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Evaluation of the confidential unit exclusion on Iranian blood donors: An 11-year experience

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Abstract:

BACKGROUND: Confidential unit exclusion (CUE) was recommended by the Food and Drug Administration to permit blood donors confidentially exclude their donation for transfusion. However, its effectiveness as a safety measure to the blood supply is debated.

AIMS: We, therefore, evaluated its benefit in identifying donors at risk of transmitting transfusion-transmissible infections (TTIs) and increasing blood safety in our population.

SETTINGS AND DESIGN: This was a cross-sectional and retrospective study. The study was performed at the South Khorasan Blood Transfusion Center.

MATERIALS AND METHODS: In this descriptive and retrospective study, data of CUE use and data of confirmed positive TTI markers were analyzed for the study period 2006–2016.

STATISTICAL ANALYSIS: Data were analyzed using SPSS software version 16.

RESULTS: Out of 165,267 donations, the CUE option was selected by 493 (0.3%) donors, most frequently by first-time blood donors, by men, by donors with <12 years schooling, and by 18–24-year-old donors. The data revealed that donations from CUE donors had no higher infection rates. Moreover, CUE showed low sensitivity (0.6%) and low positive predictive value (0.6%) in detecting TTI markers.

CONCLUSION: The data do not provide any indication of a safety advantage from CUE; thus, we recommend that the procedure of CUE can be discontinued.

Keywords:

Blood safety, confidential unit exclusion, donor risk factors

Introduction

Blood transfusion is a lifesaving procedure that can also have disastrous health consequences on recipients.^[1] There are steps toward obtaining a safe donation, including a predonation health history questionnaire, physical examination, and the laboratorial screening for the transfusion-transmissible infections (TTIs).^[2,3] Confidential unit exclusion (CUE), recommended by the Food and Drug Administration in 1986,^[4]

is a mechanism by which donors have the opportunity to confidentially exclude the donated unit from being used for transfusion.^[5] It has been considered that such an approach could be of great importance in countries where Nucleic Acid Technology (NAT) is not performed routinely,^[6] resulting in a longer TTIs window period and considerably greater transfusion risk.^[7]

In Iran, since 2003, the use of CUE is obligatory for all donations according to the guidelines of Iranian Blood Transfusion Organization (IBTO).^[8] Since NAT screening

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is not carried out routinely in IBTO, CUE seems to be useful in improving blood transfusion safety.^[6]

Few studies have been conducted on the efficacy of CUE in Iran which were usually regional during a short period and reported contradictory results.^[1,6,9] South Khorasan Province is the third largest province in Iran; however, no study has evaluated CUE effectiveness in this region.

Therefore, the aim of this study was to evaluate the efficacy of CUE procedure in identifying donors at risk of transmitting TTIs and increasing blood safety. Therefore, the prevalence of TTIs among blood donors was determined in CUE and non-CUE blood donors in South Khorasan Blood Transfusion Center (SKBTC). Moreover, the frequencies of the replies to the CUE were calculated with respect to age, gender, marital status, level of education, and donation status.

Materials and Methods

In this descriptive and retrospective study, the efficacy of the CUE option was evaluated among 165,267 voluntary blood donors who donated between 2006 and 2016 at the SKBTC. Demographic characteristics, CUE status, and the laboratory findings were extracted from a database representing all donations at SKBTC.

The clinically eligible donors completed a health assessment questionnaire and physical examination procedure. Donors were classified into three groups: first-time donors, repeat donors, and regular donors.

Prior to donation, donors were asked to confidentiality fill out the CUE form. This form has two options, and all CUE responses were divided into two groups: CUE positive and CUE negative. "CUE positive" denoting the option "My blood can be used for patients" and "CUE negative" denoting the option "My blood should not be used for patients."

The prevalence rates of hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, human T-lymphotropic virus (HTLV), and syphilis among first-time, regular, and repeat donors in both "CUE positive" and "CUE negative" groups were then calculated. The screening tests for hepatitis B surface antigen (HBsAg), HCV-antibody (Ab), HTLV, HIV, and syphilis (Ag/Ab) were done. Confirmatory tests were performed on all repeatedly reactive donations. Table 1 shows the screening and confirmatory test kits used in detection of TTIs.

