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ORIGINAL RESEARCH

TRANSFUSION

Reduction of anti-K-mediated hemolytic disease of newborns after the introduction of a matched transfusion policy: A nation-wide policy change evaluation study in the Netherlands

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Abstract

Background: During pregnancy, maternal red blood cell (RBC) antibodies can lead to life-threatening fetal hemolysis and anemia. Women can become immunized by a pregnancy or an unmatched transfusion. Our aim was to quantify the effect of a nationwide K-matched transfusion policy for women of childbearing age potential to prevent K-immunization in pregnancy.

Study Design and Methods: In this nation-wide policy change evaluation study we determined the occurrence of RBC antibodies before and after introduction of a K-matched transfusion policy and evaluated the cause K alloimmunization 10 years after introduction of this measure. K-matched transfusion for females under 45 years of age is advised in the Dutch transfusion guideline since 2004. We used laboratory data from pregnancies with RBC antibodies identified in the period 1999-2018 obtained as part of a population-based screening program in the Netherlands.

Results: Tests of 36 286 pregnancies produced a positive antibody screening result which concerned anti-K in 1550 pregnancies. The occurrence of anti-K decreased from 67.9 to 20.2 per 100 000 pregnancies. The relative risk reduction was 0.70 which largely exceeded the relative risk reduction of 0.27 for antibodies against RBC antigens for which no preventive matching is required. The number of pregnancies at risk for anti-K-mediated disease decreased from 9.7 to 4.2 per 100 000 pregnancies.

Conclusions: A K-matched transfusion policy is associated with a major decrease in a number of pregnant women with anti-K and pregnancies at risk for anti-K-mediated disease. A relatively simple measure is now shown to impact prevention of hemolytic disease in the fetus and newborn.

1 | INTRODUCTION

Maternal antibodies against the K (KEL1 and often referred to as Kell) blood group antigen on the fetal RBCs can lead to life-threatening hemolytic disease of the fetus and newborn (HDFN).[1] Anti-K-mediated HDFN has a severe disease course in over 50% of cases[2] and is after anti-D, the second most important antibody in causing severe HDFN. During pregnancy severely affected fetuses need to be treated with intrauterine transfusion to prevent a fatal outcome. In fact, compared to anti-D, in anti-K complicated pregnancies intrauterine transfusions are needed 3.5 times more often, and the first intrauterine transfusion is given 3 weeks earlier in pregnancy.[3] Also after birth, transfusions are often needed in the first months of life.[4]

A pregnant woman can have RBC antibodies, such as anti-K, due to a previous pregnancy or due to a RBC transfusion.[5–7] To prevent RhD alloimmunization, RhIg prophylaxis is given to an RhD-negative mother during and after pregnancies with an RhD-positive child and transfusions to RhD-negative women are RhD-matched. Prophylaxis to prevent K alloimmunization in pregnancy does not exist and thus in theory only a K-matched transfusion policy can lower the frequency of K alloimmunization in pregnancy. However, the efficiency of this measure has been questioned and has yet not been implemented in all western countries.[8–10] Although the high immunogenicity of the K antigen[11–14] leads to a high number of women developing anti-K after a K-positive transfusion, this will only lead to anti-K-mediated HDFN in a minority of cases. Due to the 9% prevalence of the K-antigen in the Caucasian population, a K-negative woman has only a 4.5% chance that a subsequent pregnancy will concern a K-positive fetus. A recent international observational study compared the cause of K alloimmunization in pregnant women treated in tertiary care centers for HDFN and found no effect of a K-matched transfusion policy.[10] Given the disease severity of anti-K-mediated HDFN and the ample availability of K-negative units since 91% of Caucasian donors are K-negative, many blood centers and hospitals have implemented or are considering the implementation of a K-matched transfusion policy.[9,15–18] To provide our experience and herewith to contribute to this decision, we performed a nation-wide policy change evaluation study. Our aim was to estimate the reduction in anti-K antibodies in pregnancy and the risk of anti-K-mediated HDFN since the introduction of a national K-matched transfusion policy for women of childbearing potential in 2004.

2 | MATERIALS AND METHODS

2.1 | Study design

We performed a nation-wide policy change evaluation study to evaluate the effect of a change in transfusion policy introduced in 2004, aimed to prevent K alloimmunization among pregnant women. We used laboratory test results on RBC antibodies and K-type of women, their partners and children, which are obtained as part of a nation-wide population screening program covering the period 1999-2018, as outlined later under "Occurrence of RBC alloantibodies in pregnancy" and "Occurrence of anti-K in pregnancies with a risk for a K-positive fetus." In part of the cohort, taken 10 years after introduction of the preventive K-matching measure (2013-2015), we evaluated the cause of K alloimmunization by a structured telephone interview with alloimmunized women (see "Cause of K alloimmunization"). Data on pregnancy outcome were not routinely available and not collected during this study.

