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

Mohammad Reza Ameli, Seyed Hossein Hosseini, Fariba Rad, Seyed Mehdi Sajjadi

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...
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 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).

### 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)   |                                 |
| 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) |
| HIV       | Anti-HIV I/II (Biotest)        | HIV Blot 2.2 (Genelabs)         |
|           | Genscreen HIV 1/2 (Bio-Rad)    | HIV Blot 2.2 (MP Diagnostics)    |
|           | Vironostika HIV Uniform II Ag/Ab (Biomérieux) | Inno-LIA HIV II Score (Innogenetics) |
|           | Genscreen plus HIV Ag-Ab (Bio-Rad) |                                 |

HBV=Hepatitis B virus, HCV=Hepatitis C virus, HBsAg=Hepatitis B surface antigen
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 $\geq 12$ 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.

### 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

**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. Higher rates have been described for Brazil and Iran. 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.

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. 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.

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 and Brazil. 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.
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.[6]

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.

**Acknowledgments**

We would like to thank the staff of South Khorasani Blood Transfusion Center for their valuable contribution.

**Financial support and sponsorship**

None.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Kafi‑abad SA, Rezvan H, Abolghasemi H, Talebian A. Prevalence and trends of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus among blood donors in Iran, 2004 through 2007. Transfusion 2009;49:2214-20.
2. Dilsiz G, Venicesu I, Belen FB, Celik B, Ozturk G. Trends in hepatitis B and hepatitis C virus seropositivity among blood donors over 15 years screened in the blood bank of a university hospital. Transfus Apher Sci 2012;47:95-100.
3. Kleiman S, Williams AE. Donor selection procedures: Is it possible to improve them? Transfus Med Rev 1998;12:288-302.
4. FDA. Memorandum to Blood Establishments. Additional Recommendations for Reducing Further the Number of Units of Blood and Plasma Donated for Transfusion or for Further Manufacture by Persons at Increased Risk of HTLV-III/LAV Infection; 1986.
5. Zou S, Notari EP 4th, Musavi F, Dodd RY; ARCCNET Study Group. Current impact of the confidential unit exclusion option. Transfusion 2004;44:651-7.
6. Omidkhoda A, Gharehbaghian A, Jamali M, Ahmadbeigi N, Hashemi SM, Rahimi A, et al. Comparison of the prevalence of major transfusion-transmitted infections among Iranian blood donors using confidential unit exclusion in an Iranian population: Transfusion-transmitted infections among Iranian blood donors. Hepat Mon 2011;11:11-3.
7. de Almeida‑Neto C, Liu J, Wright DJ, Mendrone‑Junior A, Takecian PL, Sun Y, et al. Demographic characteristics and prevalence of serologic markers among blood donors who use confidential unit exclusion (CUE) in São Paulo, Brazil: Implications for modification of CUE policies in Brazil. Transfusion 2011;51:191-7.
8. Cheraghali A, Gharehbaghian A. Commentary: Effectiveness of confidential unit exclusion option in blood transfusion services needs reevaluation. Hepat Mon 2011;11:295-8.
9. Kasraian L, Karimi MH. A study on confidential unit exclusion at Shiraz blood transfusion center, Iran. Asian J Transfus Sci 2016;10:132-5.
10. Vandewalle G, Baeten M, Bogaerts K, Vandenekerkhove P, Compernolle V. Evaluation of 6 years of confidential unit exclusion at the belgian red cross also blood service. Vox Sang 2014;106:354-60.
11. Vogler H, Saito M, Spinosa AA, da Silva MC, Munhoz E, Reiche EM. Effectiveness of confidential unit exclusion in screening blood donors of the regional blood bank in Londrina, Paraná state. Rev Bras Hematol Hemoter 2011;33:347-52.
12. Farhadi E, Gharehbaghian A, Karimi G, Samiee S, Tavasolli F, Salimi Y. Efficacy of the confidential unit exclusion option in blood donors in Tehran, Iran, determined by using the nucleic acid testing method in 2008 and 2009. Hepat Mon 2011;11:907-12.
13. Kean CA, Hsueh Y, Querin JJ, Keating LJ, Allensworth DD. A study of confidential unit exclusion. Transfusion 1990;30:707-9.
14. Javadzadeh Shahshahani H. Why don’t women volunteer to give blood? A study of knowledge, attitude and practice of women about blood donation, Yazd, Iran, 2005. Transfus Med 2007;17:451-4.
15. Mousavi F, Tavabi AA, Golestan B, Ammar‑Saeedi E, Kashani H, Tabatabaei R, et al. Knowledge, attitude and practice towards blood donation in Iranian population. Transfus Med 2011;21:308-17.
16. Petersen LR, Lackritz E, Lewis WF, Smith DS, Herrera G, Raimondi V, et al. The effectiveness of the confidential unit exclusion option. Transfusion 1994;34:865-9.
17. Sajjadi SM, Pourfathollah AA, Mohammadi S, Nouri B, Hassanzadeh R, Rad F, et al. The prevalence and trends of hepatitis B, hepatitis C, and HIV among voluntary blood donors in Kohgiluyeh and Boyer‑Ahmad transfusion center, Southwestern Iran. Iran J Public Health 2018;47:944-51.
18. O’Brien SF, Fan W, Xi G, Yi QL, Goldman M. Evaluation of the confidential unit exclusion form: The Canadian blood services experience. Vox Sang 2010;98:138-44.
19. Kasraian L, Tavasoli A. Positivity of HIV, hepatitis B and hepatitis C in patients enrolled in a confidential self-exclusion system of blood donation: A cross-sectional analytical study. Sao Paulo Med J 2010;128:320-3.

20. Korelitz JJ, Williams AE, Busch MP, Zuck TF, Ownby HE, Matijas LJ, et al. Demographic characteristics and prevalence of serologic markers among donors who use the confidential unit exclusion process: The retrovirus epidemiology donor study. Transfusion 1994;34:870-6.

21. Cheraghali AM, Abolghasemi H. Plasma fractionation, a useful means to improve national transfusion system and blood safety: Iran experience. Haemophilia 2009;15:487-93.