



Intrauterine transfusion versus Corticosteroids for treatment of immune fetal hydrops secondary to Rh incompatibility with 6 months postnatal follow-up: Case series with review of literature

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ABSTRACT

Introduction: Immune hydrops fetalis is still a challenging condition in fetal medicine. Corticosteroids are established for immune suppression in auto-immune disorders. Their use in cases of Rh isoimmunization is not fully studied so the aim of our study was to evaluate its role in fetal hydrops.

Methods: This study included six patients recruited from January 2015 to December 2015 at fetal medicine center-Alexandria, Egypt. Patients were multiparous women with Rh negative blood group and history of successful full term delivery once before. They had clinical history of fetal hydrops and subsequent intrauterine fetal death at 26-28 weeks of gestation in the subsequent pregnancies. Patients were referred to the center at gestational age 22-32weeks gestation. Three cases were treated by Cordocentesis and transfusion of irradiated O negative red blood cells, Three cases were treated by administration of prednisolone 20 mg tab twice a day for suppression of maternal anti-Rh antibodies production. Ultrasonographic examination was repeated every week. For cases whose fetuses survived till 34 weeks gestation, 4 doses of Dexamethasone 6 mg were given intramuscularly and cases were delivered by elective caesarian section.

Results: Three progressed into sudden intrauterine fetal death; two of them treated with transfusion and one with corticosteroids. One, treated by transfusion, improved and was delivered at 33 weeks gestation after full course of dexamethasone administration to the mother. For the other two cases treated by corticosteroids, both were delivered at 34 weeks gestation, none developed hydrops fetalis. Follow-up of the three surviving neonates was done till 6 months after birth showed normal growth and neurological development.

Conclusions: Corticosteroids could be of benefit in treating fetal hydrops but this needs to be evaluated more in a large studies.

Keywords: Steroids, Hydrops, Ultrasound, Anemia, Pregnancy

SOMMARIO

L'idrope fetale immunomediata in medicina fetale è ancora una condizione clinica indaginosa. I corticosteroidi sono somministrati nei disordini immuno mediati come terapia immuno soppressiva. Il loro uso in caso di isomimmunizzazione Rh non è ancora stato studiato a fondo, quindi lo scopo del nostro studio è quello di valutarne il possibile ruolo nel trattamento dell'idrope fetale.

Questo studio include sei pazienti che sono state reclutate da gennaio 2015 a dicembre 2015 nel centro di medicina fetale di Alessandria, in Egitto. Le pazienti erano pluripare con gruppo sanguigno Rh negativo ed in anamnesi una gravidanza portata fino al termine con successo. Le pazienti incluse hanno avuto una gravidanza con feto affetto da idrope fetale e successiva morte intrauterina tra 26-28 settimane e sono giunte al nostro centro tra le 22 e le 32 settimane di gestazione. Tre dei casi inclusi nello studio sono stati trattati mediante cordocentesi e trasfusione di globuli rossi irradiati O negativo. Tre sono stati trattati con somministrazione orale di prednisolone 20 mg per due volte al giorno ai fini della soppressione della produzione materna di anticorpi anti Rh. Gli esami ecografici sono stati ripetuti ogni settimana. Le pazienti i cui feti sono sopravvissuti oltre le 34 settimane di gestazione sono state trattate mediante 4 dosi da 6 mg di desametasone per via intramuscolo ed in questi casi è stato eseguito un taglio cesareo elettivo.

Tre pazienti hanno avuto morte intrauterina fetale; due di queste erano state trattate con trasfusione e una con corticosteroidi. Una paziente trattata mediante trasfusione è andata incontro a miglioramento e ha partorito a 33 settimane dopo aver concluso la terapia con desametasone. Per i due casi che sono stati trattati con corticosteroidi, entrambi hanno partorito a 34 settimane senza sviluppare idrope fetale. I neonati sopravvissuti sono stati sottoposti a follow up fino ai 6 mesi di vita e hanno mostrato un normale sviluppo fisico e neurologico.

I corticosteroidi potrebbero essere di beneficio nel trattare l'idrope fetale ma sono necessari studi con una più ampia coorte di pazienti.

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INTRODUCTION

Immune hydrops fetalis is still a challenging condition in fetal medicine. Incidence has decreased dramatically in last decades after introduction of the use of anti D immunoglobulins after delivery, at 28-30 weeks gestation and after any bleeding incidence during gestation⁽¹⁾. Screening for Rh isoimmunization is through anti-Rh antibodies, using indirect Coomb's test. Screening for fetal anemia is feasible using values of peak systolic velocity in middle cerebral artery⁽²⁾. Established treatment is serial intrauterine transfusion of irradiated O negative red blood cells, whether into the umbilical vein or intraperitoneal. These routes carry the risk of intrauterine infection, preterm birth, intrauterine fetal death and others⁽³⁻⁵⁾.

Corticosteroids are established for immune suppression in auto-immune disorders. Their use in cases of Rh isoimmunization is not fully studied so the aim of our study was to evaluate its role in fetal hydrops.

