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Original Article

Comparative evaluation between Mindray BC-6800 and URIT 5500 hematology analyzers, with emphasis on the ability to detect blasts in patients with acute leukemia

Avaliação comparativa entre analisadores hematológicos Mindray BC-6800 e URIT 5500, com ênfase na capacidade de detecção de blastos em pacientes portadores de leucemia aguda

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RESUMO: Comparar a capacidade dos analisadores hematológicos BC-6800 (Mindray) e URIT 5500 em sinalizar a presença de blastos em pacientes portadores de leucemia aguda. Foram analisadas 13 amostras de sangue periférico contendo blastos mielóide ou linfóide, provenientes de um hospital oncológico de Belém – Pará, previamente imunofenotipados por citometria de fluxo para verificar a capacidade dos equipamentos Mindray BC-6800 e URIT 5500 em sinalizar a presença dessas células no *scatter* leucocitário ou por emissão de *flags*. Para avaliação da existência de diferença estatística entre os resultados de hemácias, hemoglobina, leucócitos e plaquetas obtidos pelos equipamentos BC 6800 (Mindray) e URIT 5500 foi aplicado o teste não paramétrico ANOVA para análise de variância das amostras, o qual mostrou que não havia diferença estatística entre esses analitos. Não foi aplicado método estatístico para as contagens da diferencial leucocitária, pois o equipamento URIT 5500 não gerou dados numéricos para as amostras patológicas. Os dois equipamentos foram capazes de gerar *flags* e mudanças espacial do *scatter* leucocitário para amostras patológicas, contudo, o analisador BC 6800 (Mindray) foi o único a mudar a cor da população de blastos no *scatter* leucocitário. Os analisadores BC-6800 (Mindray) e URIT 5500 mostraram boa capacidade em sinalizar, através *flags* e do *scatter* leucocitário, para a presença de blastos mielóides ou linfóides em amostras patológicas.

Palavras-chave: Contagem de células sanguíneas; Alarmes clínicos; Células precursoras de granulócitos; Células progenitoras linfoides**.**

ABSTRACT: Compare the ability of the BC-6800 (Mindray) and URIT 5500 hematological analyzers to signal the presence of blasts in patients with acute leukemia. Thirteen samples of peripheral blood containing myeloid or lymphoid blasts, from a cancer hospital in Belém - Pará, previously immunophenotyped by flow cytometry were analyzed to determine the capacity of the Mindray BC-6800 and URIT 5500 equipment in signaling the presence of these cells in the leukocyte scatter or by emitting flags. To assess the existence of statistical difference between the results of red blood cells, hemoglobin, leukocytes and platelets obtained by the BC 6800 (Mindray) and URIT 5500 equipments, the non-parametric ANOVA test was applied for analysis of variance of the samples, which showed that there was no statistical difference between these analytes. Statistical method was not applied for leukocyte differential counts, as the URIT 5500 equipment did not generate numerical data for the pathological samples. Both devices were able to generate flags and spatial changes from the leukocyte scatter to pathological samples, however, the BC 6800 (Mindray) analyzer was the only one to change the color of the blast population in the leukocyte scatter. BC-6800 (Mindray) and URIT 5500 analyzers showed good ability to signal, through flags and leukocyte scatter, for the presence of myeloid or lymphoid blasts in pathological samples.

Keywords: Blood cell count; Clinical alarms; Granulocyte precursor cells; Lymphoid progenitor cells.

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INTRODUCTION

The complete blood count (CBC) or hemogram is one of the essential clinical-laboratory screening exams in diagnosing and controlling diverse hematological, infectious, and chronic diseases. However, its efficiency was possible due to the occurrence of technological advances throughout the years regarding the number of samples analyzed per minute, reduction of overhead, and the capability of automated analysis of parameters such as red blood count, hemoglobin concentration, hematocrit, hematimetric indexes; leucocytes, and differential leukocytes; and the platelet count and platelet indexes; as well as the morphological abnormality markings (flags) in blood samples[1-9].

