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수혈 전 검사 장비인 AutoVue Innova와 Techno TwinStation의 평가

신소연 · 권계철 · 구선회 · 박종우 · 고지선 · 송정훈 · 성지연

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Evaluation of Two Automated Instruments for Pre-transfusion Testing: AutoVue Innova and Techno TwinStation

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Background : Despite the advances in total laboratory automation, a considerable amount of work in blood banks is still done using outdated manual methods. Some automated pre-transfusion testing instruments have recently been developed. Of these, we evaluated and compared the AutoVue Innova (Ortho, USA) and the Techno TwinStation (DiaMed AG, Switzerland).

Methods : Forward and reverse ABO/Rh typing and unexpected antibody screening and identification tests were performed on 4,628 samples using the manual method and the two automated instruments. Two different anticoagulants (EDTA and citrate) were compared in ABO/Rh typing and unexpected antibody screening tests. Titrating studies were conducted on the following 7 dilutions using 5 samples of irregular antibodies with anti-E, anti-E & -c, anti-D, and anti-Le^{a} with anti-Fy^{a}: 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, and 1:128. The test throughput per hour, the time required to perform 1 and 100 tests, and a simulation test for total events occurring in 1 day were also measured.

Results : No erroneous results were reported between the two instruments and the manual method. Discrepancies observed in 10 cases (0.4%) of ABO/Rh typing were of higher intensity with AutoVue Innova than with the manual method. AutoVue Innova exhibited the highest sensitivity in the titrating study and throughput performance compared with the manual method and the Techno TwinStation. Especially in the throughput and time required to complete 100 antibody screening tests, AutoVue Innova had a 3.3- and 3.5-fold higher performance, respectively, than Techno TwinStation.

Conclusions : Because both of the two fully automated instruments (AutoVue Innova and Techno TwinStation) had high levels of accuracy and performance, it is expected that use of fully automated instruments will reduce human labor, turnaround time, and operator error in the blood bank. *(Korean J Lab Med 2008;28:214-20)*

Key Words : *AutoVue Innova, Techno TwinStation, Pre-transfusion test*

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INTRODUCTION

Some of the advantages for automating laboratory testing include an increase in the quality of the pre-analytical steps, a reduction in error rates, a reduction in operator exposure to potentially hazardous biological materials, and

an elimination of repetitive stress injuries by minimizing non-value-added steps and increasing available time for value-added steps in the laboratory testing process[1]. Despite efforts to mechanize and automate whole regions of the laboratory, a considerable amount of the work in blood banks is still performed in an outdated manner, i.e., by hand. Additionally, the responsibility of the operator for the data in blood banks is more critical than in the other laboratories because an operator error can result in a fatal outcome immediately after transfusion. When using column agglutination technology (CAT) for the detection of unexpected antibodies, the results of tests have occasionally been interpreted differently between observers because difficulties in standardization and differences in operating conditions, including the operator and the equipment, can cause imprecision. Because of these problems, a number of automated instruments have been developed and marketed recently. During a one month period, we evaluated and compared two automated pre-transfusion testing instruments, the AutoVue Innova (Ortho, Raritan, NJ, USA) and the Techno TwinStation (DiaMed AG, Cressir Sur Morat, Switzerland), with respect to accuracy and rapidity. In addition, the automated instruments were compared to manual processes.

MATERIALS AND METHODS

1. Reagents and equipments

For the manual technique, NOVACLONE™ anti-A, anti-B, and anti-D (Dominion Biologicals Limited, Nova Scotia, Canada) and DiaCell ABO (DiaMed AG) for ABO/Rh typing, ID-DiaCell I-II, ID-Card "LISS/Coombs", ID-DiaPanel, ID Incubator 37 SI and ID centrifuge 12 SII (DiaMed AG) for unexpected antibody screening and identification were used. For the AutoVue Innova, 0.8% Affirmagen A1, B Grouping Red Blood Cell, and ABO/Rh Reverse cassette for ABO/Rh typing, and 0.8% Selectogen I & II Screening Red Blood Cell, 0.8% Resolve Panel A, and Polyspecific Anti-Human Globulin cassette for unexpected antibody screening and identification (Ortho-Clinical Diagnostic) were used. For the Techno TwinStation, DiaClon ABO/D with reverse grouping, ID-DiaCell A1-B and ID-Diluent 2 for ABO/Rh typing, DiaMed ID-Card 'LISS/Coombs', ID-DiaCell I-II and ID-DiaPanel for unexpected antibody screening and identification, and Wash solution A, B (DiaMed AG) were used.

