al., 2020).

Conclusion

Intrauterine transfusion is a safe procedure, less perinatal complications and harm. However, the technical procedure must be performed with great care and requires thorough preparation. Intrauterine transfusion can maintain fetal development in the mother's womb and viability until birth. Evaluation of fetal hemoglobin before and after intra-uterine transfusion is important for successful therapy. Accurate fetal blood sampling is crucial for intrauterine transfusion.

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