ORIGINAL ARTICLE

Point-of-Care Testing of White Blood Cell Count and C-Reactive Protein in a Pediatric Emergency Department

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Abstract

Introduction: Laboratory workup is often required to assess patients admitted to the pediatric emergency department. Among the blood testing, the white blood cell count and C-reactive protein are commonly used markers. Few studies report point-of-care tests performance in a pediatric clinical setting. The main goal of the study was to assess the accuracy and clinical applicability of point-of-care tests for white blood cells and C-reactive protein compared with conventional testing methods. We also assessed patient discomfort and hands-on time for both procedures.

Methods: Patients were included based on clinical criteria for blood sampling. For each patient, capillary blood samples for point-of-care tests and venous blood samples for conventional analysis were collected to measure white blood cells and C-reactive protein. Pain was assessed with age appropriate scales and both procedures were timed.

Results: A total of 242 blood sample sets were obtained, but 100 point-of-care tests for white blood cells were invalidated. Point-of-care test showed good agreement with the conventional method in all of the assessed parameters. The mean differences between the point-of-care and conventional test were 0.9 x 10^3 cells/µL for white blood cells and -0.2 mg/dL for C-reactive protein. The error rate of the point-of-care test was 5% for C-reactive protein and 17% for white blood cells. The pain score and hands-on time for sampling were lower in the capillary puncture ($p < 0.001$).

Discussion: Point-of-care tests were considered accurate. Overall, capillary blood sampling was less painful and time-consuming than venipuncture. Point-of-care testing can be a useful tool in the assessment of patients in a pediatric emergency department.

Keywords: Blood Tests/methods; C-Reactive Protein/blood; Child; Emergency Service, Hospital; Leukocytes/blood; Point-of-Care Systems; Point-of-Care Testing

Introduction

When blood workup is required in a hospital setting, the collected blood sample is sent over to the laboratory to be processed. Technological evolution has made it possible to reduce the size and simplify the use of laboratory equipment, which enabled the use of bedside testing by non-laboratory professionals.[1]

Point-of-care (POC) tests have many potential advantages compared to conventional laboratory tests (CLT), namely equipment mobility and a shorter turnaround time.[2,3] This can potentially reduce the length of stay in health services. These devices require a smaller volume of biological product, and the blood samples are generally obtained by a finger prick.[4,5]

In the pediatric emergency department, the C-reactive protein (CRP) concentration and white blood cell (WBC) count are useful biomarkers used in the evaluation of acute infectious disease, namely in the differential diagnosis between viral and bacterial etiology.[6,7] Several POC tests are available on the European market for both tests, but there are few published studies on their accuracy in a pediatric emergency department.[3,6,8-10]

In POC testing, capillary blood sampling is preferentially used. It is known to be less invasive than venipuncture, but the literature is still lacking objective data in the POC setting.[2,4]

Our main purpose was to compare the POC and CLT tests for C-reactive protein and white blood cells measurement regarding their accuracy and clinical applicability. We also assessed blood sampling time and discomfort experienced by the patient during the procedures.

Methods

Study sample

A prospective study was conducted at the pediatric emergency department of a level 2 university hospital

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in Portugal. The patients were either referred to the emergency service by primary care physicians or admitted by the caregivers' initiative. The study was conducted from March 2016 to December 2016. All of the children admitted to the pediatric emergency department, which after clinical assessment required blood sampling, were eligible for participation. Hemodynamically unstable patients were excluded from the study.

Data collection

All of the participants underwent two blood draws, one by venipuncture for CLT and another by capillary puncture for POC tests. The order of the procedures was attributed by the order number in the study. Patients with odd-order number were first submitted to venipuncture and those with even-order number were first submitted to a capillary puncture.

For CLT, a variable amount of blood was drawn according to age, in two tubes, one dry and one with ethylenediaminetetraacetic acid (EDTA) that were transported to the hospital central laboratory. For POC tests, blood was drawn into two pipettes (one with 5 µL for CPR, one with 15 µL for WBC) and inserted in disposable discs ready to be analyzed in the devices physically located at the pediatric emergency department.