Those technological advances have made it possible to launch diverse automated hematological equipment (Beckman Coulter®, Sysmex Corporation®, Roche Products Ltd®, Abbott Diagnostics®, Siemens Healthcare Diagnostics/Bayer®, Horiba Diagnostics/Horiba ABX®, and others) employing different analysis technologies (impedance, flow, fluorescence, and spectrophotometric cytometry). Thence it is necessary to choose a hematological analyzer to perform a clinical analysis laboratory routine while considering the peculiarities of each procedure. Especially when performing these procedures in diagnostic centers and onomatological follow up, namely, laboratories that work on recognizing pathological samples[8,10-19].

This study opted for evaluating two different brands of equipment, from distinct manufacturers, using standard analysis technologies for determining the concentration of hemoglobin, total leucocyte, red blood cell, and platelet count; and specific technologies for five types of differential leukocyte counts (neutrophils, lymphocytes, monocytes, eosinophils, and basophils). One type of equipment was the URIT-5500 that determines the differential leucocyte by flow cytometry and optical laser dispersion at four angles (size and complexity) similar to the Coulter equipment description[3,8,11,12].

And the other equipment was the BC-6800 (Mindray) that detects the differential leucocyte by flow cytometry associated with "SF Cube" cellular analysis technology and is based on a DNA/RNA content reaction of the blood cells with reactants patented by the manufacturer and enables information on the dissemination of the laser light from two angles (complexity and the DNA/RNA content fluorescence signs, at an extremely high rate of precision of mature and immature cells as described for the Sysmex equipment[2,3,8,11,13,14,16,18,19].

Both the granularity characteristics/internal complexity and size (URIT-5500) or the internal granularity/ complexity and fluorescence signs of the DNA/RNA content of the cells (BC-6800, Mindray) can be monitored through a bi-dimensional graphic representation of the leucocyte dispersion based on five types (scatter/ cytogram), as each population of leucocytes is defined by a specific plotting area within the scatter according to its characteristics. Thereby, any changes in the cellular plotting in the leucocytic scatter, jointly with the issuance of flags (alerts), determine the criteria for verifying cellular morphology in the blood smear[2,5,8,11].

Thus, the purpose of this study has been to compare the capability of the BC-6800 (Mindray) and URIT 5500 hematologic analyzers in graphically marking in the leucocytic scatter or through issuing flags (alarms), the presence of myeloid blasts or lymphoids previously phenotypes by flow cytometry.

MATERIALS AND METHODS

Casuistic and Samples

It is a pilot, clinical, and randomized study, based on analyzing 25 samples of peripheral blood from patients of both genders, ranging in age from 0 to 17 years old, who were referred to an oncological hospital for clinical analysis laboratory for support in the city of Belém, Pará.

A total of thirteen samples from patients were selected after performing immunophenotype by flow cytometry for defining the ontogeny of the blasts, in a characterized format as the acute leukemic samples (myeloid or lymphoid) in immunological activity, as that result showed there was over 20% of blasts. After these samples were collected, in adherence with the manufacturer's counsel up to four hours after collection, in the BC-6800 (Mindray) and URIT-5500 equipment to compare the numerical results from each part comprising the CBC and characterized by the leucocyte scatter or the issuance of flags (alarms) testing for the presence of blasts.

Immunophenotyping

The blast type characterization was performed by immunophenotyping by adding 100 μL of the sample in conical tubes and 7 μL of different combinations of commercial monoclonal antibodies that were added to that - pan-hematopoietic: CD34, CD45, HLA-DR; lymphoids B: CD19, CD10, CD20, CD22, CD79a, TdT, IgG1, IgG1, IgM, anti-kappa, and anti-lambda; lymphoids T and NK: CD5, CD7, CD2, CD1a, CD3, CD4, CD8, CD56; or myceloids: CD13, CD33, CD117, CD61, CD14, CD64, CD11b, Glycophorin A, CD42a, MPO – marked by FITC, PE, Percyp, and APC, more lysis and/or permeabilization of the samples, incubation in the dark, centrifugations and washings, and even the acquisition and analysis of 10,000 events in the BD FACSCaliburTM flow cytometer, running the BD CellQuestTM Pro software (BD, San Jose, CAL, USA), in four colors.

