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CASE REPORT

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Hemagglutination of preoperative blood donation in patients with rheumatoid arthritis

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Abstract We gave preoperative blood transfusions to 37 patients with rheumatoid arthritis (RA) and 35 patients with osteoarthritis (OA), including some whose baseline hemoglobin level was less than 10 g/dl. Transfusion packs can preserve whole blood containing citrate phosphate dextrose (CPD) for 3 weeks. The baseline hemoglobin level of RA cases was 10.4 g/dl (range 8.4–13.1 g/dl), and that of OA cases was 11.9 g/dl (range 10.4–15.0 g/dl). By collecting 200–400 g every week before the operation, the total was 800–1200 g. Erythropoietin was given to patients intramuscularly when their hemoglobin was less than 13 g/dl after blood had been collected. Hemagglutination, with diameters of more than 1 cm, made filter occlusions in 11 RA cases (30%) and one OA case (3%) ($P < 0.0031$) after retransfusion. There were no differences between hemagglutination patients (agglutination group) and nonhemagglutination patients (nonagglutination group) regarding baseline C-reactive protein (CRP), white blood cells, platelets, or fibrinogen. We could not predict the formation of macrohemagglutination in the packs collected during the clinical course. In RA cases, allogenic transfusions were performed for four cases (36%) in the agglutination group and for one case (12%) in the nonagglutination group. Preoperative transfusion for the RA patients showed hemagglutination in some cases, and highlighted the need for modifications to reduce these hemagglutinations.

Key words Agglutination · Blood donation · Rheumatoid arthritis (RA)

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Introduction

Preoperative autologous blood collections for scheduled surgery are frequently performed.[1–3] The utility of preoperative blood collections with the use of erythropoietin has been established to avoid allogenic blood transfusions. However, these procedures pose several problems for cases of rheumatoid arthritis (RA) with preoperative anemia, resulting in a low response of erythropoietin in comparison to osteoarthritis (OA) cases.[4,5] These problems have led to a low number of preoperative blood transfusions because the guidelines for blood collection do not recommend collections from patients with anemia. Currently, even for cases of RA with anemia, preoperative autologous blood transfusions can be performed. In our series, we experienced filter occlusions due to large hemagglutinations which obstructed the collection pack tube, making it difficult for blood to return to the patients. In this article, we report the frequency and degree of hemagglutination in transfusion packs from patients with RA and OA.

Patients

A retrospective study was carried out on 72 patients who underwent preoperative autologous blood transfusions between January 1999 and December 2001. A preoperative diagnosis was made in 35 OA cases (6 men, 29 women) and 37 RA cases (4 men, 33 women). Surgery consisted of 15 total hip arthroplasties, 56 total knee arthroplasties, and one spinal surgery. Cases undergoing more than one operation were excluded from this study. Preoperative blood transfusions were performed for 92.5% of the joint arthroplasty cases.

OA patients

The average age of the patients with OA whose blood was collected preoperatively was 71.0 years (range 49–86 years).

Nonsteroidal anti-inflammatory drugs were prescribed for 25 OA patients. The following anticoagulants were prescribed: a low dosage of aspirin (81 mg/day) for three cases, limaprost alfadex at 90 μg/day for one patient, and cilostazol at 200 mg/day for one patient. The average age of the patients with OA who did not give blood preoperatively (two cases) was 84 years.

RA patients

All 37 RA cases were diagnosed according to the American College of Rheumatology revised criteria of 1987. The average age of the RA patients who had blood collected preoperatively was 64.0 years (range 41–77 years). The duration of disease was 9 ± 3 years (range 1–21 years). The radiological findings were expressed by the Steinbrocker's stage classification. The patients' hands were classified as follows: stage I, 0%; stage II, 10%; stage III, 24%; stage IV, 66%. Prednisolone at 2–10 mg/day was prescribed for 28 of the 37 RA patients (76%). Nonsteroidal anti-inflammatory drugs were prescribed for all patients. The following anticoagulants were prescribed: a low dosage of aspirin (81 mg/day) for two cases, limaprost alfadex at 90 μg/day for three cases, and cilostazol at 200 mg/day for one case. The average age of RA patients who did not give blood preoperatively (4 cases) was 78 years (Table 1).