2.2 | Setting

In the Netherlands a free-of-charge population screening program is offered to every pregnant woman early in pregnancy (before week 13). This comprises of screening for RBC alloantibodies, typing for ABO, RhD, and Rhc antigens, and screening for infectious diseases. The program is coordinated by the National Institute for Public Health and the Environment (RIVM) and 99% of pregnant women participate.[19] If a positive RBC antibody screening result is obtained in a local laboratory, the sample is sent to one of the two designated Dutch reference laboratories for confirmation and determination of the antibody specificity: Sanquin Diagnostic Services in Amsterdam (~90% of Dutch pregnancies) and the transfusion laboratory from the University Medical Centre Groningen (UMCG) (~10% of Dutch pregnancies). Screening for RBC alloantibodies in the Netherlands is mainly performed by Bio-Rad (Bio-Rad Laboratories, Hercules, CA, USA), Ortho BioVue (Ortho Clinical Diagnostics, Raritan, NJ, USA), or Cellbind (Sanquin Reagents, Amsterdam, The Netherlands) column agglutination techniques. During the time period considered for the study, antibody identification remained unchanged and was performed using polyethylene glycol (PEG) indirect antiglobulin tests and column agglutination techniques. If a clinically relevant RBC alloantibody such as anti-K is detected phenotyping of the father for the

relevant antigen (eg, K) or genotyping of the fetus is performed, using cell-free fetal DNA from maternal plasma[20] to judge the risk for HDFN.

K-matched transfusion was possible from 1999 onward with the donor's K-type label printed on all blood products. The transfusion guideline prescribes K-matched transfusion for women under 45 years of age since 2004, however, some hospitals already implemented this policy before 2004. To assess the year of implementation, an inquiry was sent to the blood transfusion committee in each of the 85 Dutch hospitals. Data on blood use in hospitals was obtained from the Sanquin Blood Bank[21] and was used to determine the proportion of K-matched transfusion over time.

The occurrence of alloimmunization could be influenced by the number of pregnancies over time. A reduction in this number lowers the risk for alloimmunization because only a previous pregnancy will lead to anti-K detectable early in pregnancy. Besides, a previous delivery is a risk factor for an incompatible transfusion.[5] A lower number of pregnancies also limits the possibility to detect alloimmunization in a subsequent pregnancy. Therefore, the number of first pregnancies, the number of pregnancies per women, and the total number of pregnancies in the Netherlands, were obtained from Statistics Netherlands (CBS).[22] From the birth rate, the number of pregnancies was calculated by correction for miscarriages after the first trimester antibody screen using a miscarriage rate of 3.8%.[19] Regional birth rates for the nine provinces for which Sanquin Diagnostic Services performs antibody testing were calculated from the nation-wide birth rate and the number of children born alive in these provinces. To adjust for changes in the national pregnancy rate, the yearly numbers of pregnancies were used to express the number of antibodies as occurrence per 100 000 pregnancies.

2.3 | Occurrence of RBC alloantibodies in pregnancy

The data set was derived from the Sanquin Diagnostic Services Laboratory Information System for the period January 1, 1999 to December 31, 2018. The more restricted transfusion policy with an accepted hemoglobin threshold of 4 mmol/L or less for healthy women as advised in the transfusion guideline of 2011 could have resulted in a reduced overall risk for transfusion induced alloimmunization.[23] Therefore, we compared the occurrence of anti-K antibodies in comparison to other type of RBC alloantibodies for which no preventive matching is required. Variables were: the RBC antibody screen in pregnancy was performed as part of the population screening program, the presence of anti-K and the year of its detection, the year of first detection of anti-K (study group) or the presence of another type of RBC alloantibody for which no preventive policies are in place: anti-Fy^a, Fy^b, Jk^a, Jk^b, S, or s (reference group) and the moment of detection of these antibodies. Pregnancies from women with both anti-K and an antibody in the reference group were counted in both groups. Pregnancies with other antibodies were not included because it either concerned antibodies for which other preventive measures were in place (anti-D immunoglobulin prophylaxis and a matched transfusion policy for c and E since 2011), there was no routine detection (eg, anti-Wr^a), or confirmation tests were negative.

