Giorn. It. Ost. Gin. Vol. XXXII - n. 4
Luglio-Agosto 2010

articoli originali

The presence of antibodies in anti-Lewis system in our pregnant women

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SUMMARY: **The presence of antibodies in anti-Lewis system in our pregnant women.**

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In this paper we have shown 3625 testing blood samples of pregnant women from 2005 to 2010 on the presence of irregular antibodies in Lewis system, which was done by routine methods, and by using appropriate "screening" tests and the panel for identification of antibodies. In addition to other antibodies, anti-Lewis antibodies were found in 0.2%, as follows: anti- Le^a in 5, anti- Le^b in 2, but anti- Le^{a+b} weren't found. We have confirmed that the phenotype Le (a-b-) in pregnant women is significantly more active versus tested population. If the anti- Le^a antibodies (IgM class) are harmless, the rare anti- Le^b antibodies (IgG class) could be dangerous for the fetus. Although the clinical significance of anti-Le antibody has not been fully proven, and although their immunogenicity is low, we suggest test these antibodies in all pregnant women in relationship to their essential role in the transfusions, the sensitization of the fetus and the risk of hemolysis.

RIASSUNTO: **La presenza di anticorpi di Lewis nelle nostre donne in gravidanza.**

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In questo lavoro sperimentale riportiamo i risultati di uno studio, effettuato negli anni dal 2005 al 2010, su 3.625 donne in stato di gravidanza in cui è stata esaminata la prevalenza di anticorpi del sistema Lewis. Gli anticorpi anti-Lewis sono stati evidenziati in 7 donne (0,2%): in 5 gli Anti-Le-^{a} e in 2 gli anti-Le-^{b} (mentre gli anti-Le^{a+b} non sono stati riscontrati). Se gli anti-Le^a anticorpi (classe IgM) risultano innocui, gli anti- Le-^{b} (classe IgG), possono risultare pericolosi. Pertanto, sebbene l'importanza clinica degli anticorpi anti-Le non è stata pienamente comprovata e sebbene la loro immunogenicità sia inferiore agli altri anticorpi, sarebbe auspicabile esaminarli in tutte le donne in gravidanza anche per l'importante ruolo che rivestono nelle trasfusioni di sangue con la possibile sensibilizzazione del feto e il conseguente rischio di emolisi.

KEY WORDS: Lewis antibodies - Pregnancy - Sensitisation.
Anticorpi anti-Lewis - Gravidanza - Sensibilizzazione.

Introduction

Lewis blood group system was first discovered by Mourant in 1946. Andersen with his partners continued to work on this significant research in1948 (1). There are two antigens, Le^a and Le^b and appropriate antibodies: anti- Le^a, anti- Le^b and very rare anti- Le^{a+b}. The Lewis system is characterized by the production of antigens in secretion, which then successively absorb the erythrocytes (1, 6). Lewis antigens are in special conjunction with secretions and they are present in secretions such as glycoproteins and / or as an ABH-group of specific substances (1, 6, 7). People who have H -antigen in itself are called secretors, and those who do not are called non- secretors. Secretion otherwise is exclusively related to the occurrence of ABO antigens in secretions, regardless of the presence of other antigens (2).

Le^a antigen is present in red blood cells in approx-

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imately 22%, and Le^b antigen in about 72% of the white race in the world. A Very small number of people have both antigens or not at all.

Possible phenotypes of Lewis blood group erythrocytes are:

Le (a+b-), Le(a-b+) and Le(a-b-)(1,6).

European average in the percentage of these phenotypes looks like this(6):

Le (a+b-)=20-22%

Le (a-b+)=70%

Le (a-b-)=8-10%

It was found that Lea positive people are non- secretors, and that almost all Le^a negative people are secretors of substances ABH. Most people of Leb excrete substance A, B or H (10).

