Short Communication

HOSPITAL PHARMACOLOGY
International Multidisciplinary Journal

ISSN 2334-9492 (Online)

Hospital Pharmacology. 2019; 6(2):794-799

UDC: 615.38.06:616-09

doi:10.5937/hpimj1902794N

The Role of the Kidd-Antibodies in Posttransfusion Reactions

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SUMMARY

Topic: The Kidd blood group (Jk) was discovered in 1951 and according to International Society for blood transfusion (ISBT) the Kidd (Jk) blood group is registered under the number 009. Antigens of the Kidd system are detected only on RBCs and kidney. Incompatibile transfusion in Jk blood group can provoke sensitization and appearance of anti-Jka or anti-Jkb antibodies. Jk antibodies are common cause of delayed hemolytic transfusion reactions (DHTRs). Although Kidd antibodies can lead to acute reactions, kidney damage and hemoglobinuria are very rare. More important is Kidd-antibody ability for delayed hemolytic reactions. The aim is to underline Jka antibodies laboratory characteristics, their role in delayed posttransfusion reactions and possible complications of blood transfusions.
The topic position in scientific/professional public: Kidd-antibodies, usually, destroy transfused red cells after a variable period of between 7 and 21 days. DHTR is the result of anti-Jka antibodies tendency to fall rapidly to undetectable levels even after incompatible transfusion. Anti-Jka has been reported as reason for kidney transplant rejection. There were examples of anti-Jka that react only when preservatives such as p-hydroxybenzoic acid (parabens), Na-azide or related compounds, antibiotics are present in the reaction mixture. Also, patient's therapy with antibiotics and monoclonal antibodies could cause false positive RBC antibody.
Further action needed for better topic covering in future: Except in life threatening condition, reduction of allogenic blood transfusion is recommended. Increase the number of autologous transfusions in all cases when the patient's clinical condition allows. Antigen-free RBC ie universal RBC would be the best choice for transfusion. It is essential to perform extended erythrocyte phenotyping prior to initiation of monoclonal antibodies therapy. As a minimum blood typing for Rh, K, Jka,Jkb, Fya, Fyb and Ss antigens should be done for every patient who is planned to be treated with monoclonal antibodies.Overcoming this problem is very important for patients who are transfusion-dependent or candidates for monoclonal antibody therapy, or candidates for kidney transplantation.

Keywords: transfusion, Kidd system, Jka antibodies, parabens, transplantation, antibiotics

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TOPIC

The Kidd blood group (Jk) was discovered in 1951 and according to International Society for blood transfusion (ISBT) the Kidd (Jk) blood group is registered under the number 009. It was named after a patient, a pregnant woman Mrs. Kidd [1]. Antigens of the Kidd system are detected only on RBCs and kidney [2,3]. They are carried by an integral membrane glycoprotein, which transports urea through the RBC's membrane [4]. Jka antigen is known as urea transporter UT-B (synonyms: UT3, UT11) [5]. Kidd antigen and UT-B are coded by gene chromosome 18q11-q12 [6]. The null phenotype Jk(a-b-) is usually results from homozygosity for a silent gene at the Jk locus and it is rare in most populations. Incompatibile transfusion in Jk blood group can provoke sensitization and appearance of anti-Jka or Jkb antibodies [7-9]. Jk antibodies are common cause of delayed hemolytic transfusion reactions (DHTRs) [8]. Alloimmunization is more common in females (2.38%) than males (1.68%). One in 1200 transfused patients experience a delayed haemolytic transfusion reaction [10,11].

It is quite intriguing for clinical practice that in approximately 50% of patients with detected Jka antibodies neither clinical nor laboratory signs of transfusion hemolytic reaction were not found [10,11]. Clinical and laboratory signs of a haemolysis reaction will not be demonstrated in 2 cases: 1) if the present Ig antibodies belong to the IgG2 or IgG4 class, which do not bind complement, and 2) in cases of detecting positivity to Jka, in fact, it is a reaction caused by preservatives present in using reagents. The aim is to underline Jka antibodies laboratory characteristics, their role in delayed posttransfusion reactions and possible complications of blood transfusions.