2.4 | Occurrence of anti-K in pregnancies with a risk for a K-positive fetus

Pregnancies with anti-K were studied separately using the combined data from both reference laboratories to determine the nation-wide reduction in pregnancies from women that were at risk for anti-K-mediated HDFN, hence with a K-positive father, and with anti-K detected for the first time. Pregnancies at risk for HDFN were defined as pregnancies with a K-positive typing result of the father or the fetus. We anticipated that not all K-typing results of fathers would be available in the registration at the reference laboratories, for example, because early miscarriage shortly after the first trimester antibody screen or because K negativity of the father as determined locally did not require further laboratory investigation. Since K-typing of the father was only missing in 6% of cases, the analysis was not adjusted for these missing data.

2.5 | Assessment of the cause of K alloimmunization

To evaluate the cause of anti-K formation we asked women with anti-K identified between January 1, 2013 and December 31, 2015 to participate in a structured telephone interview. Upon receipt of informed consent, the women were asked for previous transfusions and pregnancies including miscarriages, and whether previous pregnancies concerned the same fathers. Subsequently, transfusion data were collected from the treating hospitals and K-type of the involved donors was obtained from the Sanquin's blood bank management system eProgesa (MAK-system, Paris, France). When women had a previous transfusion as well as a previous possible K-positive pregnancy, the woman and her partner were asked for

informed consent to perform K genotyping of previous children using buccal swab DNA.

2.6 | Ethical approval

Pregnant women are informed about the tests and data registration of the population screening program by their obstetric care giver and a standard information flyer. Our observational cohort study was performed with pseudonymized data, which is allowed without informed consent according to the rules of the Dutch Medical Treatment Contracts Act (WGBO). To analyze the cause of K alloimmunization, obstetric care givers were informed and asked to send study information to the women involved with the question for consent. All studies were performed according to the privacy rules and the WGBO and as instructed by the Medical Research Ethics Committee (MREC) of the Leiden University Medical Center.

2.7 | Presentation of the data and analysis

The relative risk reduction (RRR) between the first and the last 5-year period was calculated for the occurrence of anti-K during pregnancy and the occurrence of first time K-alloimmunized pregnant women at risk for HDFN. To calculate the change in occurrence of the reference group of RBC alloantibodies the second 5-year period with the highest rate of occurrence was compared with the last 5-year period. The grouping in 5-year periods reduced variation in the first years after implementation of the screening program and before the K-matched blood transfusion policy was advised in the transfusion guideline in 2004, and thereby prevented an overestimation of the reduction of anti-K immunized pregnancies over time. Moreover, grouping also reduced variation because of the low occurrence of first time K-alloimmunized pregnant women at risk for HDFN.

3 | RESULTS

To evaluate the effectiveness of a K-matched transfusion policy for women under 45 years of age which was published in the Dutch blood transfusion guideline in 2004, we first determined its rate of implementation. Information on the year of actual implementation of the K-matched transfusion strategy was obtained from 65 (77%) of 85 hospitals, representing 85% of the national blood use. This measure was implemented in 31 hospitals before 2004, in 15 hospitals in 2004, and in 19 hospitals between 2004 and 2011. This represented 48%, 28%, and 24% of blood use respectively when considering the responding hospitals as being representative for the Netherlands. The year of implementation of the K-matched transfusion strategy as function of national blood use is shown in Figure S1.

From 1999 to 2018, from approximately 3.4 million screened pregnancies 36 286 antibody identifications were performed at Sanquin Diagnostic Services after a positive antibody screening result at one of the local laboratories (Table 1). Anti-K was detected in 1550 pregnancies and any (or a combination) of the reference group antibodies: anti-Fy^a, Fy^b, Jk^a, Jk^b, S, or s in 1834 pregnancies. In 76 pregnancies (4.9% of anti-K affected pregnancies) both anti-K as well as reference group antibodies were detected, and these were included in both groups. Anti-K was registered for the first time during pregnancy in 1080 out of the 1550 pregnancies.

