Clinical Exper. Obst. & Gynecology
Jan. 1974 Vol. I, pp. 48-53

*Symp. Foeto-Placental Unit.* Milan, september 1968, Excerpta Med. I.C.S. 170, Abstract n. 79. - 11. Genazzani A. R.: *Proc. VII Internat. Congr. Clin. Chemistry.* Geneva, Sept. 1969, ed Karger, Basel - New York. - 12. Genazzani A. R., Coccola F., Casoli M., Neri P., Fioretti P.: *Proc XXIII Congr. Fed. Soc. Gyn Obst. de Langue Franç.* Bruxelles, September 1970. - 13. Haour F., Cohen M., Bertrand J.: *C. R. Soc. Biol.* 4, 164, 1970. - 14. Haour F., Cohen M., Bertrand J.: *Europ. J. Clin. and Biol. Res.*, 1970. - 15. Kaplan S. L., Grumbach M. M.: *Science.* 47, 751, 1965. - 16. Samaan N. A., Bradbury J. T., Goplerud C. P.: *Am. J. Obst. Gyn.* 104, 781, 1969. - 17. Saxena B. N., Emerson K. Jr. and Selenkow H. A.: *New Engl. J. Med.* 225, 281, 1969. - 18. Spellacy W. N., Carlson K. L., Bird S. A.: *Am. J. Obst. Gyn.* 96, 1164, 1966. - 19. Spellacy W. N., Cohen W. D., Carlson K. L.: *Am. J. Obst. Gyn.* 97, 560, 1967.

# Incidence of Rh Immunisation using Intravenous anti-Rh (D) IgG

by

D. SOTTO CORONA, A. DELUCCA and G. D. MONTANARI

## INTRODUCTION

The intravenous administration of anti-Rh (D) IgG should present certain advantages over intramuscular injection.

To eliminate the Rh positive red cells from the mother's circulation it is clearly necessary that the anti-D immunoglobulin enters the circulation itself. Injected intravenously this is reached quickly and at the full dosage. Intramuscularly, it is achieved after a delay and at a lower level. After five days about 40% of the dose injected intravenously remains in the circulation while with intramuscular injection the maximum concentration in the blood is reached only between the fifth and tenth days and represents 35-40% of the dose injected ([14]).

The prevention of immunization does not depend exclusively upon the removal of the foetus' red cells. This is, however, the only method at present available to prevent the formation of anti-D antibodies.

Intravenous injection of the passive antibodies would more quickly block the antigen action and the central inhibition on the cells capable of immunization.

The method of preparing the intravenous product ([16]) should remove the risk of transmitting viral hepatitis ([17]).

Intravenous administration of the anti-D immunoglobin is more effective in eliminating from the circulation a certain volume of Rh positive red corpuscles than the same immunoglobin injected intramuscularly ([12]).

The time of latency is in fact reduced, the half-life shorter and the destruction of the foetus' red cells more rapid ([14, 15]). Intravenous administration is therefore to be preferred especially in cases of « massive » foetal-maternal transfusions (50 ml) ([12]) while bearing in mind the risk of haemolitic reaction and consequent renal damage ([10]).

Anti-D immunoglobins can be administered intravenously in considerably re-

From University of Padua - Autonomous School of Obstetrics, Bolzano (Italy).

duced doses ([6, 7]). In this way, there is a saving of materials and money. Some think that the economic factor is the only one in favour of the use of anti-Rh (D) IgG ([10]).

Finally, intravenous injection avoids the break-down of the immunoglobulin due to local proteolysis. This partial destruction within muscular tissue is not, however, acknowledged by all authorities ([14]).

The scope of the present research is to evaluate comparatively the effectiveness of anti-D immunoglobulin injected intramuscularly or intravenously in non-immunized Rh negative women who have given birth to an Rh positive child. The effectiveness has been evaluated following successive immunological controls.

## MATERIALS AND METHODS

Between 1967 and 1972 at the Autonomous School of Obstetrics, Bolzano, 405 patients were given anti-D prophylaxis. In 133 cases, this prophylaxis was carried out intramuscularly in the form of Rh-GAM Ortho at the standard dose of 300 microgrammes. In 272 cases the prophylactic was administered intravenously (Anti-Rh Biotest) at a dosage of 200 microgrammes. This dosage is accepted as being effective in the prevention of Rh isoimmunization in 98-99% of cases and can be considered the ideal standard dose ([7, 9, 10]) when one takes into account that, intravenously, the dosage can be significantly reduced ([4, 5]). Obviously, in cases of « serious » (10-15 ml) and « massive » (50 ml) foeto-maternal transfusion and therefore in « high risk » patients treatment is repeated with doses of immunoglobulin until the foetal red corpuscles disappear from the mother's circulation. To this end, doses of 10-20 microgrammes of anti-Rh (D) IgG for each ml of foetal blood that has passed into the patient's circulation are generally recommended. Before prophylaxis, the extent of the foetal-maternal hoemorrage is in fact checked by the Kleihauer test. In the cases we have studied this criterion has only been applied since 1970. Thus, 80 of the patients treated with

