Table 8 Main causes of transfusion error

	First survey[a]	Second survey[b]
Identification error	91	27
Phlebotomy error	4	2
Prescription error[c]	19	8
Testing error by doctor	21	10
Laboratory error outside of core hours	12	6
Laboratory error during core hours	5	4
Other	14	3
Total	166	60

[a]1 January 1995 to 31 December 1999.
[b]1 January 2000 to 31 December 2004.
[c]Blood components orders of incorrect ABO blood group.

or platelet concentrate orders of an incorrect ABO blood group sent to the laboratory were undetected by laboratory methods due to the omission of the minor cross-match. No reported prescription error was associated with an RCC major mismatch.

Testing error by doctors

Testing errors by doctors were reported in 13% of cases (21 of 166) in the first survey, and 17% (10 of 60) in the second. In hospitals where these errors arose, laboratory services for blood transfusion were not available.

Laboratory error outside of core hours

Laboratory errors outside of core hours were reported in 7% of cases (12 of 166) in the first survey, and 10% (six of 60) in the second. These errors included technical testing errors in 10 cases, issuance of the wrong units in four cases, and use of the wrong patient sample for testing in one case, and, in four cases the details of errors were not reported.

Laboratory error during regular (daylight) hours

Laboratory errors during regular (daylight) hours were reported in 3% of cases (five of 166) in the first survey, and 7% (four of 60) in the second. These errors included technical testing errors in three cases, clerical error in transcription in one case, issuance of the wrong units in two cases, and use of the wrong patient sample in three cases.

Other errors

In the first survey: a wrong blood type was displayed at the bedside in one case; 11 cases had no reports about the main cause; and in two cases, a main cause could not be clearly discerned. In the second survey, two ABO-incompatible bone marrow transplant recipients received the wrong blood, and in one other case, incompatible FFP was taken from an operating room refrigerator.

Discussion

Based on data from the second survey, the risk of ABO-incompatible transfusion and that of death is about half of those reported by Serious Hazards of Transfusion (SHOT) [1]. In Japan, at least 8000 hospitals transfuse blood, perhaps more if the smallest hospitals are counted, but this investigation focused on the hospitals responsible for about 80% of the blood products transfused in Japan. The Japanese Red Cross (JRC) is the only supplier of allogeneic blood components used in Japan. The collection of allogeneic blood by a hospital transfusion service is rare and permitted in emergency cases if the JRC has failed to supply the blood products to hospitals. The total amount of all blood components supplied by the JRC corresponded to the total amount of blood components transfused in Japan. In the fiscal year of 2004, when the second survey was done, the total amount of blood components supplied by the JRC Blood Center was 16 668 784 units, and the total amount of blood components transfused in the 829 hospitals which responded to the second survey was 7 962 317 units, with about 47·8% of blood components supplied by the blood centre.

ABO-incompatible blood transfusion arises from human error [8]. Eighty per cent of ABO-incompatible blood transfusions were reported from the clinical setting of a ward or operating room and 20% were reported from a laboratory. No reported errors were associated with blood banking procedures of the JRC. There were no mislabelling of units or, weak A or B antigens typed as O. This underscores the value of an incident reporting system that collects data from hospitals, and provides analytical feedback to each facility [9–11]. Identification errors between patients and blood products provoke most RCC major mismatch transfusions. Preventive efforts are important because these errors are eminently preventable. Many hospitals had their own transfusion procedural manual, including the final identification between patients and blood products in the clinical area. In many cases, procedural deviations occurred, including half of the hospitals that maintained their own procedures. Following the first survey, a standardized blood transfusion procedure manual emphasizing the final identification between patients and blood products was developed by the Japanese Society of Blood Transfusion, and this procedure has been widely propagated through distributing a poster showing the procedural manual by the Japanese Society of Blood Transfusion and JRC [6]. The second survey collected only about 30% as many identification errors as were reported in the first survey, even with the participation of an additional 251 hospitals. It may be that the dissemination of a standard procedure contributed to a decrease in identification error. This was the main intervention undertaken to reduce the incidence of ABO-incompatible transfusion after the first survey. However, incorrect blood recipient identification at

the patient's bedside persists as the main cause of ABO-incompatible transfusion. Education programmes may be helpful to the extent that they reach all staff involved in transfusion. This is challenging under the best of circumstances, and more so where staff turnover is high. It thus behooves us to monitor employment trends in the healthcare sector. Technological interventions also have the potential to interdict human error, provided that the technology is not bypassed for reasons of expediency or lack of understanding [12–15]. The introduction of electronic correlation of patients and blood products has progressed in large-scale hospitals. Pretransfusion testing out of core hours is another problem. In 7·5% of hospitals in the first survey, laboratory services for blood transfusion out of core hours were not available, thus forcing clinicians into the role of laboratory professionals. The number of facilities where a doctor performs pretransfusion testing outside of core hours decreased from the first survey, and the number of facilities where laboratory staff perform all testing increased. Even so, laboratory staff who do not routinely perform transfusion-related testing are likely to be more error prone than those who are devoted to the blood bank or transfusion service. These were the main differences between the two surveys.

The second national survey of ABO-incompatible blood transfusion was completed 5 years after first survey. Ideally, investigative data should be collected continuously and reported at least annually, as occurs in other countries with formal haemovigilance systems [1,2]. We aspire to blend the Japanese experience described herein with international best practices described elsewhere, with the ultimate goal of mitigating the needless morbidity and mortality arising from human error.

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Development and validation of a SYBR Green I–based real-time polymerase chain reaction method for detection of haptoglobin gene deletion in clinical materials

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BACKGROUND: Anhaptoglobinemic patients run the risk of severe anaphylactic transfusion reaction because they produce serum haptoglobin (Hp) antibodies. Being homozygous for the Hp gene deletion (HP^{del}) is the only known cause of congenital anhaptoglobinemia, and clinical diagnosis of HP^{del} before transfusion is important to prevent anaphylactic shock. We recently developed a 5′-nuclease (TaqMan) real-time polymerase chain reaction (PCR) method.

STUDY DESIGN AND METHODS: A SYBR Green I–based duplex real-time PCR assay using two forward primers and a common reverse primer followed by melting curve analysis was developed to determine HP^{del} zygosity in a single tube. In addition, to obviate initial DNA extraction, we examined serially diluted blood samples as PCR templates.