THE TOPIC POSITION IN SCIENTIFIC/PROFESSIONAL PUBLIC

Anti-Jka and anti-Jkb are uncommon. They are usually warm-reacting IgG1 and IgG3 but may also include IgG2, IgG4 or IgM. Approximately 50% of anti-Jka and anti-Jkb antibodies are capable of binding complement [12]. Kidd antibodies have a tendency to fall rapidly to low or undetectable levels in the plasma, therefore they are often difficult to detect in pretransfusion testing. The Kidd antibodies react better on antiglobulin testing with polyspecific anti-IgG + anti-C3d as well as with monospecific anti-C3d since they are usually detected indirectly through the complement as they bind to RBCs. These antibodies usually give stronger hemagglutination with enzyme treated test red cells [13]. Anti-Jka antibodies show antigen dosage effect, so the most anti-Jka react more intensely with Jk(a+b-) red cells than Jk(a+b+) red cells. Kidd system antibodies are noted, in developing an anamnestic response to the antigen [8,14].

Anti-Jka antibodies may cause acute and delayed hemolytic transfusion reactions (DHTR). Although Kidd antibodies can lead to acute reactions, kidney damage and hemoglobinuria are very rare [15]. More important is Kidd-antibody ability for delayed hemolytic reactions. Kidd-antibodies, usually, destroy transfused red cells after a variable period of between 7 and 21 days [8,16].

DHTRs commonly result in posttransfusion jaundice and may significantly reduce the patient's hemoglobin level [8]. Patients may be free of any hemolytic reactions when bilirubin and lactate dehydrogenase are in the normal range, so then we are talking about laboratory DHTR. DHTR is the result of Jka antibodies tendency to fall rapidly to undetectable levels even after incompatible transfusion. It is known from literature that one-third of DHTR is caused by anti-Jka antibodies [8,10,17,18]. For this reason, it is essential to perform crossmatch before each transfusion, because this is the only way to discover anamnestic (memory) RBC antibodies [8,14]. Anti-Jka has been reported as reason for kidney transplant rejection [19]. In patient noncompliant with immunosuppressive regimes, acute graft rejection occurred simultaneously with the occurrence of a Kidd antibodies [20,21]. Overcoming this problem is very important for patients who are transfusion-dependent or candidates for monoclonal antibody therapy, or candidates for kidney transplantation [22,23].

Preservatives Na-azide and esters of parabens, and antibiotics are added to commercially available LISS(C-LISS)® to prevent microbial growth [24-26]. The additives used for the storage, preservation, and coloring of blood bank reagents can be a source of false

positive agglutination reactions [27]. Agglutination of red blood cells used for blood typing, antibody detection and identification may be related to the presence of these materials in blood bank reagents. These substances include acriflavin and other dyes; antibiotics, such as penicillin and neomycin; EDTA; caprylate; and occasionally saline [27,28]. There were examples of anti-Jka that react only when preservatives such as p-hydroxybenzoic acid (parabens) or related compounds are present in the reaction mixture [29-31]. Antibodies against preservatives like Na-azide were also reported [30,32]. When results are inexplicitly positive by using commercially reagents, the solution could be to repeat immunohematological tests using saline instead of LISS, and additionally wash commercially RBCs [24,33].

Antibiotics used for classic patient therapy and antibiotics added to blood groups reagents for immunohematological transfusion testing could be false positive to RBC antibodies [34] The most frequent antibiotics used as a preservative in diluents for commercial RBCs reagents, such as chloramphenicol, neomycin sulfate, co-trimoxazole, and gentamycin could cause false positive RBC antibodies (Ab) [26,35]. In these cases of false positive RBC Ab there were no clinical or laboratory evidence of hemolysis [5,18,26,34,36].

Antigen-free RBC ie universal RBC would be the best choice for transfusion, and using specific monoclonal antibodies would be the therapeutic choice in patients who are sensitive to erythrocyte antigens [37,38]. It is recommended, prior to initiate monoclonal antibody therapy, along with baseline ABO, RhD, DAT and IAT, to perform extended RBC phenotype: Rh, MNSs, Kell, Kidd and Duffy blood group systems. Extended RBC phenotyping is important in the provision of phenotype-matched RBC for future transfusions and thus reduces the possibility of RBC antibodies formation [22,23]. Phenotyping may be inaccurate if a patient has received a blood transfusion in the previous 3 months [39,40]. In this case, the genotype is unaffected, and blood group genotyping is the method of choice [22,41,42].