Table 1. Preoperative blood collection was performed for 37 rheumatoid arthritis (RA) cases and 35 osteoarthritis (OA) cases

	Rheumatoid arthritis (n = 37)	Osteoarthritis (m = 35)	P-value
Age (years)	64 ± 10	71 ± 8	0.0006
Male/female	4/13	6/29	
Operation			
Hip arthroplasty	9	6	
Knee arthroplasty	27	29	
Spinal surgery	1	0	

RA and OA were compared using Student's t-test for parametric demographic data

Methods

Preoperative blood collections were carried out 2 or 3 weeks before surgery, with 400 ml being collected every week. Blood collections were preserved as whole blood. The storage time-limit was 3 weeks. A 400-ml blood pack contained 50 ml citrate phosphate dextrose (CPD) (TERUMO SC-407). The constituents in 100 ml CPD were as follows: sodium citrate, 2.630 g; citrate, 0.327 g; glucose, 2.32 g; sodium dihydrogenphosphate dihydrate, 0.251 g. The needle gauge for the puncture was 17 G. Erythropoietin (24 000 units) was injected intramuscularly when the patient's hemoglobin level was lower than 13 g/dl after collection, and 100 mg ferrous sulfate tablets were prescribed. After the blood was returned to the patients, we defined a blood agglutination greater than 1 cm diameter, which caused filter occlusion, as a hemagglutination-positive case (agglutination group), and a blood agglutination less than 1 cm diameter as a hemagglutination-negative case (nonagglutination group) (Fig. 1). The results were expressed as the mean and standard deviation where applicable. Between-group comparisons were performed using Student's t-test for parametric data and Fisher's exact probability test for nonparametric data. The RA agglutination and nonagglutination groups were compared with respect to

Fig. 1. Hemagglutination is visible in the collection pack. Agglutinations are formed by glue-like fibrin

Table 2. Characteristics of 37 RA cases and 35 OA cases

	Rheumatoid arthritis (n = 37)	Osteoarthritis (m = 35)	P-value
Hemoglobin precollection (g/dl)	10.4 ± 1 (8.4–13.1)	11.9 ± 1 (10.4–15.0)	0.0001
CRP (mg/dl)	7.4 ± 7.1	0.55 ± 0.6	0.66
WBC ($\times 10/mm^3$)	7940 ± 2200	5730 ± 1800	0.09
Platelets ($\times 10^4/mm^3$)	41.6 ± 72	38.5 ± 72	0.79
Fibrinogen (mg/dl)	460 ± 100	306 ± 74	0.87

RA and OA were compared using Student's t-test for parametric demographic data
CRP, C-reactive protein

Table 3. Incidence of hemagglutination

	Hemagglutination (+)	Hemagglutination (−)	
Rheumatoid arthritis	11	1	*
Ostecoarthritis	26	34	*

RA and OA were compared using Fisher's exact probability test for the incidence of hemagglutination
* $P = 0.0031$

preoperative data and frequency of receiving an allogenic blood transfusion.