The equipment used for conventional laboratory tests was UniCel® DxC 600i (Beckman Coulter, Inc. United States) for C-reactive protein assay (analytical range 0.5-20 mg/dL)[11] and UniCel® DxH 800 (Beckman Coulter, Inc. United States) for white blood cells (measuring range 0-400 x 10^3 cells/µL).[12]

The equipment used for POC tests was spinit®[t] (Biosurfit, SA, Portugal), a small (236 × 215 × 306 mm) and easily moveable device. This is an instrument that performs different laboratory panels (hematology, immunoassays, and clinical chemistry), depending on the disposable disc used. Discs are ready-to-use, do not require any reagent preparation step and allow automated sample processing.

The spinit® BC determines the total and WBC five cell type differential values as well as hematocrit measurement in 10 minutes, with a detection range for WBC of 3-30 × 10^3 cells/µL. Neutrophil and lymphocyte differential count is based on the relative percentages and not absolute values, so we could not assess the out of range results of these two parameters. This study did not evaluate the basophil, eosinophil, and monocyte counts because of its limited clinical application in the pediatric emergency department.

The spinit® CRP determines CRP values in five minutes, with a detection range of 0.4-18 mg/dL.[13,14]

The samples for the POC test were collected by doctors or nurses working in the pediatric emergency department. There were two 1-hour practice sessions on how to use the devices, given by the POC equipment manufacturer. The first occurred prior to the beginning and the other during the study.

Biosurfit SA was responsible for regular quality check-up of spinit®, concerning the calibration and maintenance of the equipment.

Regarding the secondary aims, the blood sampling time was assessed with a chronometer. The time count was initiated at the beginning of the procedure (when all the required material was prepared) and terminated when the samples were ready to be transported to the central laboratory or inserted in the spinit® discs.

Patient discomfort with both kinds of puncture was evaluated with pain scales. Such scales were used according to the children's age or maturity, namely FLACC-R (face, legs, activity, cry, consolability, revised scale) for those who did not verbalize, the faces pain scale for preschool children and the numerical scale for school-aged or older children.[15] The different scales were uniformized for analysis.

Data analysis

Statistical analysis was performed using MedCalc® (version 15.8, MedCalc Software Ltd, Belgium). A comparison of the laboratory methods was performed using the Pearson correlation coefficient (r) and Bland-Altman plot.[16] The results above and below the equipment detection limits were omitted pairwise in the comparative analysis. A comparison of the pain discomfort and blood sampling time was made using the Wilcoxon test.

Results

A total of 230 children and adolescents were included in the study, of which 48% were male, with a median age of 6.6 years (2.3; 13.6).

Two hundred and forty-two blood samples were collected for each method. The most common reasons for blood sampling were the investigation of fever with warning signs (n = 69) and assessment of dehydration in acute gastroenteritis (n = 65). The remaining analysis were performed as complementary tests in the diagnosis of acute abdomen (n = 39), differentiation of bacterial *versus* viral respiratory infection (n = 20), in the presence of constitutional symptoms (n = 15), when anemia or thrombocytopenia were suspected (n = 11), and others (n = 23).

The first 100 white blood cell tests in the POC device were invalidated due to a systematic equipment error, which led to its substitution. During the study period, other operational errors in both methods occurred (e.g. insufficient blood in the disc, coagulated sample, system errors) that led to missing results. The error rate (representing all of the analyzed samples that did not obtain results) for POC tests was 5% for C-reactive protein and 17% for white blood cells. For conventional laboratory tests, the error rate was 2% for CRP and 2% for WBC.

C-reactive protein

There were 242 collected samples, of which 96 had out of range results, 17 generated errors, and 129 were eligible for comparative analysis. The Pearson correlation coefficient showed a strong positive correlation between the methods, with r = 0.9687 and $p < 0.0001$ (Fig. 1A). The Bland-Altman test (Fig. 1B) had a near zero mean difference between the CLT and POC test values (-0.2 mg/dL), with very good agreement between the methods. Regarding children with POC C-reactive protein out of range (91 tests values < 0.4 mg/dL and five test values > 18 mg/dL), all but four results (four samples with values < 0.4 mg/dL) were concordant with those from the central laboratory.