Both automated pre-transfusion testing instruments were applied to CAT and automated readers using digital cameras for all test profiles. Techno TwinStation consists of two same-batch systems separated as its name, 'twin' implies, and each card is installed and removed by the operator. The loading of samples was impossible during times of centrifugation or pipetting and no additional samples could be applied when the two systems were being used at the same time. AutoVue Innova only requires an initial batch installation and removes cards after all processes automatically and random access is actually possible. AutoVue Innova and Techno TwinStation incubate for 10 and 15 min and centrifugation of cassettes for 5 and 10 min, respectively. Because of the limited duration of the demonstration and the limited number of reagents held, the test scale of the Techno TwinStation was not fully matched with that of the AutoVue Innova in the accuracy studies. However, the evaluations of their performances were conducted under similar conditions.

2. ABO/Rh typing

For the AutoVue Innova, a total of 9,162 tests were performed on 3,054 samples, including 2,134 random patient samples collected in EDTA tubes, 306 samples collected in both EDTA and citrate tubes (Vacutainer System; Becton Dickinson, Meylan, France) from the same patients on the same day to compare different anticoagulant samples, and 614 samples from specific patient groups (pediatrics, rheumatology, hematology, and oncology) according to the recommendations of the British Committee for Standards in Haematology, Blood Transfusion Task Force[2]. For types A, B, O, and AB, there were 1,063, 859, 792, and 340 samples, respectively; 6 Rh-negative samples were included. For the Techno TwinStation, 3,201 tests were performed with 1,067 samples of the collected samples because of the limited number of demonstration days. For the manual

procedure, forward typing on a plate and reverse typing by tube techniques were repeat-tested by different operators[3]. The results were described as negative or positive by manual methods.

3. Unexpected antibody screening

One thousand five hundred thirty-four samples were repeat tested to verify reproducibility between repeated tests by the manual technique and the AutoVue Innova. According to the recommendations of the Blood Transfusion Task Force of the British Committee for Standards in Haematology[2], 614 samples from specific patient groups, 306 samples collected in both EDTA and citrate tubes for comparing the evaluation of different anticoagulants, and 308 randomly-selected samples were included. Additionally, QC material (DiaMed AG) and frozen sera of 23 irregular antibody-positive samples were also included. For the Techno TwinStation, 68 samples could be studied simultaneously. All of the manual screening results were recorded upon agreement of two or three skillful observers. When there was a difference in the opinions of the operators, a magnifying glass was used to provide conclusive results. According to the manufacturers, the results were classified in inverse proportion to the sedimentation in the column as '0' with complete sedimentation, and '1+', '2+', '3+,' and '4+' in which there was no sedimentation. This principal was applied to both instruments. If the positive pattern shown by the instruments showed a slant tail curve on the wall of the column as a J-curve feature, it was considered negative because it could be induced by various physiologic conditions, like tilted or dried columns.

4. Identification and titration study

Only the samples that were greater than 1+ in both of the repeated manual screening tests were used. Irregular antibodies were simultaneously detected in 40 cases by the manual method and the AutoVue Innova. Twenty-four samples were also identified on the Techno TwinStation. Four patient samples with anti-E, anti-E & -c, anti-D, and anti-Le^a antibodies, as well as the QC material from DiaMed having anti-Fy^a antibodies were clearly identified without any discrepancies among the methods used for titration comparison. Seven concentrations (1:2, 1:4, 1:8, 1:16, 1:32, 1:64 and 1:128) were used simultaneously for each method. The anti-Le^a antibody-positive sample was compared between the manual technique and the AutoVue Innova only because it was discovered after the withdrawal of the Techno TwinStation. The points showing "1+" were determined as the endpoint titer for each method.

5. Turnaround time and throughput

All of the events of ABO/Rh typing with unexpected antibody screening tests, which had been conducted on one day in the same blood bank, were recorded and simulated on another day using the two automated instruments to compare their turnaround time under routine laboratory conditions[4]. In the Techno TwinStation, the manual time to equip and discard the cassettes was required in addition, but only the time to equip the cassettes was measured as hands-on time because we compared the final times at which the results were sent. To obtain the most efficient conditions for the Techno TwinStation, two systems of the Techno TwinStation instrument were both run at the same time, according to the recommendations of the manufacturer: 1) ABO/Rh typing and 2) antibody screening. Because the laboratory information system (LIS) was not interfaced with the AutoVue Innova, the barcodes were read manually and the time required was included in the time measurement. In the manual technique, ABO/Rh typing was performed during unexpected antibody screening, which takes an extended amount of time because it requires centrifugation and incubation, making for the most efficient condition for the manual method. The time required for each of the processes was recorded, from setting up CAT cassettes for antibody screening to discarding ABO tubes after entering the screening data into the LIS. Sample reception time and centrifuge time for separating cells and serum, which did not differ between the manual technique and the automated instruments, were not included. Through-

