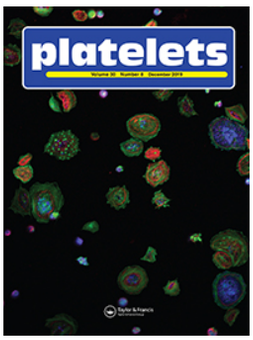

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Rapid testing of red blood cells, white blood cells and platelets in intensive care patients using the HemoScreen™ point-of-care analyzer

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Abstract

Acute major bleeding is a condition that can be encountered in critically ill patients and may require rapid transfusions. To evaluate the need for packed red blood cells (RBCs) and platelets (PLTs), it is important to have rapid test results for RBC/hemoglobin and PLTs. Recently, PixCell Medical (Yokneam Ilit, Israel) introduced the HemoScreen™, an automated hematology analyzer. It is a point-of-care device that uses single sample cuvettes and image analysis of RBCs, PLTs and white blood cells (WBCs), performing a five-part differential count. The HemoScreen™ is the first portable differential count instrument that uses image analysis. We compared the RBC, PLT, and WBC test results of the HemoScreen™ with the Sysmex XN device. In the study we analyzed 104 samples from the cardiothoracic, neuro and general intensive care units.
The HemoScreen™ technique showed good precision, with total coefficient of variation of 1–2% for RBCs and 3–5% for PLTs. Deming correlations between the HemoScreen and the Sysmex XN instrument analyzer: ($WBC_{HemoScreen™}$ = 1.061* WBC_{Sysmex} - 0.644; r = 0.995), RBC ($RBC_{HemoScreen™}$ = 0.998* RBC_{Sysmex} + 0.049; r = 0.993) for WBC and ($Platelets_{HemoScreen™}$ = 1.087* $Platelets_{Sysmex}$ – 14.80; r = 0.994) for PLT. The HemoScreen™ device provided rapid and accurate test results to evaluate the need for RBC and PLT transfusion. This new technology is promising given that it allows the analysis of WBCs, RBCs, and PLTs further out in the healthcare organization compared with laboratory infrastructure based on traditional cell counters.

Keywords

Intensive care, method evaluation, platelets, point-of-care testing, red blood cells

History

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Introduction

Hemorrhage is the second most common cause of death in trauma patients and a prevalent cause of death for those who reach the hospital after injury [1]. Injuries such as road traffic accidents and falls are also the leading causes of death in the age group of 1–44 years according to the reports of a trauma center in the United States [2] and WHO's Global Burden of Disease Report, 2016. In addition, uncontrolled hemorrhage accounts for more than 80% of all deaths in the operating room and nearly 50% of all deaths in the first 24 hours (h) after injury [3–5].

Apart from surgical control of bleeding, management of major hemorrhage may include massive transfusions to maintain adequate circulation and hemostasis [6–11]. The transfusions include packed red blood cells (RBCs), plasma, and platelets (PLTs) [12,13]. Current data indicate that trauma patients treated with higher ratios of PLTs to RBCs have better outcomes [7,9,14]. To substitute the patients optimally, it is important to monitor bleeding parameters, including PLTs and RBCs [15,16]. This procedure is facilitated by rapid test results. However, PLTs and RBCs are usually analyzed by cell counters in a centralized laboratory. Accordingly, this means long turnaround times for the processing and delivery of results. Decentralized testing would greatly reduce test turnaround times [17]. Yet, this organization is challenging in that the ability to use advanced laboratory equipment (such as cell counters) is limited in decentralized settings.

Point-of-care devices to measure blood hematocrit (HCT) and hemoglobin (HGB) have been available for years [18,19]. Recently, PixCell Medical has developed the HemoScreen™ (PixCell Medical, Yokneam Ilit, Israel), a portable point-of-care hematology analyzer that combines flow cytometry and digital imaging in a single platform [20] for full blood count. The HemoScreen™ requires a sample of 40 µL serum to measure blood cell count and employs a disposable self-contained cartridge that includes all required reagents. The blood is introduced into the single-use cartridge and then inserted into the analyzer; after approximately 5 min, the results are displayed.

The parameters analyzed by the HemoScreen™ are RBCs, white blood cells (WBCs), PLTs, HGB and HCT, as well as standard red cell characteristics and white cell differential counts.

The most important parameters to monitor in intensive care units are WBC, RBC and PLTs [21]. Current European guidelines on the management of hemorrhage following trauma [6] recommend early and repeated monitoring of PLT count to predict the proper PLT transfusion regimen. In patients with ongoing

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bleeding frequent bedside measurement of PLT count could aid the clinician in transfusing or withholding PLTs.