RESULTS: Allelic discrimination of HP^{del} yielded optimal results at blood sample dilutions of 1:64 to 1:1024. The results from 2231 blood samples were fully concordant with those obtained by the TaqMan-based real-time PCR method.

CONCLUSION: The detection rate of the HP^{del} allele by the SYBR Green I–based method is comparable with that using the TaqMan-based method. This method is readily applicable due to its low initial cost and analyzability using economical real-time PCR machines and is suitable for high-throughput analysis as an alternative method for allelic discrimination of HP^{del}.

Anaphylaxis is a severe nonhemolytic transfusion reaction, and determination of its cause is urgently needed.[1,2] The absence of a serum protein such as immunoglobulin A or haptoglobin (Hp) is one factor that can lead to anaphylactic transfusion reactions[1-4] due to production of serum antibodies against it.[5-7] At present, a homozygous deletion of the Hp gene (HP^{del}) is the only known cause of anhaptoglobinemia.[5,8]

Hp binds hemoglobin (Hb) to prevent both iron loss and kidney damage during hemolysis. Humans have a genetic polymorphism of the protein due to two codominant alleles, Hp1 and Hp2, that give rise to the three major phenotypes, Hp1, Hp2-1, and Hp2.[9,10] Because of its polymorphic nature, Hp has been used as a genetic marker for identification of individuals and determination of parentage. Anomalous inheritance of the Hp phenotypes was encountered during determinations of parentage, and HP^{del} was identified by genetic analyses of one such family in Japan.[8]

The HP^{del} allele lacks an approximately 28-kb segment of Chromosome 16 extending from the promoter region of the Hp gene to Intron 4 of the Hp-related gene (*HPR*).[5] Two different methods have been demonstrated to be useful for the detection of anhaptoglobinemia. One is detection

ABBREVIATIONS: Hp = haptoglobin; T_m = melting temperature.

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of HP^{del} allele by polymerase chain reaction (PCR) or Southern blotting,[8] and the other is quantification of Hp protein by enzyme-linked immunosorbent assay (ELISA).[11] The ELISA method is sensitive and able to discriminate efficiently between anhaptoglobinemia and hypohatoglobinemia. However, this method requires confirmation of the presence of HP^{del} by a PCR-based method. A duplex PCR method allows determination of the zygosity of HP^{del}. Using this method, frequencies of the HP^{del} allele were examined in several human populations. This allele has been found only in East and Southeast Asian populations (Chinese, Korean, Japanese, Mongols, Thais, and Indonesians) but not in African, West and South Asian, and European populations so far.[5,12-15] Detection of homozygotes for HP^{del} before blood transfusion or blood component infusion is important to prevent severe side effects of transfusion, because washed red blood cells and platelet concentrate are effective in preventing the transfusion-related anaphylactic reactions.[16]

Although isolation of genomic DNA, conventional PCR, and gel electrophoresis are routine methods in research and molecular biology laboratories, they are not suitable for large-scale analysis or diagnosis before transfusion in the clinical laboratory because they require laborious post-PCR processing steps. Real-time PCR is a high-throughput, rapid, and sensitive method that has become common.[17] It also eliminates post-PCR processing of PCR products, which reduces the chance of carry-over contamination. Recently we established a diagnostic method for detection of HP^{del} by a 5′-nuclease assay using dual-labeled (TaqMan) probes.[18] This method is highly specific due to the sequence-specific hybridization of the probe and is cost-effective when many samples are treated simultaneously, such as screening for anhaptoglobinemic patients in a blood donor pool or for large-scale screening in various populations. However, if only a few samples are examined in the clinical laboratory, the initial cost is high because two dual-labeled probes are necessary for determination of zygosity. In addition, multichannel real-time PCR machines, which are expensive compared to single-channel real-time PCR machines, are required to perform this system.

To resolve this problem, we developed a SYBR Green I–based real-time PCR method for detection of HP^{del}. SYBR Green I, an intercalating dye that binds to double-stranded DNA, is used to detect the accumulated PCR product.[17] Because an increase in the fluorescent signal is detected not only by specific amplification of the product but also by the primer-dimer or nonspecific amplified product, dissociation curve analysis is required to confirm the specificity of the PCR product. In addition, to reduce the time and cost of genomic DNA isolation, we examined serially diluted blood samples as PCR templates instead of genomic DNA.

MATERIALS AND METHODS

This study protocol was approved by the ethics committee of Kurume University School of Medicine. Fresh venous blood samples from patients who were scheduled for blood transfusion at Kurume University Hospital were used. The whole blood samples were collected in ethylenediaminetetraacetate (EDTA)- or heparin-containing tubes. We also used genomic DNA samples with known HP^{del} genotypes.

PCR was performed using the following three primers (two forward primers and one common reverse primer): Hpdel-F (5′-TATTTCTTTATGGCACTGGGGAACA-3′, sequence from 690 to 714 bp in GeneBank No. AB025320) for amplification of the regions encompassing the HP^{del} breakpoint, Hpr-F (5′-CTGCAACTATTGGAAATGAG ATCAGC-3′, sequence from 12,920 to 12,945 bp in GeneBank No. NC_000016.9, located in the 3′ end of the deleted region in HP^{del}, Intron 4 of the *HPR*) for amplification of *HPR* Intron 4, and the common reverse primer Hpdel-R (5′-GAGCAAGACACTCGTGAGTGGAAAT-3′, reverse sequence from 823-799 bp of GeneBank No. AB025320 and reverse sequence from 13,067 to 13,043 bp of GeneBank No. NC_000016.9). The HP^{del} breakpoint occurs between 782 and 783 bp in the sequence of GeneBank AB025320. The positions of the three primers are presented in Fig. 1. All primers were designed using computer software (Primer 3, http://primer3.sourceforge.net/).[19]