White blood cells

For the total WBC and differential values, 142 tests were conducted in each method. For the total WBC count, two samples were out of the detection limits and 26 were eliminated due to errors, leaving 114 samples for analysis. The point-of-care test correlated well with the CLT (r = 0.9022, $p < 0.0001$). In the Bland-Altman plot, the mean difference was 1 x 10^3 cells/µL and the 95% confidence interval of agreement limits included almost all results and were deemed compatible (-3.5 x 10^3 to +5.5 x 10^3 cells/µL) (Figs. 2A and 2B).

Of the two samples with POC test values outside the detection threshold, only one was concordant with the central laboratory.

Regarding the neutrophil count, of the 142 samples, 61 were excluded (36 errors and 25 out of detection limits) and 81 were analyzed. We obtained an almost linear positive correlation (r = 0.9077, $p < 0.0001$) and a mean difference between the methods according to the Bland-Altman plot of -0.2 x 10^3 cells/µL (Figs. 2C and 2D).

In the lymphocyte count analysis, 74 subject samples were studied (32 excluded samples for out of range limits and 36 errors). The point-of-care tests also achieved a strong correlation (r = 0.8738, $p < 0.0001$) and in the Bland-Altman plot, the difference between the two methods was 0.8 x 10^3 cells/µL (Figs. 2E and 2F).

Blood sampling time

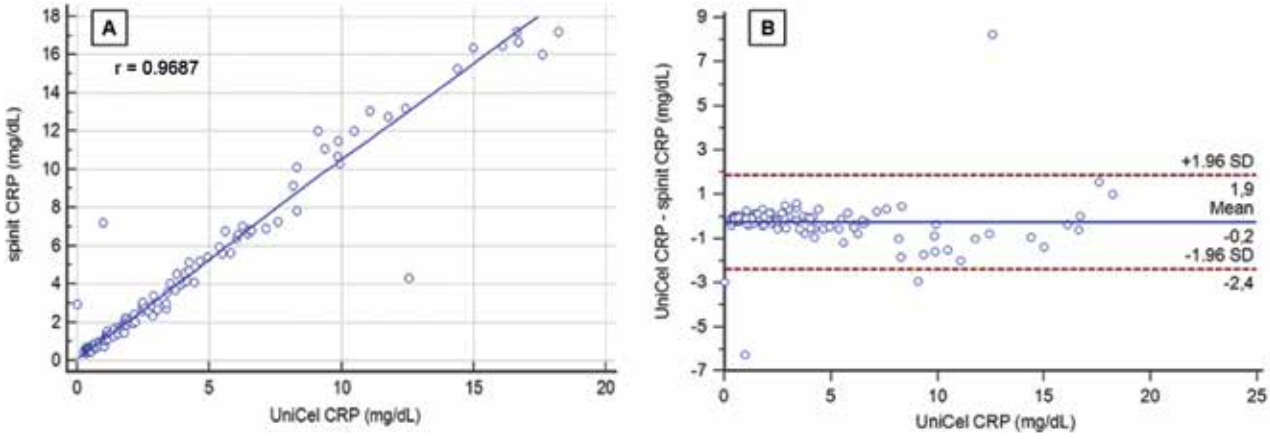
The blood sampling time was assessed in 234 procedures. Venipuncture was significantly higher than in the capillary puncture ($p < 0.001$) (Table 1).

Patient discomfort in puncture

A total of 236 pain scale scores were evaluated (110 FLACC-R, 117 numerical scales, 8 revised face scale and 1 visual analogue scale). The pain was considerably more intense in the venipuncture procedure ($p < 0.001$) (Table 2).