Antibodies anti- Le^a and anti- Le^b are mostly natural, and a form of immune antibodies Le^a has been found. Anti- Lea are common in the serum of people who are non- secretors ABH and whose phenotype is Le(a-b-) (6,8,10). This phenotype has a large number of pregnant women with blood group A1 (the largest in the ABO system) where during pregnancy disappearance of Le^b antigens has occurred and they acquired the phenotype in this way. It typically happened during the 24th weeks of gestation, while the return of the same antigens Le in erythrocytes occurred six weeks after giving birth. These antibodies are relatively more frequent in pregnant women, due to the depression of Lewis antigens given the increased concentrations of lipoproteins in plasma (8,9). The optimum temperature for the anti-Le antibodies is somewhat lower and it ranges between 16-20^{0}C. Anti-Le mostly belong to the IgM class, they are more frequent and harmless because they do not pass the placental barrier, while the rare anti-Le of IgG class are hemolytic and dangerous, because they pass through the placenta and can sensitize mother and lead to damage of the fetus and result in its death. They are detected by indirect Coombs test (5,6,7).

The aim of the work

The aim was to determine the frequency and the presence of antibodies in the Lewis blood-group system in pregnant women, within a specified time period, with emphasis on the possible discovery of irregular, dangerous anti-Le antibodies, their monitoring as well as the possibility of sensitization through them, which would led to significant birth defects. Also, we tried to confirm the allegations of some authors that there is greater percentage of blood type phenotype Le (a-b-), compared to the control group from the population in pregnant women. We have tried, with phenotypic standardization of pregnant women, to discover any rare immune antibodies of Lewis system, whose presence, among other causes, could be connected with sensitization of pregnant women who gave birth to dead children.

Materials and methods

3.625 blood samples of pregnant women were tested over a period of five years, from 2005 to 2010, in the Blood Transfusion Service of General Hospital in Bar. In parallel, we examined in the same way a control group of 100 voluntary blood providers. All of them were determined as being of the Lewis system blood group with phenotypical characteristics as well as identification of Lewis system antibodies in pregnant women, who had these antibodies in the blood. Laboratory tests were made routinely with "screening" tests in all environments and in the cases with positive findings, we identified antibodies with a panel of red blood cells. Lewis phenotypization was made by specific serum (anti-Lewis), in all pregnant women where we had found anti-Lewis antibodies (3, 4). The Blood group of Lewis phenotype was determined by serum tests of animal origin (anti- Le^a and anti Le^b) of foreign companies like "Ortho".

Results

In an examined number of 3625 blood samples in pregnant women it was found seven with anti-Lewis antibodies were found which is 0.19%.

TABLE 1 - LEWIS PHENOTYPE IN 3.625 PREGNANT WOMEN.

Fenotype	No	Percentage
Le^a	765	21,1%
Le^b	2.545	75,10%
Le(a-b-)	315	8,7%

TABLE 2 - LEWIS PHENOTYPE IN THE CONTROL GROUP OF 100 VOLUNTARY BLOOD DONORS.

Fenotip	No	Percentage
Le^a	20	20,0%
Le^b	75	75,0%
Le(a-b-)	5	5,0%

TABLE 3 - FINDINGS OF LEWIS SYSTEM ANTIBODIES.

Anti-Le^{a}	5	71,42%
Anti-Le^{b}	2	28,58%
Anti-Le^{a+b}	0	0%

TABLE 4 - LEWIS PHENOTYPE IN 7 PREGNANT WOMEN WITH ANTI-LEWIS ANTIBODIES.

Antibodies	**No**	**Fenotype**
Anti-Le^{a}	1	4
Anti-Le^{b}	1	1
Anti-Le^{a+b}	0	0

Discussion

Comparing the results given in Table 1 and 2, a significant difference can be seen in the frequency of phenotype Le (a-b-) in the study group. This supports opportunity for the creation of anti-Lewis antibodies. In a large number of pregnant women, mainly of blood group A, there is a disappearance of antigen Le^{b} from erythrocytes and with an acquired phenotype Le(a-b-) (6, 8). This usually happens during the 24th week of gestation (5, 6). Return of the same Le antigens from erythrocytes can been perceived six weeks after childbirth. Antibodies Le^{a} quite often appear in the serum of people who are non-secretors ABH and whose red blood cell phenotype is Le (a-b-). These antibodies are usually natural of IgM class and they are active at temperatures lower than 37^{0}C. Extremely rarely, they may belong to the IgG class, when they create hemolysis of erythrocytes in vivo. Anti-Le^{b} can also be found in people who are Le (a-b-), but who do not make secret of ABC antigens. Thus, both antibodies produce almost only individuals with Le (a-b-) phenotype (6, 8).