Exclusion Criteria

Twelve samples were excluded: patients who were older than 17 years old; acute leukemia carriers who were not in immunological activity, that means after performing morphological analysis, there were less than 20% blasts on the slide from the peripheral blood; non-leukemia disease carriers; or even coagulated or derived from the bone marrow.

Ethical Aspects

All these procedures were performed in a private laboratory in Belém, Pará, after getting approval from the umbrella and pilot project by the Research Ethics Committee at the "Fundação Pública Estadual Hospital de Clínicas Gaspar Vianna" (the Gaspar Vianna State Clinical Hospital Public Foundation), ruling # 732,668, dated May 22, 2014.

Statistical Analysis

The ANOVA non-parametric test was applied for independent variance analysis by running the Bioestat 5.0 software. The $p \leq 0.05$ value was considered significant.

RESULTS

There was a total of over 20% of the analyzed samples with blasts in the morphological analysis on the slide. They were immunophenotyped by flow cytometry. Among those, 6/13 samples displayed the presence of myeloid blasts, and 7/13 samples showed the presence of lymphoid blasts. There was no statistical difference observed for these analytes regarding the quantitative results from the red blood cells, platelets, leucocytes, and hemoglobin concentration from the analysis from the samples obtained in the BC 6800 (Mindray) and URIT 5500 equipment (Table 1).

Table 1. The representation of the absolute values on the total of red blood cells, platelets, leucocytes, and the hemoglobin concentration from the peripheral blood samples containing over 20% of myceloid or lymphoid blasts and, were analyzed in the BC 6800 (Mindray) and URIT 5500 equipment.

Patients / Analytes	WBC (10^3/uL)		RBC (10^6/uL)		HB (g/dL)		PLT (10^3/uL)	
	BC 6800	URIT 5500	BC 6800	URIT 5500	BC 6800	URIT 5500	BC 6800	URIT 5500
1	52,41	16,9	2,47	2,31	6,8	6,3	13	32
2	78,28	33,52	3,69	3,48	10,5	8,8	97	74
3	53,64	34,33	3,35	3,11	9,8	9,0	25	33
4	3,83	3,98	3,34	3,10	9,9	8,8	20	33
5	9,03	7,16	3,42	3,14	9,8	8,4	13	20
6	40,49	45,03	4,39	4,18	13,6	12,0	83	134
7	18,42	18,52	3,78	3,48	11,9	10,0	14	27
8	344,77	113,37	2,80	2,64	6,7	7,0	41	46
9	33,47	33,1	3,47	3,17	8,9	8,0	8	20
10	4,77	4,31	2,39	2,23	6,5	6,0	36	62
11	12,59	11,7	3,48	3,62	10,7	10,7	5	10
12	11,14	11,07	2,97	2,69	8,5	7,0	22	67
13	23,8	20,39	3,37	2,04	9,9	6,0	28	110
p	0,6576		0,2167		0,1310		0,1272	

Legend: WBC – Total Leucocytes; RBC – Red Blood Cells; HB- Hemoglobin; PLT – Total Platelets; p – statistical value obtained after variance analysis from the ANOVA test.

However, in this study, it was not possible to perform statistical analysis on the results from five types of differential leucocytes due to the operation of the BC 6800 (Mindray) equipment, as only the complete count of this differential was performed on 6/13 of the samples. Differently from the URIT 5500 equipment that performed the differential leucocyte count on all the samples.

Regarding the capacity of the BC 6800 (Mindray) equipment and URIT 5500 equipment to mark the presence of blasts in pathologically recognized samples, both could perform that observation by issuing flags, as described in Table 2 and thus assuring the necessity for a morphological revision of the leucocytes on the slide. The same equipment was also capable of marking the presence of lymphocytosis, neutropenia, leukocytosis, thrombocytopenia, and other qualitative changes in the same samples.

Table 2. The presentation of original qualitative flags issued by the BC 6800 (Mindray) and URIT 5500 equipment for marking the presence of blasts in a peripheral blood sample and its meaning for the operator.