Statistical analyses were carried out by using SPSS 16 software (IBM corporation, New York, USA), and comparisons of proportions were evaluated with Chi-square or Fisher exact tests. $P < 0.05$ was considered

Table 1: The screening and confirmatory test kits

Infection	Screening kits (manufacturer)	Confirmatory kits (manufacturer)
HBV	Enzygnost HBsAg 5.0 (Dade Behring)	HBsAg confirmatory test DiaSorin
	Enzygnost HBsAg 6.0 (Siemens)	Dade Behring
HCV	Anti-HCV (Avicenna)	HCV RIBA
	HCV 3.0 with enhanced SAve (Ortho)	Inno-LIA HCV Score (Innogenetics)
	Hepanostika HCV Ultra (Biomérieux)	HCV BLOT 3.0 (Genelabs) HCV Blot 3.0 (MP Diagnostics)
HIV	Anti-HIV I/II (Biotest)	HIV Western Blot
	Genscreen HIV 1/2 (Bio-Rad)	HIV Blot 2.2 (Genelabs) HIV Blot 2.2 (MP Diagnostics)
	Vironostika HIV Uniform II Ag/Ab (Biomérieux)	Inno-LIA HIV I/II Score (Innogenetics)
	Genscreen plus HIV Ag-Ab (Bio-Rad)	

HBV=Hepatitis B virus, HCV=Hepatitis C virus, HBsAg=Hepatitis B surface antigen

statistically significant. Rates of positive or negative CUE option were compared between age groups by means of a logistic regression model.

All experiments were performed in compliance with relevant laws and institutional guidelines. The study was approved by the Ethics Committee of the Birjand University of Medical Sciences.

Results

Over the 11 years of the study, there were 165,267 donations at the SKBTC from 2006 to 2016. The CUE option was selected by 493 (0.3%) donors, and 155,774 (99.7%) individuals did not choose the option. The data clearly show that donations from CUE donors had no higher infection rates. Accordingly, over the 11-year period, there were three HBsAg positive cases with the CUE designation. On the other hand, the prevalence of confirmed HBsAg among CUE-positive and CUE-negative donations was 0.63% (3/493) and 0.24% (406/164,793), respectively ($P = 0.11$, odds ratio [OR]: 2.45, 95% confidence interval [CI]: 0.79–7.67). All three CUE-positive infected donors were first-time, single, and male donors. No HCV, HIV, HTLV, or syphilis was found in CUE-positive donations. Table 2 compares the prevalence rates of TTIs among CUE-positive and CUE-negative donations.

CUE selection in the first-time donors was significantly higher than in regular ($P < 0.001$, OR = 44.33; 95% CI: 28.02–70.14) and repeat donors ($P < 0.001$, OR = 33.24; 95% CI: 17.18–64.29); however, the difference between regular and repeat donors was not statistically significant ($P = 0.47$, OR = 0.75; 95% CI: 0.34–1.66).

Variations in CUE positive according to demographic characteristics, including age group, gender, marital status, and level of education during the study are shown in Table 3. Most of the CUE-positive donors were in the range of 18–24 years ($P < 0.001$).

More male donors than female donors used the CUE option, and a significant correlation was identified ($P = 0.007$, OR = 1.77; 95% CI: 1.17–2.69). Likewise, a significant association was observed for marital status. Using details, among the 133,105 (80.5%) married donors and 32,162 single donors (19.5%), 231 (0.17%) and 262 (0.81%) were, respectively, CUE-positive donors; single donors were more likely than married donors to use the CUE ($P < 0.001$, OR = 0.21; 95% CI: 0.18–0.25).

In this study, the CUE rate was higher among donors with <12 years schooling. These donors were almost twice as likely to choose the CUE option as those with ≥ 12 years schooling ($P < 0.001$, OR = 1.98; 95% CI: 1.65–2.37). Finally, the use of CUE showed

extremely low sensitivity (0.6%) and positive predictive value (PPV) (0.6%) for detecting infection.