It is considered that due to the reduced Lewis antigen expression on red blood cells of pregnant women during gestation the formation of phenotype Le (a-b-). Occurs there a change yakes place in the distribution of Lewis glycolipids between plasma and erythrocytes in the favor of increasing the level of plasma lipoproteins in relation to the mass of red blood cells which is illustrated during pregnancy (6, 10).

Clinical significance of antibody specificity Lewis is very small (7, 8, 9). The main reason is temperature optimum, at which the antibodies act. Then, Le antigens in plasma donors often inactivate Le antibodies in the recipient's plasma so erythrocytes aren't affected (5). These antibodies rarely cause Hemolytic disease of the newborn. Only if the anti- Le occur in the form of IgG can they pass through the placental barrier and damage fetal erythrocytes. It usually does not happen, as the erythrocytes of a newborn usually do not manifest Le antigens, however-even if it is a small number, it is usually enough to inactivate immune antibodies of Lewis system, which originate from the mother. However, there is a possibility of sensitization. In practice, it should take care of it (9, 10).

Conclusion

The presence of anti-Lewis antibodies in the blood of pregnant women is relatively common (5, 6).

The presence of phenotype Le (a-b-) in pregnant women who had antibodies of anti-Lewis type is evident, and be useful, when possible in the generative period to give Transfusions of phenotypically matched Lewis blood.

Lewis antibodies should be detected and monitored because of the possibility of applying a blood transfusion either to the mother or the newborn. It can often be an obstacle in the detection of other antibodies, but also be a rare cause of sensitization and heavy damage to the fetus, usually with lethal consequences.

However, the clinical significance of Lewis antibodies is very small, because of its poor immunogenicity compared to the other group systems (Rh, ABO, Kell...) on which come off the highest percentage of frequency and sensitization in practice.

References

1. Harmening DM, Taghizadeh M. The Lewis System. In Harmening DM, (ed): Modern Blood Banking and Transfusion Practices. FA Davis, Philadelphia 1994, pp. 133-145.
2. Pittiglio DH. Genetics and Biochemistry of A,B,H, and Lewis antigens. In Wallace ME and Gibbs FL (eds.). Blood Group systems: ABH and Lewis. Arlington, VA, American Association of Blood Banks. 1986; 1-56.
3. Dracker RA, Lauenstein KJ, Davey FR. Immunohematology. In Nelson DA, Tomar RH, Washington JA (eds.): Clinical Diagnosis and Management by Laboratory Methods. WB Saunders Co., Philadelphia, 1991, pp. 992-993.

4. Widman FK Technical Manual, 9th edition. Arlington, VA, American Association of Blood Banks, 1985.
5. Gabbe: Obstetrics - Normal and Problem Pregnancies, 4th ed New York, NY, Churchill Livingstone; 2002.
6. Balint B. Transfuzija krvi. ZUNS Beograd, 2004; 105-8.
7. Hauser R. Lea and Leb tissue glycosphingo-lipids. Transfusion 1995; 35, 577-581.
8. Campos MM, Miranda MJ, Fleming R., Galvao M. Change of the antigenic Le a expression in pregnancy. Vox sang 1995; 68;254.
9. Moilison PL. Blood transfusion and clinical medicine. Oxford, BSP 1997. 128-135.
10. Henry S, Oriol R, Samuelsson B. Lewis Histo-blood group system and Associated Secretory Phenotypes. Vox Sang 1995; 68; 254.