Results

The average age of RA cases receiving a transfusion of preoperative blood was 64.0 years, which was lower than the average age of 71 years in OA cases ($P = 0.0006$). The average precollection hemoglobin of the RA group was 10.4 g/dl (range 8.4–13.1 g/dl), average C-reactive protein (CRP) was 7.4 mg/dl (range 0.11–30.38 mg/dl), average white cell count 7940/mm^3 (range 3900–12 500), average platelet count 41.6 × $10^4/mm^3$ (range 24.2–54.6 × 10^4), and average fibrinogen 460 mg/dl (range 272–695 mg/dl). The average precollection hemoglobin of the OA group was 11.9 g/dl (range 10.4–15.0 g/dl), average CRP 0.55 mg/dl (range 0.11–2.77 mg/dl), average white cell count 5730/mm^3 (range 2900–9400), average platelet count 38.5 × $10^4/mm^3$ (range 10.7–44.4 × 10^4), and average fibrinogen 306 mg/dl (range 195–441 mg/dl). The precollection hemoglobin of RA patients was 10.4 g/dl, which was lower than the 11.9 g/dl of osteoarthritis patients ($P = 0.0001$). White blood cells, CRP, and fibrinogen were relatively high in RA patients due to the chronic inflammation of RA (Table 2). The incidence of hemagglutination in preoperative blood collection packs was 11 of 37 RA cases, and one of 35 OA cases. The incidence of hemagglutinations was higher in the RA than in the OA group ($P = 0.0031$). One of the RA hemagglutinations spoiled all of one patient's blood collection due to severe tube occlusion (Table 3). Comparing the agglutination group with the nonagglutination group of RA patients, the baseline hemoglobin of the agglutination group was 10.4 g/dl and that of the nonagglutination group was 10.5 g/dl. The average age of the agglutination group was 68 years, while that of the nonagglutination group was 62 years. The white blood cell count of the agglutination group was 8870 ± 2500/mm^3, against 7550 ± 1900/mm^3 in the nonagglutination group. There were no differences among fibrinogen, platelets, and CRP between the two groups (Table 4). The hemoglobin of post-operative day 1 for the agglutination group was 9.8 ± 1 g/dl, while that for the nonagglutination group was 9.5 ± 1.4 g/dl. The hemoglobin 2 weeks after the operation was 10.2 ± 0.8 g/dl and 10.7 ± 1.5 g/dl for the agglutination and nonagglutination groups, respectively. In RA cases, allogenic transfusions were performed in four cases (36%) in the agglutination group, and in one case (12%) in the nonagglutination group after an operation for postoperative progressive anemia (Table 5).

Discussion

In our series there were some macrohemagglutinations in the packs of preoperatively collected blood, as reported above. In general, collected blood was not subject to filter occlusion due to microhemagglutination. We found macrohemagglutinations which caused filter occlusion in blood collected from patients. These macrohemagglutinations were more frequently found in blood from RA patients than that from OA patients. From these results, we speculated that large agglutinations were formed under chronic inflammation. No reports concerning macrohemagglutination in RA were found in the literature. Generally, hemagglutinations were formed by fibrin concentrated on white blood cells contained in whole-blood collections. Complement and platelet activation contribute to the formation of agglutination.[6,7] Secondary abnormal functions of coagulation and fibrinolysis have been observed in rheumatic disorders due to chronic inflammation.[8,9] We believe that chronic inflammations and the aging of rheumatoid patients triggered the formation of hemagglutination in our series. There were no differences between the agglutination and nonagglutination groups regarding baseline CRP, white blood cells, platelets, or fibrinogen. This study suggested that patients with large hemagglutinations in collection packs could not be clearly distinguished from those without agglutination on the basis of the usual tests performed for coagulation, fibrinolysis, and inflammation.

Other causes of hemagglutination can originate in the collecting procedures. RA cases often have fragile vessel

Table 4. Comparison clinical data in the hemagglutination group and the nonhemagglutination group of RA cases

	Hemagglutination (+) (n = 11)	Hemagglutination (−) (m = 26)	P-value
Age (years)	68 ± 8	62 ± 10	0.076
Male/female	1/10	3/23	
Hemoglobin precollection (g/dl)	10.4 ± 1	10.5 ± 1	0.90
CRP (mg/dl)	8.2 ± 5	7.0 ± 8	0.66
WBC ($\times 10/mm^3$)	8870 ± 2500	7550 ± 1900	0.09
Platelets ($\times 10^4/mm^3$)	38 ± 7	43 ± 48	0.79
Fibrinogen (mg/dl)	464 ± 71	469 ± 111	0.87