put performances per hour with total consumed time for each test and for 100 tests were studied in three categories: 1) forward and reverse ABO/Rh typing, 2) antibody screening only, and 3) forward and reverse ABO/Rh typing with antibody screening. For one test comparison study, the results of 20 repeated tests were averaged for each method. The time for 100 tests was measured from the time of the report of the first tests to the result of the last test. Analysis of variance was employed for statistical analysis using SPSS software version 13.0. *P*-value <0.05 was considered significant.

RESULTS

1. ABO/Rh typing

In comparing the automated test results with the manual results, the concordance rates were 100, 99.6, and 100% for the AutoVue Innova and 100, 100, and 100% for the Techno TwinStation with respect to forward ABO typing, reverse typing, and Rh typing tests, respectively. Ten cases with discrepancies were detected in comparison with AutoVue Innova, all of which occurred during reverse typing (Table 1). Two cases were false positives with a J-curve feature pattern of a slant tail curve on the wall of the column (cases 1 and 2). The other false positives were all of higher intensity in the AutoVue Innova compared with the manual method; one of these eight cases involved an ABO mismatched bone marrow transplant, two cases revealed irregular antibodies, and the other cases included samples from patients who were healthy, or had breast cancer, lung cancer, diabetes, nephritis, congestive heart failure, and incontinence. Microaggregations were observed via a magnifier using the manual method of these discrepant cases. The Techno TwinStation also had a discrepant case which was revealed in the AutoVue Innova (case 7). In the comparison study with different anticoagulants, 9 cases among 306 patients in the AutoVue Innova and 1 case among 51 cases in the Techno TwinStation had differences in intensity between anticoagulants. In the AutoVue InnoVa, 1 case had a stronger reaction intensity in the EDTA sample (3 +) than in the citrate sample (1 +), but the reverse situation was not observed. The other 8 cases all involved "J-curve" features which had been marked with a "?" or a "0.5" positive in the AutoVue Innova. The case observed in the Techno TwinStation had a higher intensity of cell and Rh typing in EDTA.

2. Unexpected antibody screening and identification study

The reproducibility rate of the repeated screening tests results was 100% in each instrument, but 92% in the manual method using CAT. One hundred twenty-three cases showed changed results from negative-to-positive or positive-to-negative in repeated manual tests and were negative in identification tests. In the comparison study of different anticoagulants in screening tests, no significant

Table 1. Discrepant cases in ABO typing between the AutoVue Innova and the manual method using both cell- and back-typing

No.	AutoVue Innova					Manual method				
	Anti-A	Anti-B	Anti-D	A1 cell	B cell	Anti-A	Anti-B	Anti-D	A cell	B cell
1	4	0	4	?*	3	+	−	+	−	+
2	4	0	4	0.5*	3	+	−	+	−	+
3	0	4	4	0	2	−	+	+	−	−
4	4	4	4	3	2	+	+	+	−	+
5	0	4	4	3	0.5	−	+	+	+	−
6	0	4	4	4	0.5	−	+	+	+	−
7	4	4	4	2	0.5	+	+	+	−	−
8	4	0	4	0.5	4	+	−	+	−	+
9	4	0	4	0.5	3	+	−	+	−	+
10	4	4	4	0.5	0.5	+	+	+	−	−

*, J-curve feature of a slant tail curve on the wall of the column.

Table 2. Unexpected antibodies identified and compared in this study

Antibody type	Number of cases	Antibody type	Number of cases
Anti-E	11	Anti-Fy^b	2
Anti-E & -c	9	Anti-Fy^a	1
Anti-D	1	Anti-M	1
Anti-c	1	Anti-Jk^a & -Le^b	1
Anti-Le^a	4	Anti-E & -Fy^b	1
Anti-Le^b	4	Anti-Jk^a & -Fy^b	1
Anti-Le^a & -Le^b	3		

Table 3. Comparison of titrating studies conducted using the manual method, the AutoVue Innova, and the Techno TwinStation

Case no.	Antibody	M	A	T
1	Anti-E	8	16	8
2	Anti-E & -c	8	64	16
3	Anti-D	Negative in 2	4	Negative in 2
4*	Anti-Fy^a	8	64	16
5	Anti-Le^a	32	32	Not done

*, QC materials of DiaMed.
Abbreviations: M, manual method; A, AutoVue Innova; T, Techno TwinStation.