3.1 | Occurrence of anti-K and other RBC antibodies

Figure 1 shows the decline in occurrence of anti-K alloantibodies over time and later start of this decline for the reference group of other type of RBC alloantibodies. The occurrence of anti-K in pregnancy was in the same range in the period 1998-2003 (Figure S2). The occurrence of anti-K in pregnancy decreased from 67.9 per 100 000 pregnancies in 1999-2003 to 20.2 per 100 000 pregnancies in 2014-2018 (Relative Risk Reduction = 0.70). Figure 1 shows that the reduction in anti-K was both earlier and much more profound compared to the change in occurrence of the set of reference RBC antibodies in pregnancy, which decreased from 64.0 per 100 000 in the 5-year period with the highest occurrence (2004-2008) to 46.9 per 100 000 in 2014-2018 (RRR = 0.27) (Figure 1). The decreased occurrence of reference group antibodies indicates that also other effects than antigen-matching of transfusions influenced the decline in the occurrence of

TABLE 1 Inclusion of pregnancies with anti-K or other type of RBC alloantibodies

Antibody identifications 1999-2018	**n = 36 286**
Study group: Pregnancies with anti-K*	n = 1550
First registered anti-K	n = 1080
Anti-K known from previous pregnancy or testing	n = 470
Reference group: Pregnancies with anti-Fy^a, Fy^b, Jk^a, Jk^b, S, or s*	n = 1834
Pregnancies with other antibodies	n = 32.978

*In 76 pregnancies (4.9% of anti-K affected pregnancies) there was anti-K as well as an antibody from the reference group present.

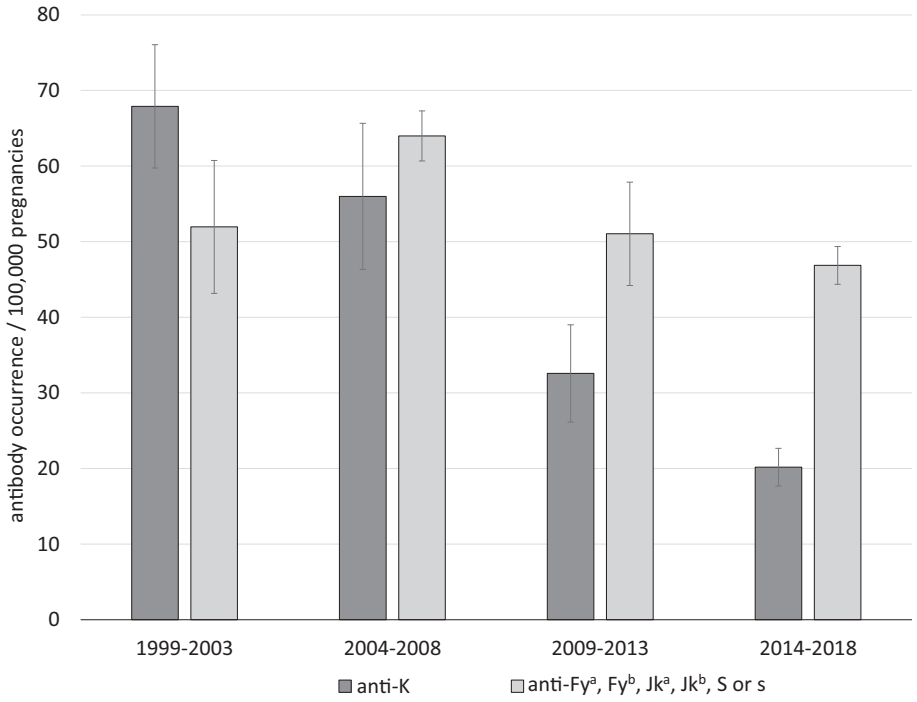

FIGURE 1 Occurrence of anti-K and reference antibodies per 100 000 pregnancies per calendar year