The amplification was performed in a volume of 20 μL containing 10 μL of 2× SYBR Premix Ex Taq II (perfect real time; Takara, Shiga, Japan), 75 nmol/L Hpr-F primer, 500 nmol/L Hpdel-690F, 250 nmol/L Hpdel-823R primer, and 1 μL of the template (severalfold diluted fresh venous whole blood or genomic DNA). Wells without a template were included as negative controls. For determination of optimal PCR conditions, amplifications were performed using a 96-well thermal cycler (Veriti, Life Technologies Japan, Tokyo, Japan). Determined optimal conditions in the real-time PCR are as follows: 1) place the 96-well plate in a real-time PCR system (Mx3000P, Agilent Technologies, Tokyo, Japan); 2) heat the plate at 95°C for 30 seconds; 3) repeat the following for 40 cycles, 95°C for 5

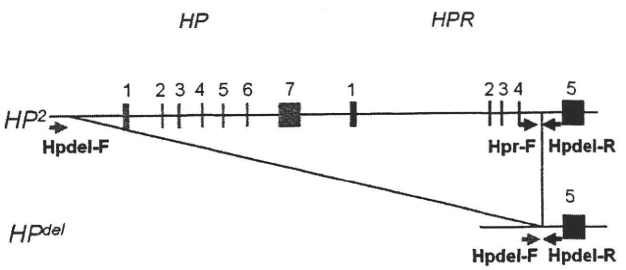

Fig. 1. Structures of the HP^2, and HP^{del} alleles and relative positions of the Hpdel-F, Hpr-F, and Hpdel-R primers.

seconds, and 65°C for 30 seconds; and 4) melting curve analysis performed as follows: heat the plate at 95°C for 1 minute, rapid cooling to 70°C, 70°C for 30 seconds, and heat the plate at 0.2°C/second to 90°C. The accumulation of PCR products and melting curve analysis were monitored by measurement of the level of SYBR Green I fluorescence with excitation/emission filters of 492/516 nm (using an FAM filter set).

After the dissociation curve analysis, we determined the length of PCR products using a microchip electrophoresis system (MCE-202 MultiNA, Shimadzu, Kyoto, Japan). In addition to SYBR Green I real-time PCR method, the zygosity of the *HP*^{del} allele was also determined in parallel using TaqMan-based real-time PCR method as described previously.[18]

RESULTS AND DISCUSSION

Duplex real-time PCR of *HP*^{del} and HPR

We investigated duplex real-time PCR, which permits discrimination of *HP*^{del} zygosity in a single tube, to determine if the melting temperature (T_m) values of the two PCR products are sufficiently different to distinguish them from each other. In the previously reported conventional PCR method, the lengths of the PCR products were 476 and 315 bp for detection of *HP* Exon 1 and *HP*^{del}, respectively.[5] These lengths are suitable and convenient for gel electrophoresis but too long to amplify in the buffer containing SYBR Green I, particularly when using a blood sample directly as a template. Thus, we planned to amplify smaller PCR products in the present SYBR Green I–based real-time PCR method. For detection of the nondeleted allele, we selected the 3′ end of the deleted region (Hpr-F; 107-82 bp upstream of the 3′ breakpoint of the *HP*^{del}) as a forward primer and reduced the length of the PCR product to 148 bp using a Hpdel-R primer as a reverse primer. We also reduced the length of the PCR product of the *HP*^{del} breakpoint to 134 bp using Hpdel-F as a forward primer and Hpdel-R.

To evaluate this real-time PCR method, genomic DNAs whose genotypes were already known to be lacking *HP*^{del} (*HP/HP*), heterozygous for *HP*^{del} (*HP/HP*^{del}), and homozygous for *HP*^{del} (*HP*^{del}/*HP*^{del}) were used as templates. We failed to establish an applicable duplex PCR method with similar peak intensities for *HP*^{del} and *HPR* signals when the three primers were adjusted to the same concentration (100-500 nmol/L). This is probably due to the apparent preferential binding of SYBR Green I to selected amplicons, as suggested previously.[20] Accordingly, we used several different ratios of concentrations of the three primers and obtained almost similar peak intensities for *HP*^{del} and *HPR* signals when we used 75 nmol/L Hpr-F, 500 nmol/L Hpdel-F, and 250 nmol/L Hpdel-823R primers. The annealing temperatures and number of cycles for two PCR assays for allelic discrimination of *HP*^{del} using blood samples were optimized to determine the PCR condition that gave the best specificity without a reduction in yield. The optimal annealing and extension temperature and numbers of cycles for both amplifications were found to be 65°C and 40 cycles, respectively (data not shown).

An increase in the fluorescent signal in the amplification plot was observed in all three samples tested. The dissociation curve analysis revealed a single peak (T_m = 84.3-84.7°C) corresponding to 148 bp of *HPR* Intron 4 product in genomic DNA samples from *HP/HP* individuals. Two different peaks (T_m = ~80.3 and 84.5°C) corresponding to the 134-bp *HP*^{del} product and *HPR* were observed in the genomic DNA sample from *HP/HP*^{del} individuals, while a single peak (T_m = 80.3-80.7°C) corresponding to the *HP*^{del} was observed in genomic DNA sample from the *HP*^{del}/*HP*^{del} individual (Fig. 2). After the dissociation curve analysis, microchip electrophoresis using MCE-202 MultiNA was performed and the characteristic length of PCR products for *HPR* Intron 4 at 148-bp (estimated sizes by microchip electrophoresis were between 156-159 bp) and the *HP*^{del} product at 134 bp (estimated sizes by microchip electrophoresis were between 140-142 bp) were detected (data not shown). No increase in the fluorescent signal was detected in the negative control (data not shown).

Evaluation of templates and plates

We then applied this method using a blood sample as a template. We first examined the effects of the anticoagulants in blood collecting tubes and dilutions of blood samples on the efficiency of PCR amplification. Blood was diluted with PCR grade water (later, we used 50 mmol/L NaOH instead of water, as mentioned below). Like the TaqMan real-time PCR method,[18] the SYBR Green I real-time PCR method worked well on blood samples collected in EDTA-containing tubes using 1 μL of undiluted and 1:4, 1:16, 1:64, 1:256, 1:1024, and 1:4096 dilutions of the whole blood sample as a template. The Ct values were not proportional to the amount of the blood template (Fig. 3). This is partly because both the fluorescence and the amplification seemed to be inhibited by blood component(s) such as Hb. Specific PCR products were observed in all blood samples diluted up to 1:1024 but not in the 1:4096 dilution. Instead, undesired PCR products with the T_m value of 76.8°C (as described below) were occasionally observed in 1:4096 dilution samples.