There were no differences between the agglutination group and the nonagglutination group in baseline C-reactive protein (CRP), white blood cells (WBC), platelets, and fibrinogen levels of RA patients by Student's t-test

Table 5. Comparison between the hemagglutination group and the non-hemagglutination group for pre- and postoperative course in RA cases

RA	Hemagglutination (+) (n = 11)	Hemagglutination (−) (m = 26)	P-value
Hemoglobin precollection (g/dl)	10.4 ± 1	10.5 ± 1	0.90
Hemoglobin 1 day after the operation (g/dl)	9.8 ± 1	9.5 ± 1.4	0.29
Hemoglobin 2 weeks after the operation (g/dl)	10.2 ± 0.8	10.7 ± 1.5	0.37
Allogenic transfusion	4/11 (36%)	3/26 (12%)	0.163

There were no differences between the agglutination group and the nonagglutination group in pre- and postoperative hemoglobin levels using Student's t-test, and allogenic transfusion with Fisher's exact probability test

walls with low elasticity, which makes blood access difficult and leads to coagulation. The most severe agglutination cases showed large masses in the collection pack which were not visible immediately after collecting the blood. This suggested that degenerative agglutination formed gradually in the packs due to the pathologic blood quality caused by the chronic blood inflammation in RA cases.

The utility of preoperative blood collection for elective surgery is well documented, but few studies have analyzed blood transfusion guidelines.[10–12] Currently, preoperative blood collection has become common even for RA patients with preoperative anemia. In these cases, there is a risk of ischemic hazards in preoperative management. In our series, the baseline hemoglobin level before collection was 10.4 g/dl in the RA cases, although there were hemoglobin levels ranging from 8 g/dl to 9 g/dl in a few cases. Autologous transfusion guidelines recommend a baseline hemoglobin of more than 11 g/dl, and careful consideration for patients older than 70 years. Some of our RA cases did not meet these guideline criteria. We could not find any differences between the agglutination group and the nonagglutination group regarding baseline hemoglobin levels. We could not predict the formation of macrohemagglutination in collection packs from the clinical findings.

However, the rate of allogenic transfusion in the agglutination group (36%) was not as high as that in the nonagglutination group (12%). In addition, we should consider the possible negative effects of the formation of hemagglutination. In some cases, macrohemagglutinations in collection packs spoiled the blood and caused even more severe anemia when compared with the predonation hemoglobin level. In general, RA cases have low responses to erythropoietin compared with OA cases. Spoiled blood is a serious issue for these RA patients, given that they are more likely to have anemia than OA patients.

Patients with RA suffer pain in multiple joints, which leads to debilitating conditions over the long term. They face the possibility of undergoing multiple operations. Multiple operations with allogenic transfusions raises the issue of the associated risks of these transfusions. The possibility of autologous transfusions for RA cases has created high hopes in both patients and medical staff.

Several procedures have been proposed to prevent allogenic transfusion, for example, by prescribing steroids before surgery to improve anemia, retrieving drainage blood, and giving erythropoietin. The Japanese health insurance program allows the use of erythropoietin in preoperative blood collections of more than 800 g. Patients with RA sometimes cannot give 800 ml owing to anemia and cannot use erythropoietin. Thus, they do not have the opportunity for preoperative collections according to the current transfusion guidelines. The results of this study have shown that

even if rheumatoid patients with preoperative anemia do give blood preoperatively, it might not be possible to retransfused the blood in some cases because of hemagglutination. We propose that an automated blood component collection, utilizing a cell separator or filter for white blood cells, should be used to prevent agglutination in collection packs and encourage the Japanese health insurance system to advocate the use of erythropoietin without collections. We recommend that more attention should be given to preoperative blood collections in RA cases, and that comprehensive plans should be agreed as soon as possible.

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