Obviously, these can be confusing or may be a source of problems in the interpretation of results in various ways. Due to the low incidence of existing undiscovered Kidd antibodies, the authors suggest a multicentric academic observation studies, that would save the data in database which give the chance to upgrade the guidelines. Data exchange among world-renowned experts would make this problem more understandable and easier to fix [43-45].

FURTHER ACTION NEEDED FOR BETTER TOPIC COVERING IN FUTURE

Except in life threatening condition, reduction of allogenic blood transfusion is recommended. Increase the number of autologous transfusions in all cases when the patient's clinical condition allows.

Antigen-free RBC ie universal RBC would be the best choice for transfusion.
Using specific monoclonal antibodies against RBC antibodies would be the therapeutic choice in patients who are sensitized to erythrocyte antigens.

Transfusiologist has to perform crossmatch in order to make transfusion decision, because this is the only way to discover unexpected RBC antibodies.

It is essential to perform extended erythrocyte phenotyping prior to initiation of monoclonal antibodies therapy or renal transplantation. As a minimum blood typing for Rh, K, Jka,Jkb, Fya, Fyb and Ss antigens should be done for every patient who is planned to be treated with monoclonal antibodies.

In patients treated with monoclonal antibodies who were already transfused in the last 3 months period, the method of choice would be genetic blood group testing.

Multicentric academic observation studies would form database which will upgrade the blood transfusion guidelines in testing and improve transfusion safety.

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Uloga Kidd-antitela u posttransfuzijskim reakcijama

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KRATAK SADRŽAJ

Tema: Kidd krvnogrupni sistem je otkriven 1951. godine, a po Internacionalnom udruženju za transfuziju (ISBT) Kidd krvno grupni sistem je registrovan pod brojem 009. Antigeni Kidd sistema su detektovani na eritrocitima i u bubrezima. Incompatibilna transfuzija u Kidd sistemu dovodi do senzibilizacije i formiranja anti-Jka ili anti-Jkb antitela. Anti-Jka antitela retko mogu dovesti do akutne reakcije pa i oštećenja bubrega i hemoglobinurije. Najčešće anti-Jka antitela dovode do odložene hemolitičke transfuzijske reakcije. Cilj rada je da se naglase karekteristike anti-Jka antitela, njihova uloga u posttransfuzijskoj reakciji i mogućim kliničkim komplikacijama.
Pozicioniranje teme u medicinskoj stručnoj javnosti: Kidd antitela obično razaraju transfundovane inkompatibilne eritrocite u periodu od 7 i 21 dan. Odložena transfuziona hemolitička reakcija je posledica osobine anti.Jka antitela da brzo padnu do nemerljivih nivoa čak i nakon inkompatibilne transfuzije. U literature su opisani slučajevi odbacivanja transplantovanog bubrega u slučajevima pojave anti-Jka antitela. Takođe, postoje slučajevi kada se anti-Jka antitelo detektuje samo u prisustvu konzervansa kao šro su parabeni, Na-azid i druge supstance iz ove grupe; antibiotika koji su dodati u komercijalne reagense.Takođe, kod pacijenata na terapiji antibiotcima ili monoklonskim antitelima, mogu se pri testiranju pojaviti lažno pozitivna anti-eritrocitna antitela.
Predlog budućih aktivnosti: Osim u životno ugražavajućim stanjima, potrebno je redukovati primenu alogene krvi. Klinički je opravdano povećati broj autolognih transfuzija u slučajevima kada stanje pacijenta to dozvoljava. Najbolji izbor bi bio primena univerzalnih eritrocita koji su lišeni eritrocitnih antigena. Kod svih pacijenata planiranih za terapiju monoklonskim antitelima ili za transplantaciju bubrega neophodno je uraditi proširenu fenotipizaciju eritrocita. Smatra se minimumom fenotipizacija na Rh, K, Jka, Jkb, Fya, Fyb i Ss antigene.

Ključne reči: transfuzija, Kidd sistem, Jka antitela, parabeni, transplantacija, antibiotici

Received: July 02, 2019
Accepted: July 27, 2019