We also used heparin-containing tubes and observed almost identical results for the same serial dilutions of blood samples as those of EDTA-containing tubes (data not shown). These results suggested that blood sample dilutions between 1:64 and 1:1024 collected in both EDTA- and heparin-containing tubes seemed to provide a good template for this real-time PCR method. Thus, we used

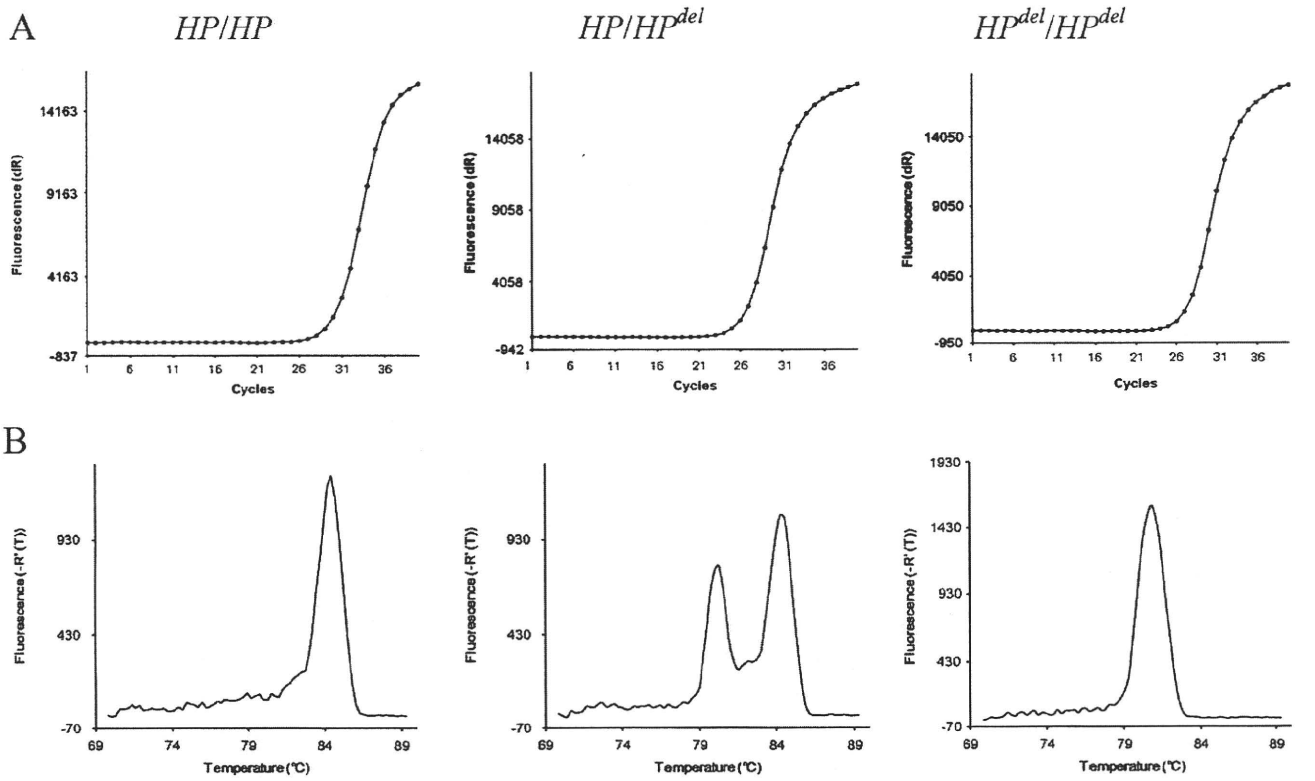

Fig. 2. SYBR Green I–based real-time PCR analysis for detection of *HP*^{del} and *HP*. Genomic DNA whose genotypes are *HP/HP* (left), *HP/HP*^{del} (middle), and *HP*^{del}/*HP*^{del} (right) were used as templates. (A) Duplex real-time amplification plot for *HPR* (intron 4) and *HP*^{del} as targets. (B) Dissociation curves provide a graphic representation of the PCR product after the amplification process. A single peak or two peaks with different T_m values were observed. T_m values of *HPR* products were approximately 84.5°C, and those of *HP*^{del} were approximately 80.3°C.

1:100 dilutions of blood samples as templates for further studies. We also compared the results of PCR amplification using frozen blood (obtained in EDTA-containing tubes) diluted 1:100 to freshly drawn blood samples as templates. We observed almost identical PCR amplification in both samples (data not shown). In addition, this method can be applied to blood samples that were collected from patients and stored for at least 10 days at 4°C.

We examined the effects of type of PCR plates on the fluorescent signal. A white PCR plate (Sorenson ultraAmp PCR semiskirted 96-well white plates, Nippon Genetics, Tokyo, Japan) increased the fluorescent signal approximately threefold compared with a transparent one (data not shown).

Validation of the method

We then examined blood samples from 2231 patients who were scheduled for blood transfusion at Kurume University Hospital. Diagnosis of the *HP*^{del} allele was performed in parallel using the TaqMan-based real-time PCR method.[18] The real-time PCR method was performed in duplicate assays for each of 45 samples using a white 96-well plate in both the SYBR Green I and the TaqMan-based methods. During this large-scale experiment, fluorescent signals of some samples (particularly in TaqMan-based real-time PCR method) were too small to be detected for presently unknown reason(s). This phenomenon was not reproducible; that is, although the signal of one sample was too small to detect, another well of a duplicate sample showed adequate signal strength. To resolve this problem, blood was diluted to 100-fold with 50 mmol/L NaOH instead of water, treated at 95°C for 5 minutes, and then used as a template. This procedure seemed to improve the signal strength significantly, although signals of some samples seemed to be still a little reduced. The results of duplex assays of the present SYBR Green I real-time PCR method were completely identical to those of the TaqMan-based real-time PCR method[18] (i.e., 2163 individuals with *HP/HP*, 67 individuals with *HP/HP*^{del}, and one *HP*^{del}/*HP*^{del}). Accordingly, the frequency of *HP*^{del} is calculated to be 0.015 in the Kyushu area (western Japan), and the incidence of individuals homozygous for the *HP*^{del} was expected to be 1 in every 4200 individuals. When we used blood samples treated with

