Letter to the Editor

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Preliminary evaluation of complete blood cell count on Mindray BC-6800

Keywords: differential; evaluation; flow cytometry; hematology.

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To the Editor,

Laboratory hematology provides an essential contribution to diagnostics and therapeutic management of most – if not all – hematological disorders. The introduction of automated flow cytometry has represented a remarkable advancement for laboratory workout, enabling several drawbacks of manual microscopy for enumeration and classification of blood cells to be overcome, which is typically plagued by a low throughput, high inter-observer variability and unsuitability for statistical testing [1], along with the possibility to generate post-analytical errors for manual transcription of results [2]. Nevertheless, due to the rather different technological approaches, an accurate evaluation of analytical performance and diagnostic accuracy of the single hemocytometers is necessary before they can be broadly introduced for routine testing. The aim of this study was a preliminary evaluation of complete blood cell (CBC) count on Mindray BC-6800, including white blood cell (WBC), red blood cell (RBC) and platelet (PLT) counts, hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean platelet volume (MPV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and RBC distribution width (RDW).

The Mindray BC-6800 (Medical Systems S.p.A., Genova, Italy) is a novel hematological analyzer specifically designed for routine CBC, which also provides a five-part differential WBC testing along with nearly 30 additional reportable parameters. The throughput is approximately 125 tests/h, with 100 tubes capacity, 150 μL aspiration via manual mode (i.e., open vial) and 200 μL aspiration via autoloader mode (closed vial). In the BC-6800, the CBC and WBC differential are performed with a flow cytometric technique that is based on laser light scattering at two angles (forward laser scatter for assessing cell size and side laser scatter for cellular complexity, respectively) combined with fluorescence signals. After construction of a 3D scattergram, WBC subpopulations are further classified according to size, cellular complexity, and nucleic acid content. The total WBC count is primarily based on the "Baso" channel, with additional comparison of WBC information from three other optical channels to eliminate interference from nucleated RBCs (NRBCs), which are counted on a dedicated channel.

In this study, the imprecision of the BC-6800 was assessed according to the Clinical and Laboratory Standards Institute (CLSI) document EP5-A2 [3], by analyzing three K_2EDTA anticoagulated specimens selected among those referred for routine analysis in 20 consecutive runs (Table 1). For the comparison studies, 125 consecutive samples referred from the Department of Hematology for routine hematological analysis over 1 week were analyzed. All samples were collected in 2.0 mL, K_2EDTA anticoagulated tubes (Becton Dickinson Italia S.p.A., Milan, Italy). The specimens were appropriately mixed by gentle inversion six to eight times, divided into three identical aliquots and further subjected to analysis by optical microscopy and automated flow cytometry within 2 h from arrival to the laboratory. Manual microscopic analysis was performed on blood smears by two independent and skilled laboratory professionals according to the H-20 CLSI guideline [4], and results were finally averaged. Routine flow cytometric analysis was performed with BC-6800 and Siemens Advia 2120 (Diagnostic Solutions, Milan, Italy). The comparison of results between BC-6800 and Advia 2120 for CBC, or between BC-6800 and manual microscopy

	Sample 1 (CV%)	Sample 2 (CV%)	Sample 3 (%)
WBC, 10^9/L	5.0±0.1 (2%)	6.4±0.1 (2%)	7.0±0.1 (2%)
RBC, 10^{12}/L	2.91±0.03 (1%)	4.01±0.03 (1%)	6.54±0.05 (1%)
PLT, 10^9/L	165±5 (3%)	209±6 (3%)	449±11 (2%)
Hemoglobin, g/L	90±1 (1%)	123±1 (1%)	165±1 (1%)
Hematocrit, %	28.0±0.3 (1%)	39.1±0.3 (1%)	56.3±0.4 (1%)
MCV, fL	86.1±0.1 (0%)	96.3±0.1 (0%)	97.5±0.1 (0%)
MCH, pg	25.2±0.1 (1%)	30.7±0.3 (1%)	31.1±0.3 (1%)
MCHC, %	29.3±0.3 (1%)	31.5±0.3 (1%)	32.1±0.3 (1%)
RDW, %	12.3±0.1 (0%)	15.5±0.1 (0%)	22.8±0.1 (0%)

Table 1 Imprecision (expressed as coefficient of variation, CV) of Mindray BC-6800 for evaluation of white blood cell (WBC), red blood cell (RBC) and platelet (PLT) counts, hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean platelet volume (MPV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and RBC distribution width (RDW).
Values are shown as mean±standard deviation.

for WBC differential, was assessed by Pearson's correlation. The bias [(and 95% confidence interval (CI)] was calculated by means of the Bland-Altman analysis. The statistical analysis was performed using Analyse-it for Microsoft Excel (Analyse-it Software Ltd, Leeds, UK). The study was carried out in accordance with the Declaration of Helsinki, under the terms of all relevant local legislation.

