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Original Research Article

Efficacy and Safety of Monoclonal Anti-RHD Immunoglobulin with Polyclonal Anti-RHD Immunoglobulin for the Prevention of Maternal RH-Isoimmunisation: A Comparative Study

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Abstract

Aim and Objective: To compare the efficacy and safety of monoclonal anti-Rhesus (anti-D) immunoglobulin (IgG) with polyclonal anti-D IgG in the prevention of maternal Rh-soimmunisation.

Material and Methods: A comparative clinical trial was conducted in the obstetric inpatient department of 3 hospitals in Patna, Bihar between January 2018 to December2019.100 Rh-D negative women, not sensitized to Rh antigen, and delivering Rh positive babies, received postpartum intramuscular administration of monoclonal or polyclonal anti-DIgG.The main outcome was assessed by the proportion of subjects protected from Rh-isoimmunisation, identified by a negative indirect Coombs test(ICT) result at day 180 after anti-D IgG administration and the incidence of adverse
effects.

Results:50 subjects each were allotted to monoclonal and polyclonal group. ICT results at day 180 was negative in all 50 of monoclonal gp whereas 1 had positive and 49 had negative ICT among polyclonal gp.5 minor adverse events were reported all unrelated to the interventional drug(3 in monoclonal and 2 in polyclonal gp). None developed immunogenic reaction to the monoclonal Anti-D.

Discussion and Conclusion: The efficacy and safety of the monoclonal and polyclonal preparation of Anti-D were comparable to each other in the prevention of maternal Rh-isoimmunisation.

Keywords: Monoclonal, Polyclonal, Rhesus Immunoglobulin, Isoimmunisation

Aim and Objective:

In the 1960s began the clinical practice of passive immunization of Rhesus (Rh) negative pregnant women with anti-Rh immunoglobulins(IgG) for the prevention of sensitization to the Rh(D)antigen. [1-3]

Sensitisation mostly occurs with detachment of placenta during delivery which can be immunosuppressed by Anti-DIgG prophylaxis most probably acting by accelerated destruction of Rh-positive red blood cells. [3,4]

The incidence of postpartum anti-D sensitisation has reduced from 13-19% to 0.9-1.8% with postpartum immunoprophylaxis and further to 0.1-0.3% with addition of antenatal immunoprophylaxis [5-7].

The polyclonal anti-D IgG is produced by fractionation of IgG from pooled plasma of donors and thus has limited availability while monoclonal anti-DIgG have unlimited supply as they are produced using hybridoma and recombinant DNA technologies. Both have similar physiochemical and biological properties and this study aims to compare their efficacy and safety when used for postpartum immunoprophylaxis.

Material and Methods:

The trial was conducted in the obstetric-in-patient department of 3 hospitals in Patna, Bihar between January 2018 and December 2019.Rh-negative pregnant women delivering Rh-positive baby with a negative IT(Indirect Coombs Test) test result were eligible for this study. Exclusion criteria: Positive ICT test result at baseline, h-negative blood group of husband, history of incompatible blood transfusion, history of allergic reaction to IgGs and diagnosis of abruptio placenta, placenta previa or intrauterine death.

100 selected patients were divided into 2 groups of 50 each. All were explained about the study and the need for follow up and provided voluntary, written, informed consent. 50 subjects received Monoclonal anti-D(Rhoclone, Bharat Serum and Vaccines Ltd) and the other 50 received Polyclonal anti-D(RhoGAM, Johnson & Johnson) at a dose of 300 mcg(15001U)IM within 72 hrs of delivery to protect against 30 ml of expected feto-maternal hemorrhage.

Blood samples were collected before study drug administration (baseline)and at 72hrs, 90 days and 180 days from the anti-D administration. ICT was performed on all the samples while testing for anti-drug antibodies was performed on baseline, day 90 and day 180 samples. ICT results at 72 hrs and Day90 were also assessed since anti-DIgG from administered anti D injection is present in detectable quantities upto 12 weeks and since it is not possible to distinguish between administered and immune anti-DIgG these results were considered as supportive evidence and were not carried forward for Day180.Only serial rise in tires was considered as positive result.

Adverse events were recorded throughout the study.

Results:

1. Demographics and baseline characteristics were comparable between the two treatment groups.
2. Efficacy Endpoints:

At Day 90:2 subjects from the polyclonal group and none from the monoclonal group had a positive ICT result.

At Day 180:1 subject from the polyclonal group and none from the monoclonal group had a positive ICT result.

3. Safety Outcomes:

3 subjects from monoclonal and 2 from polyclonal group developed minor adverse events like bodyache, itching and anaemia, all unrelated to the study drug and resolved without any complications or sequelae.

4. Immunogenicity: The immunogenicity testing in the monoclonal group revealed that none of the subjects developed antibodies against monoclonal anti-D.

Table 1: Efficacy data-indirect coombs test results

Time-Point and Result	Monoclonal anti-D(n=50)	Polyclonal anti-D(n=50)
Day 90		
Positive	0	2
Negative	50	48
Day 180		
Positive	0	1
Negative	50	49

Table 2: Safety data-adverse events

Adverse Event	Monoclonal anti-D group	Polyclonal anti-D group
Bodyache	1	1
Itching	1	0
Anemia	1	1

Discussion and Conclusion:

The estimated worldwide prevalence of Rh disease is 276 per 100000 [8]. In recent times, commercial availability of polyclonal anti-D IgG has been affected, primarily due to limited availability of hyperimmune plasma and increasing demand as both antenatal and postnatal prophylaxis is in use now and hence the rise in its cost. Additionally, there is increasing concern about the risk of transmission of newly emerging viruses.

Monoclonal anti-D IgG avoids the need for human donors and human products thereby decreasing the risk of disease transmission, protein impurities and batch-to-batch inconsistencies.

In this study, both monoclonal and polyclonal anti-DIgG preparations demonstrated effective protection in Rh-negative women against isoimmunization with Rh antigen from their Rh - positive babies.Despite the use of postnatal prophylaxis, antibody formation occurs in about

1-2% and thus 1 ICT positive patient in polyclonal group is not significant. No specific adverse reactions related to either preparation was reported. In addition, the monoclonal anti-D preparation did not result in an immunogenic reaction in any subject.

Coupled with the other advantages associated with monoclonal antibodies over polyclonal antibodies-better batch-to-batch consistency ,lesser protein impurities, lesser risk of disease transmission and practically unlimited supply, monoclonal anti-D provides an attractive and viable alternative to the conventional polyclonal preparations in the prevention of maternal isoimmunization.

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