Table 4. Comparison of the turnaround time conducted using the manual method, the AutoVue Innova, and the Techno TwinStation

Test profiles	Consumed time (min)	
	Total (n=88)	Average±SD* (n=11)
Manual	445	40.45±10.33
AutoVue Innova	339	32.73±7.39
Techno TwinStation	401	36.55±2.65

*, P=0.034.

Table 5. Comparison of the throughput between the AutoVue Innova and the Techno TwinStation

Comparison categories	Throughput per hour (tests/hr)		Time consumed for 100 tests (min)		Time consumed for one test (min)		
Test profiles	A	T	A	T	A	T	M
ABO/Rh typing	48	36	129	141	9	26	5
Antibody screening	158	48	38	132	23	31	30
Type and screening	40	24	148	260	23	32	30

Abbreviations: See Table 3.

difference was observed between the EDTA and citrate samples with either instrument.

Forty cases with irregular antibodies were identified. Two cases could not be clearly identified using the manual method, but were identified by the AutoVue Innova as anti-Jk^a & -Le^b and anti-Le^b. The reverse situation was not observed. Another two cases which were clearly identified in the AutoVue Innova were identified after treatment with bromelin in the manual method. Sixteen among 40 cases identified were also studied using the Techno TwinStation, and there was one discrepant case that had all positive reactions in the Techno TwinStation, but was clearly identified by the manual method and the AutoVue Innova, as well as a repeated test in the Techno TwinStation.

The frequencies of irregular antibodies in the 40 cases are shown in Table 2. The most frequent antibodies were anti-E or anti-E & -c type, followed by anti-Le^a and anti-Le^b.

3. Titration

Regarding the results of titration, all cases showed the same or more sensitive results with the instruments than with the manual method. The AutoVue Innova had higher sensitivity than the manual method and the Techno TwinStation in most cases (Table 3).

4. Turnaround time

Eighty-eight cases of 11 events were recorded in actual practice and simulated on each instrument; 106 min and 44 min less were required in the AutoVue Innova and the Techno TwinStation, respectively, compared to the manual method. In the AutoVue Innova, random access was possible, except during the pipetting of other samples, and this resulted in a reduction of 21 min more of the total time consumed for all events in this simulation. Simulated turnaround times were significantly reduced in the automated instruments (Table 4).

5. Throughput

Compared to the Techno TwinStation, the AutoVue Innova

showed much higher throughput results in all test profiles of the three categories. AutoVue Innova had a 3.3- and 3.5-fold higher performance than the Techno TwinStaion in throughput per hour and time for 100 tests of antibody screening tests, respectively (Table 5).

DISCUSSION

The AutoVue Innova and Techno TwinStation yielded no erroneous results when compared to the manual method. In fact, the AutoVue Innova had higher sensitivity in most discrepant cases compared with the manual method, and this was confirmed by the titration study. Morelati et al. [5] suggested the possibility of weak RBC antibodies that were detected in discrepancies by the AutoVue System, which was the previous model of the AutoVue Innova. Even though such weak reactions in ABO/Rh typing could be clinically insignificant findings caused by cold or allo- or auto-antibodies, such discrepancies could lead to increased costs and the potential for a delay in transfusion due to the repeat testing required to resolve the anomalous results; microaggregations missed by the tube method served as warnings of the visual limits of humans and the need for more sensitive and objective standards. Indeed, if it was discovered in a cross-matching phase, it would provide more critical information of any possibility of the presence of unexpected antibodies, which could induce significant post-transfusion complications; thus, high sensitivity is required.