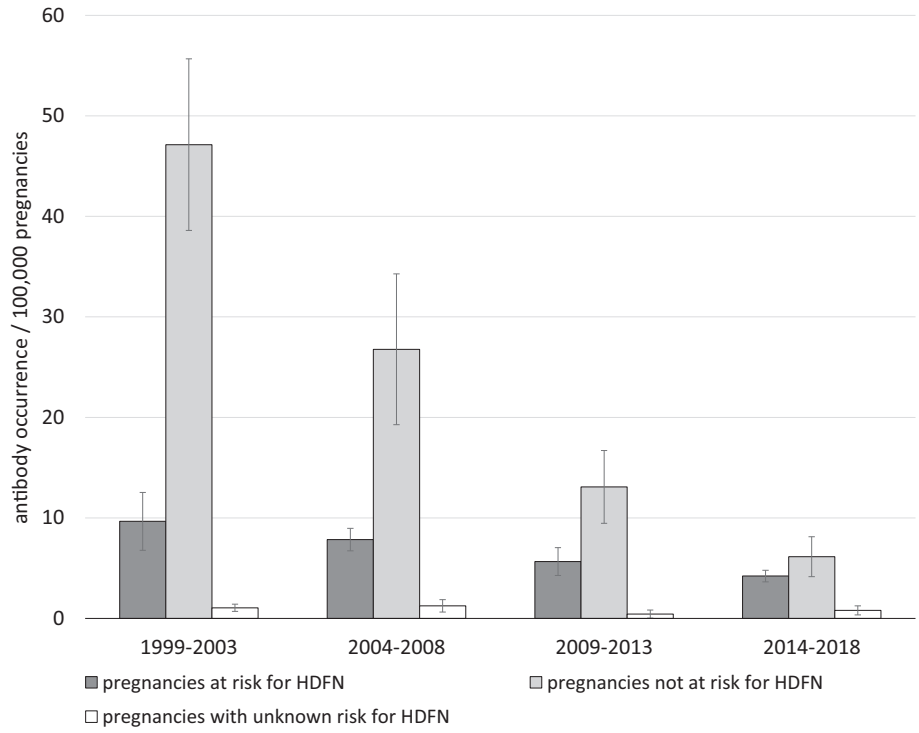

FIGURE 2 Occurrence of first time registered anti-K complicated pregnancies by risk for HDFN per calendar year

RBC antibodies. The occurrence of the separate antibody specificities is shown in Table S1.

3.2 | Occurrence of pregnancies at risk for anti-K-mediated HDFN

With the combined data from the two references laboratories (Table S2) we studied whether the K-matched transfusion policy also reduced the number of pregnancies from women with a pregnancy at risk for anti-K-mediated HDFN for the first time. In these pregnancies, anti-K may have been developed due to the contact with fetal cells in a previous pregnancy. In 264 of the 1218 (22%) pregnancies with first-time registered anti-K, the father or fetus were K-positive. The father was typed K-negative in 875 of these cases (72%) and in 79 (6%) the K-type of the father nor the fetus was known. Figure 2