Table 1. *Patients given anti-D intramuscularly as a prophylactic (Rh GAM Ortho).*

| Cases treated | Cases later checked | Subsequent Pregnancies | | |
|---|---|---|---|---|
| | | Total number | Delivered | Aborted |
| 133 | 90 (67%) | 44 | 40* | 4 |

* 33 born Rh positive and 7 Rh negative.

intramuscular anti-D immunoglobulin (Rh GAM) are excluded. The Kleihauer test and the indirect Coombs test were carried out one or more times in the days immediately following treatment. The demonstration of an excess of antibodies in the blood provides better guarantees than does the disappearance of the foetus' red cells from the mother's circulation ([14]). However, in our experience, the Coombs and Keihauer tests have an almost equal pattern in checking the effectiveness of prophylaxis.

Of 405 patients given anti-Rh (D) IgG treatment we have been able to check 296 (76%) after six months or more. Of these 296, 90 had been given intramuscularly Rh GAM Ortho as a prophylactic (Table 1) and 206 anti-Rh Biotest intravenously (Table 2).

Clinical Exper. Obst. & Gynecology
Jan. 1974 Vol. I, pp. 48-53

Table 2. *Patients given anti-D intravenously as a prophylactic (Anti-Rh Biotest).*

| Cases treated | Cases later checked | Subsequent Pregnancies | | |
|---|---|---|---|---|
| | | Total number | Delivered | Aborted |
| 272 | 206 (75%) | 40 | 38* | 2 |

* 28 born Rh positive and 10 Rh negative.

The parity and ABO compatibility of the patients given anti-D prophylaxis was then checked and is shown in Table 3.

When being followed-up, patients were asked about the possible appearance of liver dysfunction within four ([8]) months of being given anti-Rh (D) IgG.

## RESULTS

Of the 405 patients given anti-D prophylaxis (133 intramuscularly and 272 intravenously) 296 (90 of those treated intramuscularly and 206 of those treated

Table 3. *Similarity and compatibility of the patients given anti-D and the checked.*

| | Parity | | ABO Compatibility | |
|---|---|---|---|---|
| Way of administration of the anti-Rh IgG | 1 | >1 | Present | Absent |
| Intramuscular (Rh GAM Ortho) | 39 | 51 | 70 | 20 |
| Intravenous (anti-Rh Biotest) | 111 | 95 | 165 | 41 |

Table 4. *Results of blood investigations carried out 6 months or more after parturition in a group of patients treated with anti-Rh (D) IgG intramuscularly or intravenously.*

| | Immunized | Not immunized | Total |
|---|---|---|---|
| Patients treated intramuscularly (with Rh GAM Ortho) | 2 | 88 | 90 |
| Patients treated intravenously (with anti-Rh Biotest) | 1 | 205 | 206 |
| Totals | 3 | 293 | 296 |
| 2/90 = 2.2%; 1/206 = 0.4% | P> 0.05 | | |

intravenously) were followed up six months or more after giving birth. In Table 4 are shown the results of the blood test.

In assessing the efficacy of the anti-D treatment, a more significant factor is that of the absence of sensitisation in patients during a subsequent pregnancy with an Rh positive foetus ([19]). The possibility does in fact exist that the passive antibodies screen the onset of immunization and that with a subsequent pregnancy the treated patients develop antibodies. The assessment of our material from this point of view is summarised in Table 5.

Table 5. *Results of blood tests carried out at the time of delivery on patients who had given birth to another Rh positive baby and who at the time of the previous birth were being treated intramuscularly or intravenously with anti-Rh (D) IgG.*

| | Immunized* | Not immunized | Total |
|---|---|---|---|
| Patients treated intramuscularly (with Rh GAM Ortho) | 2** | 31 | 33 |
| Patients treated intravenously (with anti-Rh Biotest) | 1 | 27 | 28 |
| Totals | 3 | 58 | 61 |
| 2/31 = 6,1% 1/27 = 3,6% P> 0.05 | | | |

* All primiparous.
** An incompatible ABO pregnancy.