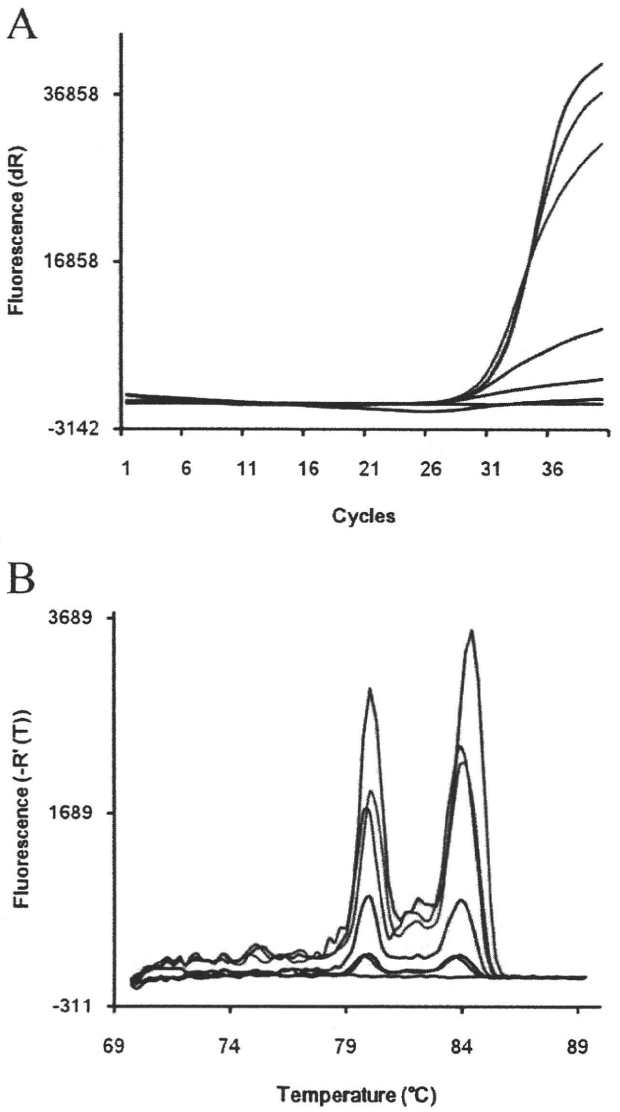

Fig. 3. Effect of dilution of blood on the fluorescent signal of real-time PCR analysis. The results of severalfold diluted blood sample from an *HP1/HP*^{del} individual are shown by navy (no dilution), red (1:4), green (1:16), gray (1:64), chartreuse (1:256), blue (1:1024), and purple (1:4096). A negative control is shown by orange. (A) Real-time amplification plot. (B) Dissociation curves provide a graphic representation of the PCR product after amplification.

50 mmol/L NaOH, the T_m value seemed to have dropped slightly (approx. 0.5°C for both products) compared to that observed when water is used as the diluent. Although undesired fluorescent signals were detected in some negative control samples (with a frequency of less than 10%), they were not reproducible, and the T_m value (76.8°C) of the undesired products was lower than that of the targets.

For safe transfusion medicine for as many people as possible, the screening test of *HP*^{del} of every potential transfusion recipient before transfusion is desirable. However, as mentioned above, the prevalence of absolute Hp deficiency is relatively low, and it is a difficult issue to include the screening test considering the cost-effectiveness, while they would only need to be tested once in their lifetime.

The advantages of the TaqMan-based method over the SYBR Green I–based are superior specificity and the possibility of determination of common Hp genotypes (*HP*^{1} and *HP*^{2}) when one probe and primers set is added.[21] However, when confirmation of the length of PCR products by electrophoresis was included, the reliability of the SYBR Green I–based method with melting curve analysis was comparable with that of the TaqMan-based method. In addition, the results of the present SYBR Green I–based method with melting curve analysis were completely concordant with that of the TaqMan-based method. When melting curve analysis is included, less than 1.5 hours after taking blood from the subject is required for allele determination like the TaqMan-based method. Thus, the present SYBR Green I–based method for diagnosis of the *HP*^{del} allele seems to be comparable to the TaqMan-based method in specificity and suitability for high-throughput analysis. It seems to be better adapted to clinical diagnosis of patients before blood transfusion or infusion of human blood components in clinical laboratories as an alternative method for allelic discrimination of *HP*^{del} to prevent anaphylactoid shock caused by anti-Hp.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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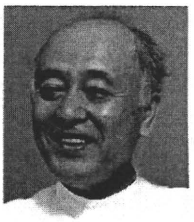
クリニカルパスに基づいた安全で適正な自己血輸血の実践

Safe and appropriate practices for autologous blood transfusion based on clinical path procedures



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◎現在，日本の多くの病院で，輸血を必要とする外科的手術を受ける患者に，自己血輸血が実施されている．日本の赤血球製剤の輸血の約8%が自己血輸血であり，日本は世界でもっとも積極的に自己血輸血を推進している国である．自己血輸血が医学的に優れている点は，同種血輸血では一定の割合で発生する同種免疫副作用が回避できること，そして既知および未知の病原体の感染を回避できることである．さらに，社会的な意味で優れている点は，本来，輸血のレシピエントである患者が輸血のドナーにもなっていることである．しかし，自己血輸血のドナーは外科的手術を受ける予定の患者であり，健康面では弱者である．したがって，この患者に対して不利益や有害事象をできるかぎり発生させないように，安全で適正な自己血輸血を実施することが肝要である．そのためのツールとしてクリニカルパスの技法は，臨床的にきわめて有用である．

Key word：自己血輸血，クリニカルパス，オリエンテーションビデオ，説明ビデオ，血管迷走神経反射

現在，日本の多くの病院で，輸血を必要とする外科的手術を受ける患者に自己血輸血が実施されている．日本の赤血球製剤の輸血の約8%が自己血輸血であるという推計があるが[1]，日本は世界でもっとも積極的に自己血輸血を推進している国である．