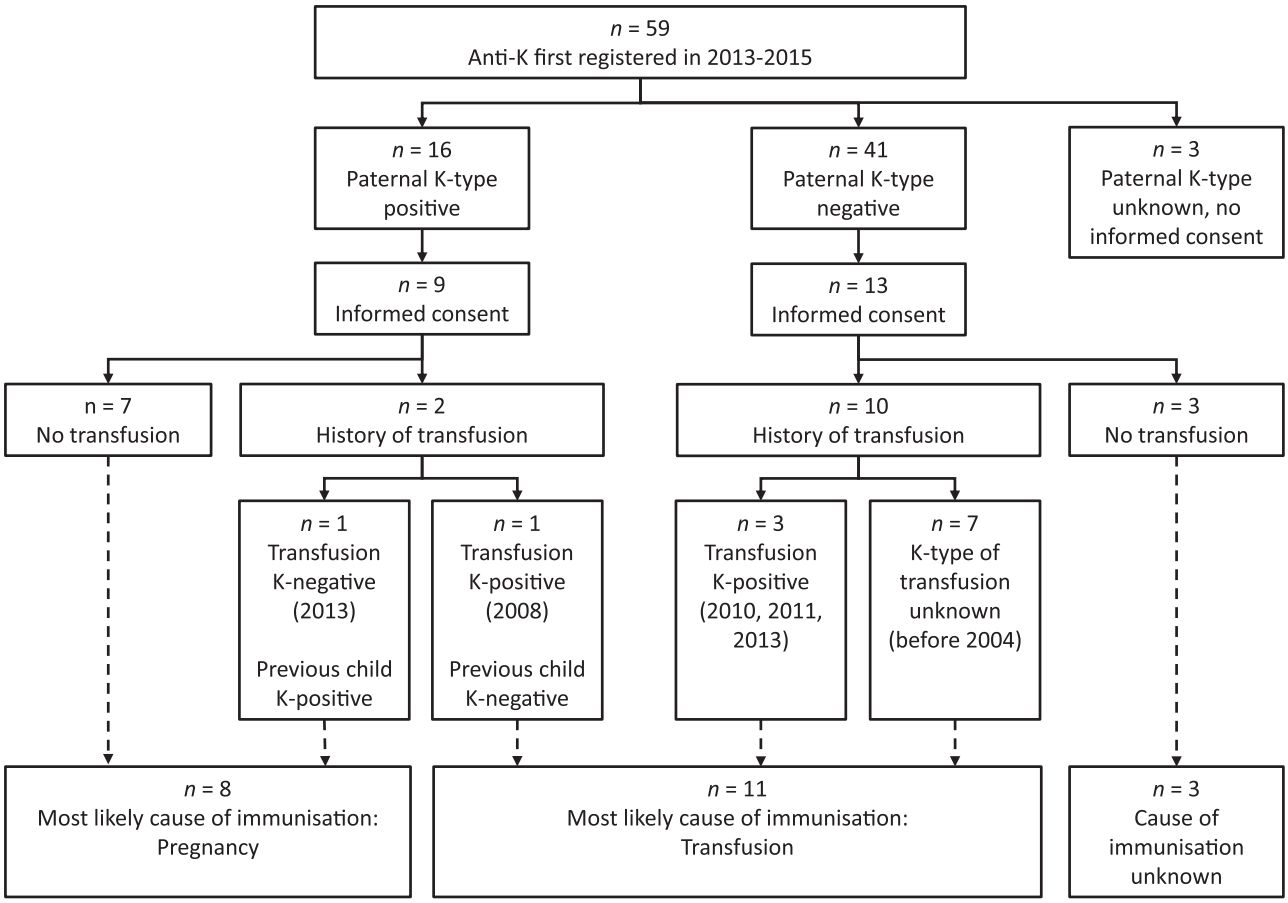

FIGURE 3 Most likely cause of K immunization of patients with first registered anti-K in 2013-2015

shows the occurrence of first time registered anti-K over time. As expected, we observed a more profound reduction in number of pregnancies with K-negative fathers compared to the group with K-positive fathers, because of the risk of alloimmunization by the foregoing pregnancy.

The occurrence of first time registered anti-K in pregnancies at risk for anti-K-mediated HDFN decreased from 9.7 per 100 000 pregnancies in 1999-2003 to 4.2 per 100 000 pregnancies in 2014-2018 (RRR = 0.56) (Figure 2). The occurrence of pregnancies with a K-negative father decreased from 47.1 per 100 000 pregnancies in 1999-2003 to 6.1 per 100 000 pregnancies in 2014-2018 (RRR = 0.87). Figure S3 shows the occurrence of first time registered anti-K cases per year.

3.3 | Cause of K alloimmunization in pregnancy

We estimated the cause of alloimmunization of women found to have anti-K in the years 2013 to 2015 to evaluate the cause of K immunization 10 years after the national policy change. First time registered anti-K was present in 59 pregnancies (Figure 3). Informed consent was given by 22 (37%) women while the others did not respond and may not have been reached. The paternal K-type was positive in nine of these 22 pregnancies. Eight of these women (36%) became immunized by a previous K-positive pregnancy: seven women were never transfused before and one was transfused with K-negative blood products only. Eleven women (50%) were most likely immunized by a K-positive blood unit. Ten women with K-negative partners received a transfusion and three of them became immunized by a documented K-positive product years after the K-matched transfusion policy change (in 2010, 2011, and 2013, respectively). One woman with a K-positive partner became immunized by a K-positive transfusion in 2008 and this resulted in HDFN in their first K-positive pregnancy. Partners of the remaining three non-transfused women were K-negative, and therefore the cause of immunization could not be determined. In the group of nine women with a K-positive partner and a previous pregnancy, only two (22%) had had an RBC transfusion previously, which points to a previous pregnancy as the main cause of K alloimmunization in this group.

4 | DISCUSSION

In this study a reduction in the risk for anti-K-mediated HDFN was seen after the introduction of K-matched transfusion for female patients of childbearing potential. We observed a decline from 67.9 to 20.2 women with anti-K per 100 000 pregnancies. A decrease in occurrence of anti-K in pregnant women who are for the first time at risk for anti-K-mediated HDFN was observed from 9.7 to 4.2 per 100 000 pregnancies.

A strength of the study is the large size of the cohort with unselected entry of pregnant women in the study after a routine screening as part of the national screening program.[19] Another strength is that possible effect modifiers, such as a more restricted transfusion policy and number of pregnancies, were considered. Also the number of first pregnancies and the number of pregnancies per women remained relatively stable over time (Figure S4). We expect these factors not to be of major influence on the occurrence of alloimmunization.

It is possible that the K-matched transfusion strategy also had an effect on alloimmunization against other red blood cell antigens, as described previously for anti-D formation in D-incompatible transfusions.[24] Therefore a decrease in reference antibodies might be partly explained by this phenomenon.