In the comparison study of different anticoagulants in ABO/Rh tying, each case among 306 cases in the AutoVue Innova and among 51 cases in the Techno TwinStation showed higher intensities in EDTA samples than in citrate samples, but we could not conclude EDTA samples were more suitable for automated instruments based only upon two cases. Besides, there was no difference in unexpected antibody screening tests using EDTA and citrate samples. The J-curve features of serial cassettes were observed not only in instruments, but also in numerous manual tests and indicated any physiologic problems like tilting and shaking in storage or handling of the serial cassettes. Weak positive results remarked with a '?' or '0.5 positive' in the instruments should be confirmed by operators to rule out J-curve features as in the manual method. To avoid such controversial results and reduce unnecessary repeat testing, more careful handling of cards in carrying or storage should be considered. The low reproducibility rate of manual unexpected antibody screening tests using CAT was embarrassing to the laboratory. The similarly with the J-curve features and physical impact on manual operation were suspected to be the primary cause of this problem. CAT is a very sensitive and discriminative method from previous manual tube methods; however, false positive results induced by human sources persist. More stable and standard operations by automated instruments are expected to prevent repeat screening tests, delay in transfusions, unnecessary identification tests, and the increased cost of manual methods due to low reproducibility. With the small discrepancies in the identification test comparison, we could not conclude whether the AutoVue Innova is superior to the manual method or the Techno TwinStation, or vice versa in unexpected antibody identification because, there could have been some differences in the composition of reagent cells between different lot numbers or between manufacturers. Further evaluation is required to compare the strengths of these methods in identification testing. The frequency of irregular antibodies was significantly different from a previous report in Korea by Han et al.[6]. In our study, the most frequent antibodies were anti-E or anti-E & -c type, followed by anti-Le^a and anti-Le^b antibodies, and the frequency was not different from the results, including transfusion candidates, but the previous report showed anti-Le^a, anti-P1, anti-Le^b, anti-I, and anti-E antibodies to be present in a decreasing order of frequency. The previously issued report was studied with samples of transfusion candidates which can reflect more transfusion requirements or a dependent condition. Even though this study was done on a much smaller scale, it might reflect a broader tendency of a more diverse population, including non-transfusion candidates. Additional studies covering a larger and broader group could add clarity to the findings. For the titration study, the AutoVue Innova and the Techno Twin-

Station showed greater sensitivity than the manual method in most cases. All the results indicated sufficient acceptability and additional studies with various types of antibodies might provide more useful information for the purposes of clinical application.

Both instruments had a definitely reduced turnaround time and throughput compared with the manual method, except for one test comparison, which was caused by reduced hands-on times of both instruments for pipetting and mixing of the samples and reagents, operating the incubator and centrifuge, and carrying the cassettes. High random accessibility of the AutoVue Innova resulted in a dramatically shortened turnaround time compared with the Techno TwinStation. The other merits of the AutoVue Innova compared with the Techno TwinStation were that it does not require equipping and disposal of cassettes by operators and applied shortened centrifugation and incubation times. Because of these differences, with more batches, the increase of the gap might be inevitable. In conclusion, the two automated pre-transfusion testing instruments, the AutoVue Innova and the Techno TwinStation, exhibited acceptable accuracy and higher performance than the manual method. Moreover, the AutoVue Innova had the highest sensitivity results in titration and outstanding throughput performance compared to the Techno TwinStation and the manual method. Automation in pretransfusion testing had high accuracy and rapidity, giving rise to three goals: 1) less error, 2) less labor, and 3) faster performance.

요 약

배경 : 검사실의 전체적인 자동화의 노력에도 불구하고 혈액은행의 많은 업무들은 여전히 수작업에 의존하고 있다. 최근 몇몇 수혈 전 검사의 자동화 장비가 출시됨에 따라, Ortho사의 AutoVue Innova와 Diamed사의 TechnoTwin Station의 유용성 평가 및 비교연구를 하였다.

재료 및 방법 : 총 4,628개의 환자혈액을 사용하여 ABO 혈구형 및 혈청형 검사, Rh형 검사, 비예기항체선별 및 동정검사를 수기법과 비교하여 정확도를 평가하였다. 항응고제에 따른 검사결과의 동일성 유무를 확인하기 위하여 EDTA와 citrate 간의 비교도 ABO/Rh형 검사 및 비예기항체선별 검사에 포함하였다. anti-E, anti-E & -c, anti-D, and anti-Le^a & -Fy^a으로 확인 동정된 5검체로 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128의 7단계의 농도로 희석하여 비교하였다. 신속성의 평가를 위하여, 한 시간당 처리속도와 한 검체 및 100검체당 처리 속도를 측정하여 비교하였으며, 본 검사실에서 하루 동안 일어난 검사들을 그대로 재현하여 소요시간을 비교하여 보았다.

결과 : 두 장비 모두 ABO 혈구형, Rh형 검사에서 수기법과 100% 일치하는 결과를 보여주었다. AutoVue Innova의 경우 ABO혈청형 검사에서 10예의 불일치 예(0.4%)가 관찰되었으나 수기법에 비해 높은 강도를 보인 예들이었다. AutoVue Innova가 가장 높은 민감도와 가장 빠른 처리속도를 보여주었다. 특히, 비예기항체선별 검사에서 시간당 처리속도 및 100검체당 소요시간에서 Techno TwinStation에 비해 각각 3.3배, 3.5배의 빠른 처리속도를 보여주었다.

결론 : 높은 정확도와 신속한 검사 처리 속도를 보이는 수혈전 검사 자동화 기기는 혈액은행의 업무량과 소요시간을 줄이고, 수작업에 의한 오류를 줄일 수 있을 것으로 사료되었다.

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