自己血輸血が医学的に優れている点は，同種血輸血では一定の割合で発生する同種免疫副作用が回避できること，そして既知および未知の病原体の感染を回避できることである．さらに，社会的な意味で優れている点は，本来，輸血のレシピアントである患者が輸血のドナーにもなっていることである．つまり自己血輸血を実施する患者は，自らが使用する輸血用血液製剤を自らの体のなかで生産して提供できるドナーでもある．

しかし，同種血輸血のドナーが健康な16～69歳の男女であるのに対して，自己血輸血のドナーは病気の治療のために外科的手術を受ける予定の患者である．しかも年齢は，年少者から80歳以上の高齢者にまで及んでいる．したがって自己血輸血のドナーの健康水準は，同種血輸血のドナーに比べて明らかに劣っている．このような条件下の患者を対象とした自己血採血であり，また自己血輸血であることを認識し，より安全で適正な自己血輸血を実施することはわれわれ医療者の責務である．

本稿では安全で適正な自己血輸血を推進するために，久留米大学病院において著者らが取り組んできた，クリニカルパスに基づいた自己血輸血について報告する．なお，日本でもっとも普及している貯血式自己血輸血を中心に記述する．

自己血輸血の利点と欠点

自己血輸血の利点，そして同種血輸血に対する優位性として，①同種免疫反応による副作用が起こりにくい，②不規則抗体が産生されない，③不規則抗体保有者であっても適合する血液が確保できる，④同種血にみられるウイルス感染症の伝播の可能性がない，⑤同種血にみられる未知の病原体の伝播の可能性がない，⑥輸血後移植片対宿主病(輸血後GVHD)の可能性がない，⑦輸血関連急性肺障害(TRALI)の可能性がない，などがあげら

表 1　貯血式自己血輸血の全体像の時系列による理解

時系列	事項	担当者	備考
1	自己血輸血の適応の決定	医師*	担当医が行う
2	インフォームドコンセントの取得	医師	担当医が行う
3	貯血計画の策定	医師，輸血部門の医師	担当医が輸血部門の医師と相談のうえ策定
4	貯血患者へのオリエンテーション	医師または看護師	主として看護師
5	貯血実施	医師，看護師，臨床検査技師	クリニカルパスに基づいたチーム医療
6	自己血の分離，保管管理	臨床検査技師	
7	自己血の適合検査	臨床検査技師	
8	自己血の払い出し	事務員または臨床検査技師	
9	自己血の受取り	看護師	
10	自己血輸血前の照合	医師，看護師	ダブルチェックが必要
11	自己血輸血の実施	医師，看護師	

*：医師は医師および歯科医師を意味する．

れる．

自己血輸血の不利な点として，①貯血のときに血管迷走神経反射が起こりうる，②心・脳血管系にリスクのある患者では循環動態への悪影響に対して配慮が必要である，③貯血時および保存期間中に細菌汚染や細菌増殖が起こりうる，④輸血過誤を起こしたときに感染症の伝播の危険性が高い，⑤輸血用血液の確保量に限界がある，⑥実施施設では採血，保存，管理などに同種血輸血実施以上の人手や技術が必要になる，などのことも考慮しておく必要がある[2]．

このような利点と不利な点を理解したうえで，安全で適正な自己血輸血を実施しなければならない．そのためには“自己血輸血の指針”[3,4]や“日本自己血輸血学会　貯血式自己血輸血実施基準(2007，2008)”[5]に則って，自己血輸血を実施すればよい．

貯血式自己血輸血の全体像の時系列による理解

医師，看護師，臨床検査技師および貯血式自己血輸血にかかわる医療者は表 1 に示すように，貯血式自己血輸血の全体像の時系列による理解が必要である．全体の流れと，それぞれの段階での医療者の役割分担や協力関係を理解し，それらを忠実に実行することによって安全で適正な，そして質の高い自己血輸血が実施できる[6-8]．

医師，看護師，臨床検査技師の共同作業による安全で適正な自己血輸血

貯血式自己血輸血は表 1 に示したように，複雑かつ多くの段階の仕事を担当する医療者がひとつひとつ着実に実行していくことによって実践できる．これらの過程には多くの職種がかかわっている．とくに医師，看護師，および臨床検査技師の共同作業が重要である．これらの共同作業はクリニカルパスの手法を活用することで，より安全で適正な実践が可能となる[6-8]．

1．適正なドナーの選択

安全で適正な自己血輸血を実施するためには，まずドナーを適正に選択することが肝要である．ドナー選択の詳細な条件については，1994 年版のマニュアル[2]および 2007 年の改訂版(案)[3]に書かれているので参照していただきたい．

著者らは後述する自己血採血のクリニカルパス(医療者用)(図 1)[9-11]のなかに，①自己血輸血の適応基準，②除外基準，③既往歴，などの欄を設けて，貯血計画を策定するときにそれらをチェックして，ドナーとして適正かどうかを医師が判定するシステムにしている．

とくに，菌血症の疑いのある患者を除外することは大切である．

2．適正な貯血計画の策定

患者の担当医または輸血部門の責任医師が患者の医学的状態を総合的に判断して，適正な貯血計画を策定する．経験の深い輸血部門の医師に相談のうえ，策定することが望ましい．手術日には医学的状態およびヘモグロビン値が許容範囲まで改

図 1　自己血採血クリニカルパス(医療者用)

採血スケジュール	1回目　年　月　日	3回目　年　月　日
	2回目　年　月　日	4回目　年　月　日

承認番号 02007A

□：Dr実施　　○：Ns実施

血液型　　型　Rh(　)
感染症　Wa(　) HBV(　) HCV(　)
その他(　)
病名
OP予定日
採血予定量　　ml
既往歴　心疾患　　身長
　　　　高血圧　　体重
□同意書
□鉄剤処方

適応基準
自己血採血の説明を受け，同意が得られている
ASA physicalstatus Ⅰ度及びⅡ度の者
NYHA Ⅰ度及びⅡ度の者
Hb 11.0g以上を原則とする
体重40kg以上

除外基準
ASA physicalstatus Ⅲ度以上
NYHA Ⅲ度以上
有熱時
明確な根拠を基に主治医が除外と判断した場合

○オリエンテーションビデオ(　)
○患者用パス説明(　)