Previous studies were not conclusive about the effectiveness of a K-matched transfusion strategy in reducing occurrence of HDFN. O'Brien et al.[8] reported a single center study and observed a decline in anti-K, and studied the effect of K-matched transfusions on the occurrence of HDFN in a small cohort during 3 years after implementation, which was found to be too limited. Our study contains sufficient high numbers and a 20-year period of time to clearly demonstrate the decline of K alloimmunization both in the general pregnant population and in those with a risk to develop anti-K-mediated HDFN. The AMIGO study[10] reported the cause of immunization (ie, transfusion or previous pregnancy) of an international cohort including 78 pregnancies with anti-K and a K-positive child. Seventeen women (22%) had a transfusion in their medical history. This is much lower compared to the rate of transfusions in a general population with anti-K and this corresponds with our observations. In 2009 Koelewijn et al. reported that 46% of women with anti-K and a K-positive partner had a history of transfusion.[5] In our study we demonstrated a gradual increase of the effect of a matched transfusion on the rare occasion of HDFN due to anti-K alloimmunization. In line with the AMIGO study, in our 2013-2015 subcohort, in the group with a K-positive partner, a previous pregnancy is a much higher risk for K alloimmunization than a previous transfusion event, but still for one woman, K alloimmunization was transfusion induced. Also, a French study concluded that preventive K matching is effective in reducing K alloimmunization.[18,25] This study involved post transfusion patients and did not provide data about the pregnant population.

In the Netherlands with approximately 172 000 pregnancies yearly the prevalence of severe anti-K-mediated HDFN decreased to approximately 2-3 cases per year.[3] It is important to realize that our study shows that a K-matched transfusion policy not only results in fewer HDFN cases but also in an overall decline in anti-K cases detected during pregnancy. This means less laboratory costs of antibody identification during pregnancy, no delay in issuing blood in emergency situations around birth, no necessity to make a risk estimate on HDFN by typing fathers or prenatal K-typing, and less concern for pregnant women and their partners.

A limitation of the study is that the effect of a K-matched transfusion policy might be underestimated, because already before the introduction of K-matching the occurrence of anti-K in pregnancy was relatively low with 67.9 per 100 000 pregnancies compared to published numbers of 100 per 100 000 pregnancies in Canada.[6] This may be explained by the early introduction of K-matching in many Dutch centers before 1999. Another limitation is that we only had information on possible events leading to K immunization (eg, transfusion or previous pregnancy) in a subcohort. Therefore, we do not know if the minimum in anti-K-mediated burden in our pregnant population has been reached. As our study indicates, women with anti-K, who are pregnant nowadays, could still have been immunized by a transfusion before preventive K-matching was introduced or upon a recent transfusion. This demonstrates that compliance to the K-matched transfusion policy is not yet complete. In emergency situations regularly occurring around delivery, it is common practice to pre-select a set of group O, RhD-negative units, and not yet group O, RhD and K-negative units.

5 | CONCLUSIONS

We conclude that a K-matched transfusion policy for women of childbearing potential is associated with a significant reduction in occurrence of anti-K during pregnancy and also halves the risk of anti-K-mediated HDFN. Although our data indicates that it will take a long period time before a K-matched transfusion policy has completely abolished transfusion-induced anti-K in pregnant women, we now showed that it does contribute to a reduction of the risk for anti-K-mediated HDFN and thus lowers the number of severely ill babies. Since K-preventive matching can easily be achieved if the donor's

K-type is label printed, we strongly advocate to select K-negative blood products for all female transfusion recipients of reproductive age or younger.

AUTHOR CONTRIBUTIONS

M.d.H., J.L., H.S., and C.F. designed the study; J.L.,P.L., M.L., and H.M. collected data; J.L. performed the analysis; J.J.Z., M.J., C.E.v.d.S., and J.G.v.d.B. contributed to the analysis and review of the data; J.L., C.F., and M.d.H. have written the paper. M.d.H. is the guarantor.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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REFERENCES