This study aimed to investigate the correspondence between the Sysmex XN (a large, centralized cell counter) and the HemoScreen™ analyzer for WBCs, RBCs, and PLTs. A second purpose was to evaluate whether the HemoScreen™ could be used for point-of-care testing (POCT) of intensive care patients.

Methods

Study Population

The method comparison study was approved by the local ethical committee (DNR 01–367). The ethical permit limits the patient information to age and sex. The work was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Control samples used with the HemoScreen™ analyzer were obtained from R&D Systems (Minneapolis, MN, USA).

The study was performed at a tertiary hospital with a mixed general intensive care unit, a mainly surgical neurointensive care unit and a cardiothoracic intensive care unit. The samples used were from routine requests at the Uppsala University Hospital from the general intensive care (n = 27), neurointensive care (n = 36) and thoracic intensive care (n = 41) units and eventually sent to the Department of Clinical Chemistry and Pharmacology, Uppsala University Hospital, Uppsala. The samples were taken from indwelling arterial catheters and delivered to the laboratory within 30 min. The K_2-EDTA tubes (BD Vacutainer tube 354664, Becton Dickinson, Franklin Lakes, NJ, USA) were stored at room temperature and first analyzed using the Sysmex XN (Sysmex Sverige AB, Kungsbacka, Sweden), the laboratory standard instrument for full blood count, and then analyzed with the HemoScreen™ device. The Sysmex XN is a high-capacity system for central laboratories performing automated analyses using the sheath flow direct current detection method for RBCs, PLTs and flow cytometry for differential WBCs.

For the HemoScreen™, an accurate volume of 40 µL blood was acquired using dedicated capillaries provided with the cartridge unit. After cartridge insertion into the HemoScreen™ analyzer, the rest of the procedure runs in automated mode. Cells are flow focused into a single layer plane within a microfluidic chamber that facilitates optical analysis. The analyzer then captures images of the focused cells to analyze them in real time using machine vision algorithms [20].

The tests for both instruments were run at room temperature within 4 h from obtaining the samples from the patients.

To assess the variability of the measurements control samples were analyzed four times independently. These samples were then stored at 4°C and reanalyzed daily for 10 days.

Statistical Analysis

The coefficient of variation (CV) for the HemoScreen™ analyzer and the correlation between the two analytical devices were calculated with Excel 2016 (Microsoft, Seattle, WA, USA). Deming regression analysis was performed using the Method Validator software, version 1.1 for Windows (Metz, France) and In addition, Bland-Altman plots were constructed [22].

Results

Samples were analyzed from 102 patients whose characteristics are summarized in Table I. All samples were analyzed on both the Sysmex XN and the HemoScreen™ analyzers. The mean values for the two instruments were similar (Table I).

Table I. Basic values for the study population. The age and cell counts are presented as means and range.

Sex	41 females	51 males		
Age (years)	59	11–88		
	Sysmex XN™		Hemoscreen™	
RBC (10^{12}/L)	3.63	2.24–5.29	3.68	2.23–5.31
Platelets (10^9/L)	220	23–622	225	24–677
WBC (10^9/L)	10.6	3.2–25.6	10.6	3.2–26.1

Coefficient of Variation (CV) for the HemoScreen™ Analyzer

Within-day variation was calculated based on four measurements for each of the three control levels during a single day (Table II).

Ten measurements, analyzed during 10 days for each of the three controls, were used to calculate total CV. Total CV for RBCs varied between 1.55 and 2.08% and for PLTs between 3.31 and 5.59% (Table III).

Correlation between the Two Analyzers

The equation for the Deming correlation for RBC (10^{12}/L) was $RBC_{HemoScreen™} = 0.998* RBC_{Sysmex} + 0.049$; $r = 0.993$. The 95% confidence interval (CI) for the slope was 0.977 to 1.019 and for the intercept −0.023 to 0.122. The Bland–Altman plots of the comparison between the two instruments are presented in Figure 1. Bias in the Bland–Altman plots was 0.04 for the RBC count and the limits of agreement were <0.2 10/L [12]. There was no trend in the bias for the RBC count over the range of measurements.

The equation for the Deming correlation for PLT counts (10^9/L) was $Platelets_{HemoScreen™} = 1.087* Platelets_{Sysmex} - 14.80$; $r = 0.994$ [9]. The 95% CI for the slope was 1.057 to 1.117 and for the intercept −20.73 to −8.86. The Bland–Altman plots of the comparison between the two instruments are depicted in Figure 2. Bias in the Bland–Altman plots was 4.4 for the PLT count. The limits of agreement were ±30 10^9/L. At levels <300 10^9/L, the HemoScreen-Sysmex bias for the PLT count was negative while all bias values were positive >320 10^9/L.