ADL　自立
　　介助　杖
　　　　　車椅子
　　　　　難聴(左 右)
　　　　　視力障害

特記事項
(　)

月日	1回目　ベッドNo　年　月　日	2回目　ベッドNo　年　月　日	3回目　ベッドNo　年　月　日	4回目　ベッドNo　年　月　日
アウトカム	VVR Ⅰ度以上を起こさず予定量の採血ができる 採血後の注意点及び内服の必要性について理解できる	VVR Ⅰ度以上を起こさず予定量の採血ができる 採血後の注意点及び内服の必要性について理解できる	VVR Ⅰ度以上を起こさず予定量の採血ができる 採血後の注意点及び内服の必要性について理解できる	VVR Ⅰ度以上を起こさず予定量の採血ができる 採血後の注意点及び内服の必要性について理解できる
検査	□ Hb(　)	□ Hb(　)	□ Hb(　)	□ Hb(　)
採血量	□ 400ml □ 200/200 ml □ 200 ml	□ 400ml □ 200/200 ml □ 200 ml	□ 400ml □ 200/200 ml □ 200 ml	□ 400ml □ 200/200 ml □ 200 ml
指示	□ ソルアセトF 500ml (採血後)(　) □ ソルアセトF 500ml (採血と並行(　) □ ソルアセトF (200/300ml)(　) □ 5%G 16ml+フェジン2A(　) □ エスポー24000単位(　) □ 鉄剤処方	□ ソルアセトF 500ml (採血後)(　) □ ソルアセトF 500ml (採血と並行(　) □ ソルアセトF (200/300ml)(　) □ 5%G 16ml+フェジン2A(　) □ エスポー24000単位(　) □ 鉄剤処方	□ ソルアセトF 500ml (採血後)(　) □ ソルアセトF 500ml (採血と並行(　) □ ソルアセトF (200/300ml)(　) □ 5%G 16ml+フェジン2A(　) □ エスポー24000単位(　) □ 鉄剤処方	□ ソルアセトF 500ml (採血後)(　) □ ソルアセトF 500ml (採血と並行(　) □ ソルアセトF (200/300ml)(　) □ 5%G 16ml+フェジン2A(　) □ エスポー24000単位(　) □ 鉄剤処方
安全	○ 名前と血液型の確認 ○ 採血後の血液と患者の照合 ○ 止血確認	○ 名前と血液型の確認 ○ 採血後の血液と患者の照合 ○ 止血確認	○ 名前と血液型の確認 ○ 採血後の血液と患者の照合 ○ 止血確認	○ 名前と血液型の確認 ○ 採血後の血液と患者の照合 ○ 止血確認
観察 記録	前日の睡眠状況 (良 不良) 朝食 (摂取 未摂取) 体調(下痢など) (良 不良) 鉄剤内服 (している していない)	前日の睡眠状況 (良 不良) 朝食 (摂取 未摂取) 体調(下痢など) (良 不良) 鉄剤内服 (している していない)	前日の睡眠状況 (良 不良) 朝食 (摂取 未摂取) 体調(下痢など) (良 不良) 鉄剤内服 (している していない)	前日の睡眠状況 (良 不良) 朝食 (摂取 未摂取) 体調(下痢など) (良 不良) 鉄剤内服 (している していない)
	採血部位　○右　○左	採血部位　○右　○左	採血部位　○右　○左	採血部位　○右　○左
	採血開始 / / 点滴終了 : / / : T BP / / / / P 生あくび 冷汗 悪心	採血開始 / / 点滴終了 : / / : T BP / / / / P 生あくび 冷汗 悪心	採血開始 / / 点滴終了 : / / : T BP / / / / P 生あくび 冷汗 悪心	採血開始 / / 点滴終了 : / / : T BP / / / / P 生あくび 冷汗 悪心
採血状況	○ 問題なく終了 ○ ミルキングを加えた ○ フラッシュを行なった ○ 採血部位を変更した	○ 問題なく終了 ○ ミルキングを加えた ○ フラッシュを行なった ○ 採血部位を変更した	○ 問題なく終了 ○ ミルキングを加えた ○ フラッシュを行なった ○ 採血部位を変更した	○ 問題なく終了 ○ ミルキングを加えた ○ フラッシュを行なった ○ 採血部位を変更した
採血量	ml	ml	ml	ml
採血時間	分	分	分	分
説明・指導	○ 生活指導	○ 生活指導	○ 生活指導	○ 生活指導
バリアンス	有(　) 無	有(　) 無	有(　) 無	有(　) 無
サイン	Dr　Ns	Dr　Ns	Dr　Ns	Dr　Ns

H16. 8月

善されている必要がある．無理な貯血計画を立てたために，患者が悪条件で手術に臨まなければならないような事態は回避すべきである．

3. オリエンテーションビデオによる患者の理解と協力

自己血輸血をはじめて受ける患者は，実態がわからないために不安を抱えている場合が多い．その不安感が，自己血採血の場で血管迷走神経反射を誘発することもある．採血前日の睡眠不足，採血当日に朝食を摂取しないままに来院するなど，悪い状態のまま自己血採血にのぞみ，血管迷走神経反射を発症する事例も多い．これらのことを憂慮した久留米大学病院の自己血輸血にかかわっていた看護師らは，自己血輸血の実際を説明するオリエンテーションビデオを自らが製作した[9-11]．

ビデオの内容は，①担当医師からの説明“自己血輸血の安全性について”，②採血前日までの注意点，③採血当日の注意点(採血前)，④手続方法，⑤自己血採血の方法，⑥採血当日の注意点(採血後)，⑦鉄剤の服用について，⑧食事について，である．動画やイラストを利用し，大きな文字を使用し，実物の内服薬の写真や，推奨される食材のフードモデルを利用して紹介し，わかりやすさを心がけて編集している．自己血輸血外来で働いている看護師，医師が出演している．ナレーションおよび音楽も入っている．