In two cases after intramuscular, and in seven after intravenous prophylaxis, the patients reported hepatic dysfunction within four months of the anti-Rh (D) IgG being administered. In none of these cases does either the case history or the clinical and laboratory documentation (where this exists) allow a retrospective diagnosis of viral hepatitis.

## COMMENTARY AND CONCLUSIONS

The overall lack of success (immunization) in the two series of patients stands at 2,2% when the prophylaxis is administered intramuscularly and at 0,4% when it has been given intravenously. Statistical evaluation suggests that the difference between the two series is not significant (P>0,05). One arrives at the same conclusion by evaluating the most significant group of patients, i.e. those pregnant again with an Rh positive foetus: immunization rate 6,1% intramuscularly and 3,6% intravenously. P>0,05.

It can thus be stated that, with regard to efficacy, there is no difference between the two ways of administering anti-Rh (D) IgG.

Apart from the significance of the difference in the results, it seems useful to analyse the failures. These can have had various causes as a mono-transfusion

Clinical Exper. Obst. & Gynecology
Jan. 1974 Vol. I, pp. 48-53

at the time of birth. The high incidence of immunization in the cases given the prophylactic intramuscularly can also be due to the fact that in 60% of the patients coming to our attention since 1970 the extent of the foetal-maternal haemorrhaging was not assessed; these were limited to the administration of a standard dose, thought to be considerably above that necessary for protection ([7]). It is also known that failures are also observed despite the use of large doses of immunoglobin Rh (D) ([11]). The identification of cases in which there is serious or heavy haemorrage remains the only means available for trying to eliminate this type of failure. Also, immunization during pregnancy could have contributed to an increase in the rate of failure ([10]) but it is not possible to demonstrate this. On the other hand, one must exclude from our figures all causes of failure such as delayed administration of anti-Rh (D) IgG and the use of ordinary gammaglobulins during pregnancy for prophylaxis against infectious diseases since they contain small quantities of anti-D and can thus accentuate rather than suppress the immunitary response in very light foetal-maternal haemorrhages.

In conclusion, a comparative examination of the results in two groups of patients who were given anti-Rh (D) IgG prophylaxis intramuscularly and intravenously does not bring out any significant difference.

## SUMMARY

A comparative examination of the results in two groups of patients who were given anti-Rh (D) IgG prophilaxis intramuscolarly and intravenously in made. There is no difference between the two ways of administering anti-D.

*Translated by Samil Pabyrn Foundation*

## BIBLIOGRAPHY

1. Althoff ., Schellong G., Stahl M.: *Münch. Med. Wsch.* 111, 1386, 1969. - 2. Baradun S., Kistler P., Jeunet P., Isliker H.: *Vox. Sang.* 7, 157, 1962. - 3. Bishop G. J., Krieger V. I.: *Ann. Ost. Ginec.* 92, 447, 1971. - 4. Borner P., Deicher H., Hoppe H. H., Hitchold H., Holz S., Seifert A.: *Geburtsch. Frauenheilk.* 29, 203, 1969 a. - 5. Borner P., Deicher H., Hoppe H. H., Pixberg H. U., Sieg W.: *Vox. Sang.* 17, 362, 1969 b. - 6. Borner P., Deicher H.: *Ann. Ost. Ginec.* 92, 453, 1971. - 7. Clarke C. A.: *Clin. Obst. Gynec.* 14. 1971. - 8. Eibl J.: *Ann. Ost. Ginec.* 92, 461, 1971. - 9. Finn R.: *Ann. Ost. Ginec.* 92, 436/460, 1971. - 10. Gorman J.: *Ann. Ost. Ginec.* 92, 459, 1971. - 11. Gorman J.: *Clin. Obst. Gynec.* 14, 1971. - 12. Huchet J., Cregut R., Pinon F.: *Rev. Franc. Transfusion* 13, 231, 1970. - 13. Jouvenceaux A., Adenot N., Berthoux F., Revol L.: *Rev. Franc. Transf.* 13 suppl. 2, 341, 1969. - 14. Jouvenceaux A.: *Rev. Franc. Transf.* 14, 39, 1971. - 15. Jouvenceaux A.: *Ann. Ost. Ginec.* 92, 464, 1971. - 16. Logrippo G. A., Hartmann F. A.: *Bibl. Haemat.* 7, 225, 1958. - 17. Stephan W.: *Vox. Sang.* 20, 442, 1971. - 18. Vermylen C.: *Ann. Ost. Ginec.* 92, 451, 1971. - 19. Walker W.: *Ann. Ost. Ginec.* 92, 431, 1971.