The equation for the Deming correlation for the WBC count (10^9/L) was $WBC_{HemoScreen™} = 1.061* WBC_{Sysmex}$ 0.644; r = 0.995. The 95% CI for the slope was 1.031–1.091 and for the

Table II. Within-day coefficient of variation (CV) on Hemoscreen ™ for the three control samples. Each control was analyzed four times on the same occasion. The results are presented as mean and CV in percentage for white blood cells, red blood cells and platelets for each control sample.

	Mean	CV (%)	Mean	CV (%)	Mean	CV (%)
RBC (10^{12}/L)	2.74	1.5	4.77	0.8	5.51	0.5
PLT (10^9/L)	74	4.4	237	3.4	568	1.5
WBC (10^9/L)	2.9	6.8	8.1	5.7	20.8	2.5

Table III. Total coefficient of variation (CV) on Hemscreen™ for the three control samples. Each control was analyzed once daily for 10 days. The results are presented as mean and CV in percentage for white blood cells, red blood cells and platelets for each control sample.

	Mean	CV (%)	Mean	CV (%)	Mean	CV (%)
RBC (10^{12}/L)	2.70	2.1	4.78	1.6	5.56	1.6
PLT (10^9/L)	68	5.6	234	4.1	538	3.3
WBC (10^9/L)	3.0	7.8	8.2	3.5	20.9	2.5

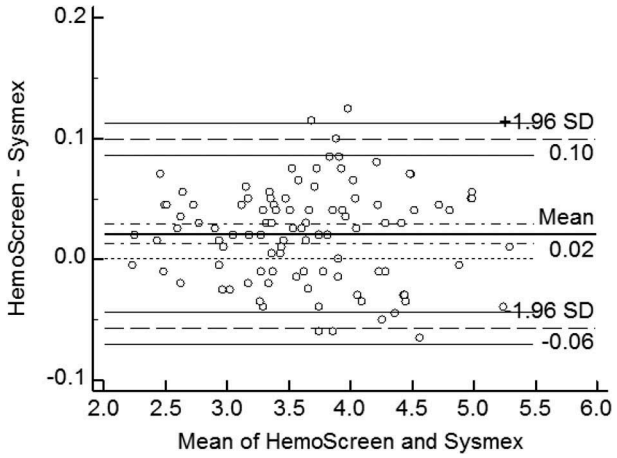

Figure 1. Bland-Altman plot for red blood cell counts (10^{12}/L) with the mean of the two methods are plotted against the differences between the two methods. The horizontal lines show the mean difference between the two methods with 95% confidence intervals and limits of agreement with 95% confidence intervals.

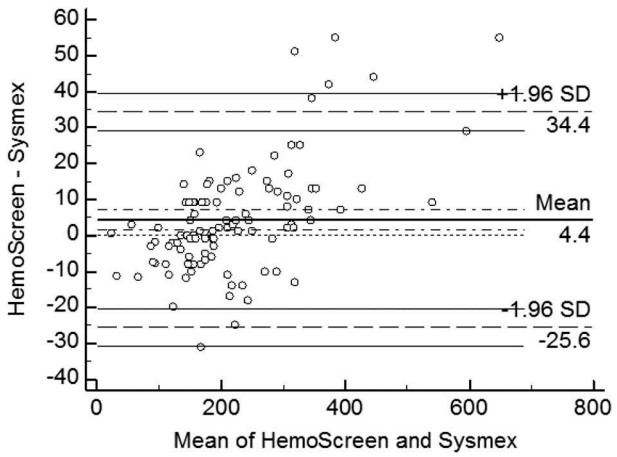

Figure 2. Bland-Altman plot for platelet counts (10^9/L) with the mean of the two methods are plotted against the differences between the two methods. The horizontal lines show the mean difference between the two methods with 95% confidence intervals and limits of agreement with 95% confidence intervals.

intercept −0.919 - −0.370. The Bland-Altman plots of the comparison between the two instruments are displayed in Figure 3. The bias in the Bland–Altman plots was 0.001 for the WBC count. The limits of agreement were ±1.15 10^9/L. At levels >19.2 10^9/L, all bias values were negative.