自己血輸血の貯血計画のために自己血輸血外来に来院した患者に，このビデオを前もってみてもらい，自己血輸血に対する理解を深めてもらう．その後，ビデオの内容に沿った図2に示す自己血採血クリニカルパス(患者用)“自己血輸血を受けられる患者さんへ”を手渡し，持ち帰っていただいて復習してもらう．そして，その内容に沿った準備をしてもらう．その結果，不安感は解消され，より安全で適正な自己血採血ができることになる．このビデオが完成して以来，ほぼ全員の患者にあらかじめ視聴してもらっているが，自己血採血時の血管迷走神経反射の発生頻度は明らかに減少した．説明ビデオの効果は明白である．多くの病院でこのようなシステムが利用されることを期待したい．このビデオ(2007年に改訂版のDVD版がつくられた)は，希望の方には提供することもできる．

4. クリニカルパスに基づいた安全で適正な自己血貯血

安全で適正な自己血輸血の実現のためには，“時系列化”，“視覚化”，“クリニカルパス”がキーワードであろう．もっとも実効性の高い方策として，自己血輸血の重要な段階ごとにクリニカルパスを作成し運用することが考えられる．

久留米大学病院では臨床検査部内の輸血部門が中心となって，自己血輸血を推進している．久留米大学病院外来部門の第1化学療法センターのなかに自己血輸血外来を開設しているが，ここで自己血の貯血計画の策定と，患者からの自己血採血を行っている．担当している職種は，医師1名，臨床検査技師1名，そして看護師4〜5名である．看護師は内科外来所属であるが，自己血輸血業務も兼務してくれている．第1化学療法センターでは，患者用の自己血採血クリニカルパス(図2)と医療者用の自己血採血クリニカルパス(図1)の2種類をつくり運用している．患者用の自己血採血クリニカルパスは，オリエンテーションビデオを視聴した患者に渡して，理解を補完するために利用してもらっていることは前述のとおりである．

貯血計画の当日および貯血の当日は，担当している医療者全員がA3版1枚に記載された医療者用の自己血採血クリニカルパス(図1)に基づいて，自己血採血業務を行っている．実施した医療行為については，担当者が該当欄にチェックマークを記入することによって確認作業を行う．このように1枚のクリニカルパス表を基盤にして作業をすることによって情報の共有化，技術の均一化がはかれ，医療者にとっても患者にとっても“安全で適正な貯血式自己血輸血”が実現できていると考えている[6-11]．

5. 血管迷走神経反射対策

自己血採血を行っていると，採血中，採血直後，あるいは採血後しばらく時間がたってから一定の頻度で血管迷走神経反射の発症に遭遇する．患者にとっても医療者にとっても不快な副作用である．この血管迷走神経反射を早期に発見し，迅速に対処することが必要である．そのために以下のことに留意し，処置および対策を実行することが

	貯血計画時	前日	当日	翌日
診察 自己血採血 注射	ビデオを見て頂きます（約７分）⇨ 医師の診察があります		受付を済ませ第１化学療法センターへおいでください ⇨ 医師の診察があります ⇨ 自己血採血をはじめます（約 20 分） ⇨ 点滴をします（約 40 分） ⇨ 診察終了後受診科へお戻りください	
食事	バランスの良い食事を心がけてください	過度の飲酒を避けてください	朝食は普段通り食べてきてください 尚、検査のために絶食で来られた場合は診察時に医師にお知らせください	バランスの良い食事を心がけてください
薬	服薬中の薬があれば医師にお知らせください		現在服用中の薬は飲んできてください 自己血採血後鉄剤が処方されます。医師の指示通り服用してください	鉄剤を服用すると便の色が黒くなりますが心配はいりません
清潔		制限はありません	入浴は短時間で済ませてください （できればシャワー程度に！）	制限はありません
活動		いつもより早めに就寝してください	採血後はエレベーターを利用してください 気分が悪くなったら受診科へご連絡ください 車の運転や激しい運動・仕事はなるべく避けてください	日常生活に制限はありませんが疲労感を感じたら休息してください

私たちの体の中を流れている血液の量は 70ml x 体重(kg)で計算できます。
血液は毎日､体の中で造られています。

鉄分を多く含む食品
レバー、肉、さんま
うなぎ、あさり、鰯
昆布、のり、わかめ
ひじき、ほうれん草
ブロッコリー、小松菜
納豆、大豆、いりこ
ごま、プルーンなど

自己血採血の予定日は　１回目：　／　　２回目：　／
３回目：　／　　４回目：　／　　です。
忘れないようにカレンダーに書き込んでください。
尚、わからないことがありましたら、遠慮なく看護師におたずねください。
久留米大学病院　第１化学療法センター
☎0942-35-3311（内線 6247）

図 2　自己血採血クリニカルパス(患者用)“自己血採血を受けられる患者さんへ”

肝要である.

① 血管迷走神経反射は 0.5〜1%の頻度で発症する.

② 初期症状を見逃さず，早期発見，早期治療が原則である.

③ 採血中に発症したときにはただちに採血を中止し，輸液ラインに切り替え，乳酸リンゲル液などの細胞外液系の輸液を急速点滴静脈注射する.

④ 頭部を下げ，下肢を上げる.

⑤ 5〜10 分でほとんどの患者は改善する．著者らの経験では，昇圧薬を使用しなければならなかった症例はない.

⑥ 採血前にオリエンテーションビデオを見せ，全体像を理解してもらい不安感を軽減させる.

⑦ 血管迷走神経反射およびその他の有害事象を起こしやすい患者を選別し，採血と輸液を並行実施するなどの対策を講じる．たとえば，右上肢から採血し，同時に左上肢から細胞外液系の輸液をする.

⑧ 発症しやすいリスクをもつ患者は，若い人，睡眠不足の人，食事抜きの人，不安感の強い人，などである.

⑨ その他のリスクのある人，心血管障害のある人，70 歳以上の高齢者などは上記と同様のリスク防止策をあらかじめ実施することを考慮する.

おわりに

自己血輸血は同種血輸血の欠点を補完できる重要な輸血の方法である．しかし，自己血輸血のドナーは外科的手術を受ける予定の患者であり，健康面では弱者である．したがって，この患者に対して不利益や有害事象をできるかぎり発生させないように，安全で適正な自己血輸血を実施することが肝要である.

そのためのツールとして，クリニカルパスの技法はきわめて有用である．なお，一般論としてではあるが，看護師はこの技法に習熟しているので，医師も臨床検査技師も看護師と共同してクリニカルパスを作成することが効率的である.

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