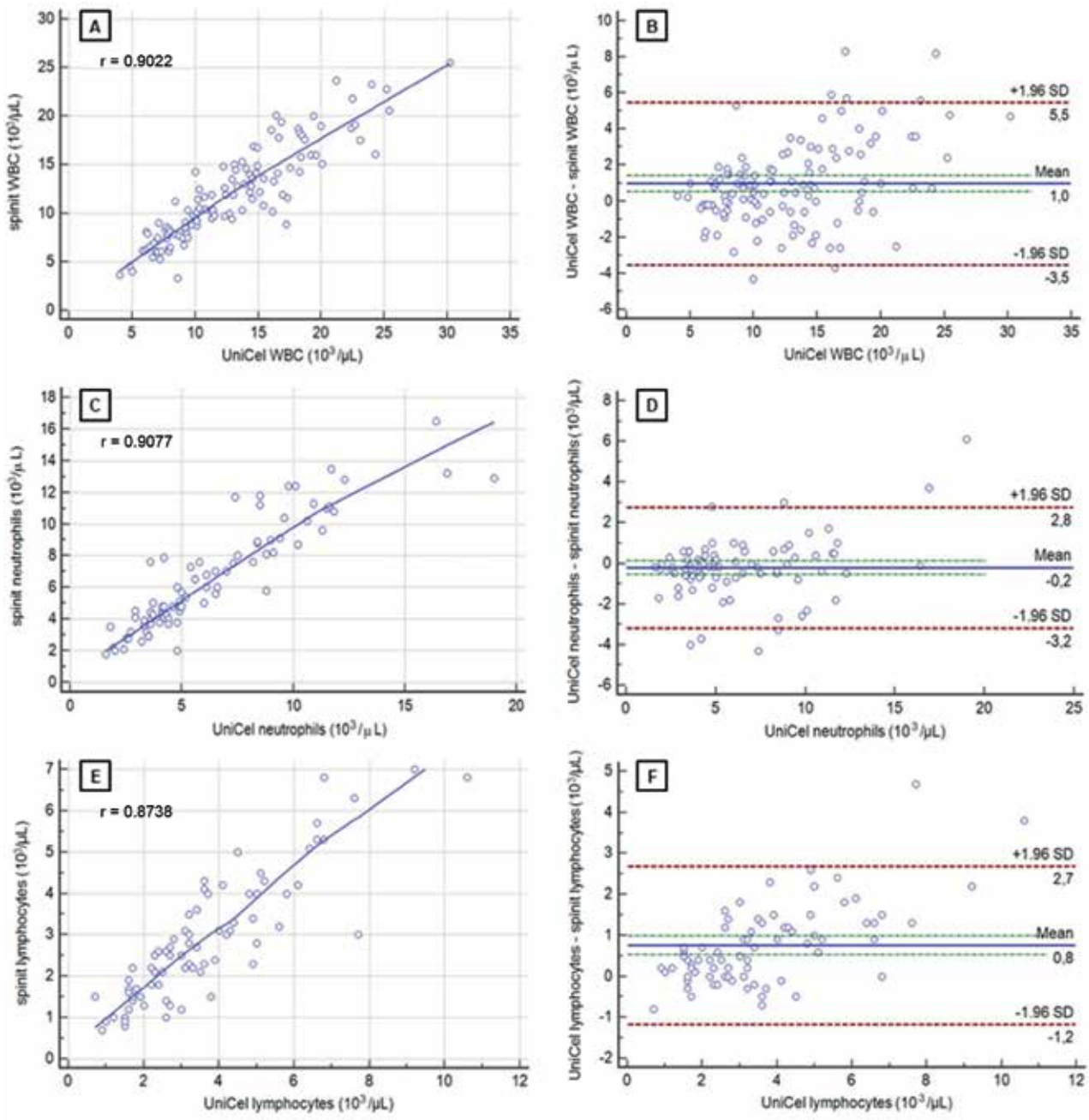
Discussion

In this study, point-of-care tests proved to be accurate in the evaluation of children in the pediatric emergency department.



CRP - C-reactive protein, POC - point-of-care, SD - standard deviation.

Figure 1. Comparison of the point-of-care and conventional tests for C-reactive protein values (n = 129). Scatterplot of the relationship between the methods and Pearson correlation coefficient (A). Bland Altman plot for the difference between the methods with a representation of the mean difference (solid line) and of 95% limits of agreement (dashed line) (B).



r - correlation coefficient; SD - standard deviation; WBC - white blood cells.