Discussion

We found strong correlations between the WBC, RBC and PLT results obtained with the HemoScreen™ and Sysmex NX instruments, with r values >0.99 for all three analytes in this intensive care patient cohort. Considering the length of stay of a few days in the intensive care unit (ICU) [23], we studied the intra-day CV, that was well below 5% for both RBCs and PLTs. At low PLT counts, the HemoScreen™ analyzer tended to underestimate PLT counts, whereas at high PLT counts, the effect of the bias was to overestimate. Other biases were of minor clinical significance.

Blood cell count is one of the most frequent requests made to hospital laboratories [21]. To cope with the large volumes, the measurements are usually performed with high-performance

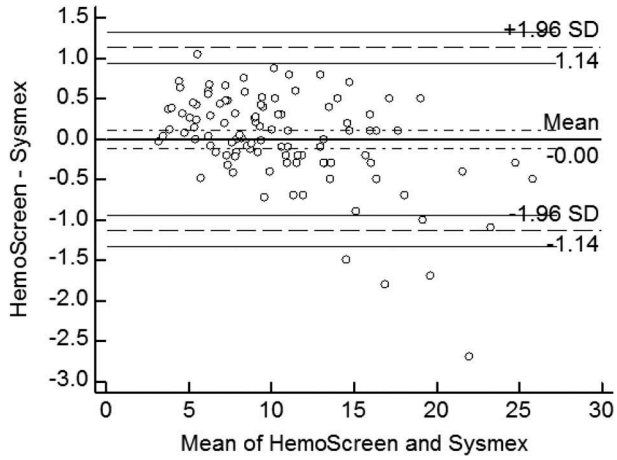

Figure 3. Bland-Altman plot for white blood cell counts (10^9/L) with the mean of the two methods are plotted against the differences between the two methods. The horizontal lines show the mean difference between the two methods with 95% confidence intervals and limits of agreement with 95% confidence intervals.

automated cell counters, counters that are expensive and complex instruments that require regular and careful maintenance. Accordingly, they are not very well suited for decentralized testing. Another problem with centralized testing is the time required to transfer the samples to the central laboratory and the possible delays in delivering results. Depending on the logistics at the local hospital, results may be available from 30 min to several hours after sampling. This is a substantial delay for intensive care patients that often require rapid decisions and actions. A way to eliminate the transport burden is to perform the analysis of blood cells as point-of-care testing [17]. Bedside analysis of HCT and calculation of HBG based on centrifugation and electrical conductivity have been available bedside for many years [18,19]. The HemoScreen™ system combines single-use sample cartridges and digital imaging [15]. One advantage of single-use cartridges for the samples is that a clot in the sample will only affect the cartridge and not the entire instrument. Accordingly, this new technology requires less maintenance and allows the analysis of WBCs, RBCs and PLTs in peripheral health care settings. Moreover, with an assay time for the HemoScreen™ instrument of approximately 5 min, the delay would be substantially reduced in comparison with centralized testing. Such a time reduction would be a formidable advantage when treating patients with major hemorrhage that requires rapid transfusions with packed RBCs and PLTs. In turn, this should lead to better optimization of the transfusion of RBCs and PLTs of which there is often a shortage in the blood bank.

Considering the need for rapid test results in the ICU and operating theater, we decided to evaluated the performance of HemoScreen™ with intensive care patient samples. Apart from blood gas measurements, the prime interest of intensive care in Sweden is WBCs, RBCs, and PLTs [21]. We therefore focused the comparison on these three parameters given that full differential WBC counts are very rarely requested by the ICUs in Sweden. The device was easy to use and operators showed a very quick learning curve, independently performing the analyses after a brief introduction. We had few technical issues with the tool. In 1% of the capillary samplings we encountered an air bubble that required resampling. There were also technical errors in approximately 1% of the tests leading to a failure message for the cuvette and thus a retest was needed. Seeing the complexity of blood cell counts, the few errors that did occur were insubstantial.

A limitation of the instrument is that the function of PLTs, HCT or WBCs is not assessed. However, PLT function is generally not offered by instruments providing full blood counts. Furthermore, although thrombocytopenia and leucopenia are not uncommon in the ICU, none of the patients presented with very low levels of PLTs and leucocytes, limiting our conclusions in these ranges. More complex tests of coagulation (e.g., thromboelastography) are available but less intuitive to interpret into clinical management.

Future studies should focus on investigating the performance of this device in remote settings (operating rooms, prehospital settings and operating theaters).

In conclusion, the HemoScreen™ point-of-care method can provide rapid and accurate analysis of WBCs, RBCs, and PLTs in an intensive care setting.

Disclosure Statement

The authors declare no conflicts of interest.

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