Optimal imprecision was observed for all the parameters tested, with coefficients of variations (CVs) always below 3% (Table 1). The comparison of WBC, RBC, PLT counts and hemoglobin between BC-6800 and Advia 2120 produced rather limited biases, i.e., 0.19×10^9/L (95% CI −0.13 to 0.52×10^9/L) for WBC, -0.15×10^{12}/L (95% CI −0.16 to -0.13×10^{12}/L) for RBCs, 14×10^9/L (95% CI 5 to 22×10^9/L) for PLT, and −2.1 g/L (95% CI −2.5 to −1.7 g/L) for Hb. The corresponding correlations were 0.99 (95% CI 0.99 to 1.00; $p<0.001$) for WBCs, 1.00 (95% CI 0.99 to 1.00) for RBCs, 0.98 (95% CI 0.96 to 0.98) for PLTs, and 0.99 (0.99 to 1.00) for Hb. The comparison of the WBC differential between manual microscopy and BC-6800 was also excellent, with mean biases of 0.21×10^9/L (95% CI 0.02 to 0.40×10^9/L) for neutrophils, -0.12×10^9/L (95% CI −0.24 to 0.00×10^9/L) for lymphocytes, 0.19×10^9/L (95% CI 0.04 to 0.34×10^9/L) for monocytes, 0.03×10^9/L (95% CI 0.01 to 0.06×10^9/L) for eosinophils and 0.00×10^9/L (95% CI −0.03 to 0.03×10^9/L) for basophils. The corresponding correlations were 0.99 (95% CI 0.98 to 0.99; $p<0.001$) for neutrophils, 0.99 lymphocytes (95% CI 0.98 to 0.99; $p<0.001$), 0.86 (95% CI 0.80 to 0.90; $p<0.001$) for monocytes, 0.83 (95% CI 0.77 to 0.88; $p<0.001$) for eosinophils, and 0.97 (95% CI 0.96 to 0.98; $p<0.001$) for basophils. As regards NRBC identification and enumeration, at the reference threshold of 1.0% as for CLSI H20-A2 recommendation [4], the overall agreement between optical microscopy and BC-6800 was 90% (kappa statistics 0.69, 95% CI 0.53 to 0.85; $p<0.001$).

The preliminary evaluation of CBC on Mindray BC-6800 suggest that this novel hemocytometer may be suitable for routine hematological analysis of most blood specimens, including those of patients with hematological disorders. This is confirmed by the fact that the optimal imprecision found on three different blood samples was even better than that claimed by the manufacturer, with coefficient of variations always lower than 3%. We have also found excellent agreement and limited bias with the current gold standard for WBC differential (i.e., manual microscopy performed according to the CLSI guidelines) after analysis of 125 pathological specimens of patients with various hematological disorders, including acute and chronic leukemias (n=72), hemoglobin disorders (n=31), multiple myeloma (n=12) and lymphomas (n=10). The BC-6800 does not generate a specific enumeration of abnormal cells as a six-part differential WBC (e.g., large and unstained cells in Advia 2120), but provides specific flags and classifies them as blast cells, atypical lymphocyte or immature granulocytes in separate submenus of the software (i.e., cells with high nucleic acid content, being positioned as a higher cluster in the scattergram). Although in this preliminary evaluation we could not assess the diagnostic accuracy of specific flags, we conclude that the performance of the five-part differential are, however, suitable for obtaining valid numerical data.

Conflict of interest statement

Authors' conflict of interest disclosure: The authors stated that there are no conflicts of interest regarding the publication of this article.
Research funding: None declared.
Employment or leadership: None declared.
Honorarium: None declared.

Received September 17, 2012; accepted October 4, 2012; previously published online March 18, 2013

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