Sinalização de *Flags*	Significado
WBC?	Graphic distribution indicator with abnormal leukocyte scattering
WBC Abnormal scattergram	
Blasts	Indicator of the possibility of the existence of blasts in the sample
Immature granulocytes	Indicator of the possibility of the existence of immature granulocytes in the sample
Atypical Lymphocytes	Indicator of the possibility of the existence of atypical lymphocytes in the sample
Abnormal Lymphocytes	Indicator of the possibility of the existence of lymphocytes with abnormal morphology or blasts in the sample

Legend: WBC – Total Leucocytes.

Concerning the visual analysis of the leucocyte scatters for these samples observed by the 6800 (Mindray) equipment, it was the only one that marked the presence of undefined cellular populations by a different one than typically viewed in normal cellular populations, which is, the presence of blasts (myeloids or lymphoids) in the scattergram marked by a gray color, while in the URIT 5500 equipment, all the scatters from these samples had superimposed blast populations in the monocyte or lymphocyte standard plotted regions.

DISCUSSION

The hematologic counters in the BC-6800 (Mindray) and URIT-550 equipment displayed statistical agreement from the results on red blood cells, hemoglobin concentrations, leucocytes, and platelets, corroborating with the data in the literature for analyzers employing similar technologies[2,3,8,11,14,16,18,19,20]. Even good capabilities in marking the presence of blasts in samples, pathological recognition, regarding hypocellular (3,830 leucocytes/mm^3) and hypercellular (344,770 leucocytes/mm^3), through changes in the leucocyte, scatter or even through the issuance of flags.

Regarding the changes observed in the blast plotting in the scattergram, we observed the main finding regarding the superimposition of these cells in the plotted regions of the monocytes or the lymphocytes. Such as what has been described in the literature[2-5,8,10-14,16,17,19,] which stated that the size, cytoplasmic granularity, and amount of DNA/RNA of the blasts, myceloids, or lymphoids were similar to the populations of normal lymphocytes or monocytes. It is also described in the literature[5,7,10-13,19,20,21] that, for the same reasons, other types of cells, like atypical lymphocytes or prolymphocytes, when observed in the samples of the peripheral blood and end up promoting superimposition of the cellular plotting within the monocyte or lymphocyte regions. This requires the close attention of the equipment operator when analyzing each sample.

We must emphasize that the BC-6800 (Mindray) equipment concerning the presence of blasts and its scattergram plotting demonstrated its capability of modifying the plotting color of the blast population in the leukocyturia scatter compared to the plotting of normal cellular populations in such a way as to make the observer pay attention to the need for performing a morphological revision of the sample.

As the complete counting analysis of the five types of differential leucocytes, the URIT 5500 equipment was the only one that performed the differential counting of all the analyzed samples, although that equipment distributed the blasts present in the samples among the populations of neutrophils, lymphocytes, monocytes, eosinophils, and basophils. For an inexperienced analyst who is not used to analyzing scattergram and verifying flag issues by the equipment, that fact can generate the false idea that the sample is not pathological and induce it to release it without reviewing it on the slide. Since the BC 6800 (Mindray) equipment only performed the complete counting of the differential leucocytes on 6/13 of the analyzed samples. It obliges the equipment analyst to verify the sample on the slide.

For example, Joshi et al.[22] confirmed in their studies that nowadays the automated analyzers in hematology are standardized to mark quantitative and qualitative changes in the CBC by issuing flags and changes in the cellular distributions in the scattergram of the pathological samples. Furthermore, regarding these markings, the operator should revise the changes indicated by the equipment to ensure the quality of the final results.

So, to emphasize the maximum the automated hematologic equipment nowadays utilizes increasingly modern technology and can help the clinical analyst in their decision making; however, these professionals must be familiarized with the counting parameters of differential leucocytes, graphical scatter analysis of leukocyturia, and flag verification proposed by the supplier of each type of equipment[4,5,6,10,11,13,16,17,22].

CONCLUSION

The BC-6800 (Mindray) and URIT 5500Os

hematological analyzers have displayed good capabilities in graphically marking in the leucocyte scatter and by issuing alarms (flags) showing the presence of blasts, myceloids, or lymphoids, in samples previously phenotyped by flow cytometry.

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