Figure 2. Comparison of the point of care and conventional tests for white blood cells values. For leucocyte analysis, n = 114. Scatterplot of relationship between the methods and Pearson correlation coefficient (A). Bland Altman plot presenting the level of agreement between the methods. For neutrophil analysis, n = 81. Scatterplot of the relationship between the methods and Pearson correlation coefficient (C). Bland Altman plot presenting the level of agreement between the methods (D). For lymphocyte analysis, n = 74. Scatterplot of the relationship between the methods and Pearson correlation coefficient (E). Bland Altman plot presenting the level of agreement between the methods (F). In the Bland Altman plots, the solid line represents the mean difference between the two methods and the dashed lines represent the 95% limits of agreement.

Comparing spinit® BC and spinit® CRP with the reference tests in the laboratory, we obtained good agreement for both white blood cells and C-reactive protein, and these results are in line with those obtained by other authors that compared spinit® with CLT.

A very good correlation was achieved between spinit® BC assay and the Sysmex XE-5000 (Pearson coefficient: WBC r = 0.937, neutrophils r = 0.928, lymphocytes r = 0.919) and the absolute mean differences for the parameters of the leukogram were rather minimal (Bland Altman plot: WBC -0.45 x 10^3 cells/µL, neutrophils -0.16 x 10^3 cells/µL, lymphocytes -0.22 x 10^3 cells/µL).[14]

In another study[13] both spinit® BC and spinit® CRP correlated well with the laboratory method (Sysmex XN and Cobas 8000, respectively), and was considered a reliable device.

Table 1. Blood sampling time comparison, measured in seconds (n = 234)

	Capillary puncture (s)	Venipuncture (s)	Wilcoxon test
Median	60	111	$p < 0.001$
IQR	30-90	70-180	-

Table 2. Patient discomfort comparison, measured with pain scales (n = 236)

	Capillary puncture (pain scale)	Venipuncture (pain scale)	Wilcoxon test
Median	2	5	$p < 0.001$
IQR	1-3	2-7	-

IQR - interquartile range.

So far, most studies comparing point-of-care with conventional laboratory tests in a pediatric context showed good correlations between the methods.[8,17] A POC was tested for CRP in 283 children with a fever of unknow origin in a pediatric emergency department with a strong, positive correlation between both methods.[6] Other authors[10] compared the POC test for C-reactive protein and white blood cells in 168 febrile children in the pediatric emergency department, also achieving good agreement with the reference methods. Similar to other authors,[18] our weaker correlation was for lymphocytes.

The values of out of detection limits of spinit® devices cannot be used to assess patients. They were not statistically analyzed but were mostly congruent with CLT, as previously reported.[6,8,10,19] In clinical practice, these values should always be carefully interpreted in conjunction with the clinical data. Regardless, we considered the range acceptable for the distinction of viral from bacterial etiology in the pediatric emergency department.

Although some studies describe rare technical errors in the POC analyses,[10] we had a non-negligible percentage of errors with spinit® equipment, mainly with WBC. Even so, it was in line with other studies that used spinit®. It was described that 19 of 115 samples of spinit® BC gave no result for one or more parameters (16% *vs.* 17% in our study).[14] This may be because POC tests are more accessible and permit an increased number of device users, thereby increasing inaccurate results due to human error.[2,5] Fingerstick may also be responsible for the high percentage of errors, as it is related to clotting and hemolysis when not collected optimally.[18]

Decreasing pain and discomfort during diagnostic procedures in children is the responsibility of health workers. Because POC tests need a lower volume of biologic products, capillary blood is a method of preference, as it is less invasive and less painful.[2,4] We found that the capillary puncture pain score was significantly lower to venipuncture, which can contribute to better screening acceptability by children and their parents.[2,20]

In this study, hands on time for sampling for the POC system was shorter than sampling for CLT (by almost one minute), freeing emergency workers up to do other tasks faster. This result is concordant with other studies.[10] Although we did not analyze this outcome in terms of patient flow in the pediatric emergency department, some studies have already concluded the potential of the POC test for decreasing the length of stay in the emergency department.[3,9,10]

Research limitations included operator dependent differences in the POC testing and blood sampling. The time until the availability of results and the impact of the POC tests in the length of stay in the pediatric emergency department were not evaluated. When assessing the pain during blood collection, we did not normalize the data for the different puncture sites.

