Intrauterine Transfusion: Indications, Complications and Optimization Techniques

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Abstract

Intrauterine transfusion has been used for various indications. The use of Rh(D) immune globulin prophylaxis led to the marked decrease in this procedure. This paper is highlighting the known indications for IUT in the era of ultrasound advances and fetal therapy revolution. This method is being done less commonly nowadays as fetal hemolytic anemia with Rh alloimmunization has decreased markedly with Rh alloimmunization prophylaxis. Nonetheless, IUT is still the cornerstone treatment for fetal hemolytic anemia and some other conditions that will be stated in this article. That being said, it is essential to maintain the updated evidence to minimize the complications and associated risks.

Keywords: IUT; Fetal Transfusion; Fetal Anemia; Rh Disease; Alloimmunisation

Introduction

Intrauterine transfusion (IUT) was first performed in 1963 by Liley using an intraperitoneal method. In 1982, the technique was upgraded to a transfusion through umbilical vein entry under direct ultrasound vision [1]. Throughout the years, IUT has been used for various indications [2]. Worldwide use of Rh(D) immune globulin prophylaxis decreased the need for IUT vividly [3]. In 1906, hemolytic disease of the newborn was first described by a French midwife in a twin delivery at the royal court of King Henry IV and Queen Marie de Medicis. However, the pathogenesis was not clear and only in 1953, Chown then linked the pathogenesis of Rhesus (Rh) alloimmunization to the cross of Rh-positive fetal red blood cells trans-placentally into maternal Rh-negative blood [4].

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Literature Review

Indications

Multiple indications for IUT are mentioned in the literature [2,5,6]. Fetal IUT is considered a pillar aspect in the management of fetal anemia [6]. Fetal hemolytic anemia per se can be seen in red cell alloimmunization complicating the pregnancy in which a progressive type of anemia may occur [7]. The mechanism of the disease was first explained in 1940 with the detection of the Rh grouping system by Landsteiner and Wiener [4,8]. A year later, in 1941, Levine announced the discovery of the Rh(D) antigen which is mentioned later as the responsible cause of the formation of the antibodies in Rh(D) negative mothers [4,9]. When fetal Rh(D) positive antigen is identified by the Rh (D) negative mother, Immunoglobulin type G will be formed, and those antibodies will be able to cross the placenta in further leading to fetal anemia in future pregnancies carrying Rh (D) positive fetuses [4].

With proper diagnosis and with the benefit of fetal IUT, survival rates in those cases generally exceed 90 percent [7,10]. One serious cause of fetal anemia other than alloimmunization includes fetal anemia from erythropoiesis suppression occurring with anti-Kell antibodies [11,12]. Unlike Fetal anemia from red cell isoimmunization with Rh(D) disease, fetal anemia from anti-Kell antibodies cannot be prevented since there is no known prophylaxis for this kind of anemia. For that reason mainly, an increasing incidence of anti-Kell related fetal anemia is being documented the United States of America [13].

Fetal anemia can be diagnosed accurately using a non-invasive method with Middle Cerebral Artery Peak Systolic Velocity (MCA-PSV) Doppler Studies [14-16]. After calculating the PSV in the MCA using Doppler Sonography, a cut off in the mean plus 1.5 standard deviations is considered very accurate in identifying fetal anemia with a very low false positive rate [15].

A third well-known indication for IUT includes fetal Parvovirus B19 infection leading to fetal anemia and hydrops [17-20]. In such cases, one study on 2012 suggested an increased risk of long-term neurological complications in children received IUT antenatally for parvovirus infection [21]. With Parvovirus B19 infection before 20 weeks of gestation, the risk of fetal death from hydrops and fetal anemia is increased. This risk can be decreased with proper, timely diagnosis and appropriate management with IUT [22].

Another IUT indication which is considered controversial includes fetal platelet transfusion in cases of Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT) [23]. Current evidence regarding diagnosed FNAIT is suggesting treatment with IVIG antenatally rather than fetal platelet transfusions with different recommended thresholds for neonatal platelets transfusion postnatally [24].

Another less common complication specifically associated with Monochorionic twins' pregnancies is the more recently prescribed disease Twins Anemia Polycthemia Sequence (TAPS) [28]. The incidence of TAPS in Monochorionic pregnancies is calculated to be ranging between 2 - 13% as per different studies including both spontaneous and TAPS post-TTTS laser treatment [28-30]. TAPS management is still controversial in the limited number mentioned in the literature [28]. IUT combined with partial exchange transfusion is thought to be advantageous in managing the anemic twin in cases of TAPS [31].

In the literature, there are multiple methods and routes mentioned with various indications and clinical scenarios. IL van Kamp., et al suggested the following Preferred order for IUT aiming to transfuse initially in the umbilical vein at the placental insertion site. If this appeared technically challenging, they were aiming for the second option which was the intrahepatic portion of the umbilical vein. Otherwise, a cord-free loop to chosen for umbilical vein insertion site. The fetal heart being used directly to access the fetal circulation was considered one of the latest or final options available for IUT. If previous routs of IUT were ineffective or undoable, intraperitoneal transfusions were performed [36].
Safety and complications

IUT benefits outweigh the risks when indicated, and the procedure is considered relatively safe [37]. Better outcomes are believed when intervention with IUT for fetal anemia is done before signs of hydrops are seen [36]. Complications of IUT continue to occur, and fetal loss from the procedure is estimated to be about 1.6 - 2% per procedure [37-39]. Some studies in the literature are meant to evaluate options to optimize the settings for IUT to minimize the known associated complications [1,39,40].

Procedure-related complications other than fetal loss with an incidence of approximated to be less than 1% include PROM, infections, emergency cesarean sections [39].

In terms of optimizing IUT settings, the following might be considered: early gestational age is known to increase almost all known procedure-related complications. Those complications are shown to be more when the procedure is done before 20 weeks gestation, and some may consider although still controversial the use of Intravenous Immunoglobulin (IVIG) to delay IUT [39].

The neurodevelopmental complications in association with IUT treatment were evaluated by the LOTUS study which is the largest cohort established worldwide. The incidence of neurodevelopmental damage in offspring managed with IUT for fetal alloimmune anemia is found in this cohort to be (4.8%). The most solid preoperative predictor for those known neurodevelopment complications such as cerebral palsy or hearing loss is the existence of fetal hydrops in those managed cases [41].

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Improving the outcomes

One of the suggested options to decrease the rate of complications is to provide an assigned team with expertise in dealing with IUT cases. With experienced hands, the pregnancy loss rate is thought to as low as 0.6% per procedure [39].

Other considerations include transfusing irradiated blood to prevent Graft versus Host disease and not to transfuse the blood straight from storage at 4°C to avoid the risk of fetal bradycardia. The calculated IUT volume should be carefully calculated depending on the gestational age using the donor, fetal and targeted hematoctrits equation (Rodeck and Deans, 2008) to avoid overload and cardiac failure. Including all the previously mentioned points, a clear hospital policy must be written in each unit to provide every possible effort that may be beneficial in minimizing the rate of the associated complications [42].

Conclusions

Incidence of IUT is dramatically decreasing with the prophylactic to administration of anti-D in Rh (D) negative pregnancies. Nevertheless, it is still being done in specialized centers with certain indications. Complications can be reduced with proper preparations and adherence to guidelines from respected organizations as well as specialized centers’ policies.

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Conflict of Interest

No conflict of interest.

Bibliography


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