1. de Haas M, Thurik FF, Koelewijn JM, van der Schoot CE. Haemolytic disease of the fetus and newborn. Vox Sang. 2015; 109:99–113.
2. Slootweg YM, Lindenburg IT, Koelewijn JM, Van Kamp IL, Oepkes D, De Haas M. Predicting anti-Kell-mediated hemolytic disease of the fetus and newborn: Diagnostic accuracy of laboratory management. Am J Obstet Gynecol. 2018;219:393 e1–e8.
3. Zwiers C, Oepkes D, Lopriore E, Klumper FJ, de Haas M, van Kamp IL. The near disappearance of fetal hydrops in relation to current state-of-the-art management of red cell alloimmunization. Prenat Diagn. 2018;38:943–950.
4. Ree IMC, de Haas M, Middelburg RA, et al. Predicting anaemia and transfusion dependency in severe alloimmune haemolytic disease of the fetus and newborn in the first 3 months after birth. Br J Haematol. 2019;186:565–573.
5. Koelewijn JM, Vrijkotte TG, de Haas M, van der Schoot CE, Bonsel GJ. Risk factors for the presence of non-rhesus D red blood cell antibodies in pregnancy. BJOG. 2009;116:655–664.
6. Goldman M, Lane D, Webert K, Fallis R. The prevalence of anti-K in Canadian prenatal patients. Transfusion. 2015;55:1486–1491.
7. Dajak S, Culic S, Stefanovic V, Lukacevic J. Relationship between previous maternal transfusions and haemolytic disease of the foetus and newborn mediated by non-RhD antibodies. Blood Transfus. 2013;11:528–532.
8. O'Brien KL, Kim YA, Haspel RL, Uhl L. Provision of KEL1-negative blood to obstetric patients: A 3-year single-institution retrospective review. Transfusion. 2015;55:599–604; quiz 598.
9. Solheim BG. Provision of K- (KEL1-) blood to women not more than 50 years of age. Transfusion. 2015;55:468–469.
10. Delaney M, Wikman A, van de Watering L, et al. Blood group antigen matching influence on gestational outcomes (AMIGO) study. Transfusion. 2017;57:525–532.
11. Evers D, Middelburg RA, de Haas M, et al. Red-blood-cell alloimmunisation in relation to antigens' exposure and their immunogenicity: A cohort study. Lancet Haematol. 2016;3:e284–e292.
12. Giblett ER. A critique of the theoretical hazard of inter vs. intra-racial transfusion. Transfusion. 1961;1:233–238.
13. Tormey CA, Stack G. Immunogenicity of blood group antigens: A mathematical model corrected for antibody evanescence with exclusion of naturally occurring and pregnancy-related antibodies. Blood. 2009;114:4279–4282.
14. Winters JL, Pineda AA, Gorden LD, et al. RBC alloantibody specificity and antigen potency in Olmsted County, Minnesota. Transfusion. 2001;41:1413–1420.
15. Blood Transfusion Guidelines. Federatie Medisch Specialisten. 2019. Available from: https://richtlijnendatabase.nl/richtlijn/bloedtransfusiebeleid/.
16. The appropiate use of group O D negative red cells, NHS Blood and Transplant (NHSBT) 2019. Available at: https://www.transfusionguidelines.org/document-library/documents/nbtc-appropriate-use-of-group-o-d-negative-red-cells-final-pdf.
17. *Guidelines for transfusion and immunohaematology laboratory practice*. Australian & New Zealand Society of Blood Transfusion Ltd (ANZSBT) 2020. Available at: https://anzsbt.org.au/guidelines-standards/anzsbt-guidelines/.
18. Arrêté du 4 août 1994 portant homologation du règlement de l'Agence française du sang relatif aux bonnes pratiques de distribution et pris en application de l'article L. 668–3 du code de la santé publique. *Journal Officiel de la République française*. 1994. Available at: https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000000732396.
19. van der Ploeg CPB, Schönbeck Y, Oomen P, Vos K. [Process monitoring prenatal screenings on infectious diseases and red blood cell alloimmunisation 2016]. National Institute for Public Health and the Environment (RIVM)/TNO. 2016. [Dutch] Available at: https://www.pns.nl/sites/default/files/2020-08/010634_113364_Monitor_PSIE_2016_V3_TG.pdf.
20. Scheffer PG, van der Schoot CE, Page-Christiaens GC, de Haas M. Noninvasive fetal blood group genotyping of rhesus D, c, E and of K in alloimmunised pregnant women: Evaluation of a 7-year clinical experience. BJOG. 2011;118:1340–1348.
21. Bloedkatern, use of blood products in the Netherlands. Sanquin Blood Supply, Amsterdam. 2015. [Dutch].
22. Geboorte; kerncijfers. Statistics Netherlands (CBS). 2019. Available from: www.cbs.nl.
23. CBO Blood Transfusion Guideline. CBO. 2011. Available at: http://www.isbtweb.org/fileadmin/user_upload/blood-transfusion-guideline.pdf.
24. Klein HG, Anstee D. Mollison's blood transfusion in clinical medicine. 11th ed. Oxford, UK: Oxford Blackwell Science, 2005;p. 79.
25. Moncharmont P, Barday G, Benamara H. Correspondants d'Hemovigilance et de securite transfusionnelle Auvergne

Rhone A. Low incidence of post-transfusion Kell (KEL1) alloimmunisation in patients under 50years old. Transfus Med. 2020;30(1):70–72.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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