Discussion

In this study, the usefulness of CUE was assessed by comparing the prevalence rates of TTIs in CUE-positive and CUE-negative donations. In our study population, 0.3% (493/165,267) of all donors were marked as CUE positive which is within the previously reported range (0.15%–0.38%) of CUE utilization in developed countries.^[10] Higher rates have been described for Brazil^[7,11] and Iran.^[6,9,12] This higher frequency may be related to low socioeducational conditions of donors, CUE selection by mistake, lack of knowledge about the criteria for donation, and physicians' insufficient explanation about an appropriate use of CUE.^[9,11,13] The CUE-positive donor tended to be first-time blood donor, and 25–34 years which was in agreement with previous studies on the demographic properties of the CUE user.^[7,11] This higher rate in first-time and young donors might indicate that they are not adequately aware of CUE and its implications. A significant association was found between male gender and CUE selection. This could be due to the lower donation by women due to their fear and attitude of becoming anemic after blood donation.^[14,15] In the present study, the use of CUE was related to the donors' level of education, which was similar to the results of the studies in Iran^[12] and Brazil.^[7]

Our data revealed that the prevalence rate of HBV between the CUE-positive and CUE-negative groups was not statistically significant. There was no positive result for other infections in our study population. It was inconsistent with most of the previous studies indicating significant higher rates of TTIs in the CUE-positive group as compared to the CUE-negative group.^[5,7,11,12,16,17]

Table 2: Use of confidential unit exclusion and prevalence rates of transfusion transmissible infections

Marker	CUE use	Number of donations	Number of positives	Positive rate (%)
HBsAg	Negative	164,774	406	0.24
HBsAg	Positive	493	3	0.63
HIV	Negative	164,774	1	0.00
HIV	Positive	493	0	0.00
Syphilis	Negative	164,774	0	0.00
Syphilis	Positive	493	0	0.00
HCV	Negative	164,774	35	0.02
HCV	Positive	493	0	0.00
HTLV	Negative	164,774	45	0.02
HTLV	Positive	493	0	0.00

HCV=Hepatitis C virus, HBsAg=Hepatitis B surface antigen, CUE=Confidential unit exclusion, HTLV=Human T-lymphotropic virus

Table 3: Use of confidential unit exclusion and demographic characteristics of donors

Demographic characteristics	Donors	CUE positive, n (%)	OR (95% CI)	P
Age group (Years)				
18-24	7136	45 (0.63)	3.18 (2.24-4.53)	<0.001
25-34	61,611	316 (0.51)	2.58 (2.06-3.24)	<0.001
35-44	50,826	101 (0.19)	1.00	
45-54	32,553	19 (0.05)	0.29 (0.18-0.479)	<0.001
55-64	13,141	12 (0.09)	0.45 (0.252-0.835)	<0.01
Gender				
Male	152,098	470 (0.24)	1.77 (1.17-2.69)	0.007
Female	13,169	23 (0.28)		
Marital status				
Single	32,162	262 (0.23)	0.21 (0.18-0.25)	<0.001
Married	133,105	231 (0.25)		
Level of education				
<12 years schooling	41,935	198 (0.41)	1.98 (1.65-2.37)	<0.001
12 or more years schooling	123,332	295 (0.19)		

OR=Odds ratio, CI=Confidence interval, CUE=Confidential unit exclusion

Regarding the previous studies, the sensitivity and PPV of CUE vary between 0.7% and 5.6% and from 0.04% to 5.3%, respectively^[10]. Similar to our results, a low sensitivity and PPV were reported in Canada,^[18] Brazil,^[7] Iran,^[19] and the USA;^[5,20] however, higher figures have been reported by Farhadi *et al.*^[12] and OmidKhoda *et al.*^[6] It is of interest to note that, compared to other studies, our study has a major advantage due to the long period of the study; thus, the results would be more reliable.

Regarding PPV, the low amount might be related to the low prevalence of TTIs among all donations, thereby reducing the probability that a CUE-positive donation being positive for an infection.^[10] Furthermore, the prevalence of TTIs is lower among blood donors as compared to the general population,^[21] resulting to a lower PPV.^[10] Likewise, errors in the selection of the CUE options by donors could be another reason for the low PPV.^[5]

Similar to ours, there are many reports indicating the minimal effectiveness of the CUE system in detecting window period donations and further reducing the TTIs.^[5,10,11,16,18]

Further studies may be necessary to discover its real impact on TTIs reduction in donation procedure and on loss of safe donations. The validity of donors' declarations is also needed to be assessed. Therefore, we recommend a national study on the effectiveness of CUE.

Conclusion

CUE use was not associated with higher rates of TTI risk, so it adds no clear safety advantage in lowering the prevalence of TTIs, in the absence of NAT testing, in our donor population. Thus, we recommend that the procedure of CUE can be discontinued in SKBTC.

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Conflicts of interest

There are no conflicts of interest.

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