The main disadvantages of the POC test were vulnerable operator-dependent steps, the error rate, and the limited detection range.

The relevance of our study lies in the fact that, in addition to reporting the correlations between the POC tests and laboratory instruments, we also assessed the impact of the POC test in clinical practice (patient discomfort and sampling time) in the pediatric emergency department. We believe our study contributes to the development and improvement of POC devices.

WHAT THIS STUDY ADDS

- Overall, a good correlation and a good agreement was demonstrated between the point-of-care and conventional laboratory tests for white blood cells and C-reactive protein analysis.
- Capillary puncture was less time consuming and associated with less discomfort than venipuncture.
- Point-of-care tests can be useful as a method of screening, helping to manage patient flow more efficiently in the pediatric emergency department.
- The use of point-of-care devices must consider the lack of studies and experience in pediatric setting, thus implying regular quality checks and user training.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

Funding Sources

There were no external funding sources for the realization of this paper.

Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Provenance and peer review

Not commissioned; externally peer reviewed

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Awards and presentations

Study presented at the 8th Excellence in Pediatrics Conference (London, United Kingdom, 2016) and at the 19º Congresso Nacional de Pediatria (Estoril, Portugal, 2018).

This study was awarded with Prémio Investigação e Formação Avançada Pfizer Vaccines – Sociedade Portuguesa de Pediatria (Programa Crescemos Consigo) for pediatrics interns, for the best studies in three different areas of pediatrics at the 19º Congresso Nacional de Pediatria (Estoril, Portugal, 2018).

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Testes de Cabeceira de Contagem de Leucócitos e Proteína C Reativa num Departamento de Urgência Pediátrica

Resumo:

Introdução: Na avaliação das crianças no serviço de urgência pediátrico podem ser necessárias colheitas de sangue. A contagem leucocitária e a proteína C reativa são marcadores de infeção aguda frequentemente requisitados. Existem testes de cabeceira para realização destas análises, mas poucos estudos sobre o seu desempenho na população pediátrica. O objetivo principal foi determinar validade e aplicabilidade clínica dos testes de cabeceira para contagem leucocitária e proteína C reativa, comparando com os testes laboratoriais convencionais. Também foram analisados o tempo de colheita e o desconforto do paciente em ambos os métodos.

Métodos: Inclusão de crianças com critérios clínicos para colheita de sangue. Em cada criança foi colhido sangue capilar para os testes de cabeceira e sangue venoso para os testes convencionais. A dor foi aferida com escalas apropriadas à idade e ambos os procedimentos foram cronometrados.

Resultados: Foram obtidos 242 conjuntos de amostras séricas, mas foram invalidados 100 testes de cabeceira para a contagem leucocitária. Os testes de cabeceira para a contagem leucocitária e proteína C reativa mostraram boa concordância com os métodos de referência. A média das diferenças entre os resultados obtidos pelos testes de cabeceira e os convencionais foi 0,9 x 10^3 células/µL para a contagem leucocitária e -0,2 mg/dL para a proteína C reativa. A taxa de erro dos testes de cabeceira foi 5% para a proteína C reativa e 17% para a contagem leucocitária. A intensidade de dor e o tempo de colheita foram inferiores na colheita capilar ($p < 0,001$).

Discussão: Os testes de cabeceira foram considerados válidos. A colheita de sangue capilar foi menos dolorosa e demorada que a punção venosa. Os testes de cabeceira podem ser uma ferramenta útil na gestão dos pacientes no serviço de urgência pediátrico.

Palavras-Chave: Criança; Leucócitos/sangue; Proteína C-Reativa/sangue; Serviço de Urgência Hospitalar; Sistemas Automatizados de Assistência Junto ao Leito; Testes Hematológicos/métodos; Testes Imediatos