METHODS

This study included six patients recruited from January 2015 to December 2015 at fetal medicine center-Alexandria, Egypt. Patients were multiparous women with Rh negative blood group and history of successful full term delivery once before. They had clinical history of fetal hydrops and subsequent intrauterine fetal death at 26-28 weeks of gestation in the subsequent pregnancies. Patients were referred to the center at gestational age 22-32 weeks gestation.

At recruitment, they were subjected to: Assessment of ABO and Rh blood grouping, Measurement of hemoglobin, postprandial blood sugar and anti-Rh antibody titer and Ultra-sonographic examination including: Fetal biometry, anomaly scan including fetal echocardiography and Peak systolic velocity in middle cerebral artery.

Three cases were treated by Cordocentesis and transfusion of irradiated O negative red blood cells, Three cases were treated by administration of prednisolone 20 mg tab twice a day for suppression of maternal anti-Rh antibodies production. Ultrasonographic examination was repeated every week. For cases whose fetuses survived till 34 weeks gestation, 4 doses of Dexamethasone 6 mg were given intramuscularly and cases were delivered by elective caesarian section.

RESULTS

All cases were Rh negative, with indirect Coomb's test showing anti-Rh antibodies titer above 1/32. Gestational ages were 22-26 weeks in the recruited cases. Middle cerebral artery peak systolic velocity was above 1.5 MoM for the gestational age in all three recruited cases. Four cases showed fetal ascites at the time of recruitment. Three of them were treated with serial cordocentesis and O negative red blood cell transfusion, guided by Peak systolic velocities in middle cerebral artery. Of these four cases, three progressed into sudden intrauterine fetal death; two of them treated with transfusion and one with corticosteroids. One, treated by transfusion, improved and was delivered at 33 weeks gestation after full course of dexamethasone administration to the mother. Fetal weight was 1800 gms, severe neonatal jaundice developed and was promptly treated by exchange transfusion and phototherapy. Neonate was discharged after 16 days. For the other two cases treated by corticosteroids, both were delivered at 34 weeks gestation, none developed hydrops fetalis. Birth weights were 1900 and 1950 grams. Newborns developed hemolytic anemia and jaundice at day one, necessitating exchange transfusion, which was repeated three times together with phototherapy. Fetuses were discharged 12 and 14 days after delivery. Follow-up of the three surviving neonates was done till 6 months after birth showed normal growth and neurological development.

DISCUSSION

Alloanti-D that is acquired during pregnancy or by transfusion is a major cause of severe and sometimes fatal haemolytic disease of newborns and haemolytic transfusion reactions, respectively. Isoimmunized mothers are destined to have immune hydrops in all future pregnancies with Rh positive fetuses. Treatment of these fetuses is currently through repeated intrauterine transfusion, Other modes of treatment include plasmapheresis to dilute the anti-Rh antibodies in maternal blood, with large volumes of plasma needed for this procedure. Pharmaceutical treatment is currently of limited use. In our case series we proposed the use of relatively high doses of corticosteroids for immune suppression versus the established transfusion therapy. The underlying principle is suppression of maternal Anti-Rh antibodies which cross the placenta and cause fetal hemolysis⁽³⁻⁶⁾.

Early use of this mode of treatment was successful to suppress antibodies, allowing the bone marrow and reticuloendothelial system of two fetuses to maintain adequate cardiovascular function and tissue oxygenation. Liver affection was not documented and no evidence of ascites, pleural effusion nor subcutaneous oedema was found in the two cases surviving on prednisolone therapy. Second case showed hepatomegaly at 33 weeks, 4 days, prompting the decision of caesarian delivery after 4 doses of corticosteroids. Conservative treatment till this age allowed shorter period of admission at neonatal intensive care unit and helped improve the outcome for fetuses of both cases. Treatment with 40 mg oral prednisolone helped save two fetuses of isoimmunized mothers. It could be used alone or in conjunction with other modes of treatment⁽³⁻⁶⁾. On the other hand, cases already presenting with evidence of fetal ascites mostly agreed to the transfusion therapy, with only one having successful outcome. This method is more effective in replacing hemolysis fetal red blood cells, without slowing down the rate of hemolysis⁽⁶⁾.

Isojima et al⁽⁷⁾ reported the successful use of plasmapheresis and high doses of gamma globulins for dilution and neutralization of anti-Rh antibodies in one case.

Houston et al⁽⁸⁾ reported another cases case managed with the same combination, none of them added corticosteroids.

In conclusion, we propose the addition of 40 mg oral prednisolone therapy to pregnant females, in addition to other modes of therapy, whether transfusion or plasmapheresis and

immunoglobulin therapy. Prednisolone therapy is cheap, it proved helpful on its own for obtaining good outcome, and in combination with other therapies prognosis could be more favorable.

CONCLUSIONS

Corticosteroids could be of benefit in treating fetal hydrops but this needs to be evaluated more in a large studies.

AUTHORS CONTRIBUTION:

All the authors contributed to protocol development, data collection and management, Data analysis and Manuscript writing/editing.

Ethical disclosure

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflict of interest. The authors declare no conflict of interest.

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