International Journal of Laboratory Hematology
The Official journal of the International Society for Laboratory Hematology

Letter to the Editor

No clinically relevant differences between capillary and venous blood cell counts in adult haematological patients using a nonautomated lancet

Sir, Physicians who treat patients suffering from haematological diseases require the determination of peripheral complete blood counts (CBC), among other tests, for making day-to-day therapeutic decisions. Venous values are accepted as the standard. The most common access site is a superficial arm vein. This situation can create problems: difficulty in finding a site for punctures, repeated attempts with considerable pain, phlebitis, haematoma and inadequate sampling. For these reasons, capillary CBC through finger pricking has been used an alternative in patients with blood sampling difficulties, particularly in infants and children. The successful use of this approach has been reported previously by many authors [1–6]. Samples are easily obtained and the results are quickly available, and trials from the last 10 years agree with the fact that capillary and venous blood CBC results are similar in both adults with haematological diseases and healthy controls; however, the procedure requires the use of an automated lancet to avoid operator mistakes. This procedure is painful, and the cost of the automated lancet is higher than that of a generic one. To our knowledge, there is no information regarding capillary *vs.* venous blood cell count in haematological patients using a nonautomated lancet.

This prospective, comparative, single-arm study was performed between March 2013 and February 2014 in patients with haematological diseases who came to the haematology service of the University Hospital 'Dr. José Eleuterio González' in Monterrey, Mexico, for routine medical evaluation. Eligible patients were 18 years or older. Participants were excluded if they had an active infection, positive serology for HIV, hepatitis C, or B infections or were pregnant. Our institution's ethics committee approved the study protocol, and all patients gave written informed consent before any procedure. Our primary outcome was the comparison between capillary and venous blood cell counts.

Two blood samples were obtained from each patient at the same time; the first sample was obtained by puncture of a finger and the second sample was obtained by puncture of the antecubital vein. The procedure consisted in a finger prick on the lateral aspect of the pulp of the third or fourth finger of one hand, using a safety lancet (mediLance®3 mm blade, Monterrey, México); the first drop of blood was discarded to minimize excess tissue fluids. An aliquot of 200–500 μL of blood was collected in a tube with ethylenediaminetetraacetic acid (EDTA) for anticoagulation (BD Microtainer, NJ, USA). If necessary, the finger was gently massaged to obtain the required volume. Venous blood was procured from an antecubital vein into a vacuum tube (5 mL BD Vacutainer, Armonk, NY, USA) with EDTA. The punctures were performed by three operators (medical technicians) who attended the patients randomly. The same operator took capillary and venous blood samples from each subject. Both samples were assessed using the haematology analyser Sysmex XT-2000i (Sysmex, Kobe, Japan).

Results are presented as means with standard deviation, among other central tendency measures. Venous and capillary measurements were contrasted according to the normality in the Kolmogorov–Smirnov test using either Student's *t*-test or analysis of variance (ANOVA) for paired samples. Correlations between capillary and venous samples were determined using Spearman or Pearson's tests according to the normality as well. Cohen's kappa was obtained in order to compare each sample's ability to diagnose low, normal or high values in each variable according to our laboratory's reference values. Table 2 notes. Specificity was calculated by dividing 'true-negative' capillary results (i.e. normal capillary results confirmed in venous testing) by all negative results in the venous sample. The relation between 'true-positive' (i.e. altered capillary results confirmed in venous testing) and all altered venous values determined sensitivity. A *P*-value of 0.05 was considered significant, and all tests were two-sided. Statistical analysis was performed using SPSS software version 20.0 for Mac (IBM, Armonk, NY, USA).

We included 107 patients, 15 were excluded from the analysis; three were considered healthy and 12 because their samples were taken by two different operators. Ninety-two patients were analysed. The median age was

46.6 years (range 18–90.9); 51 were women and 41 were men. The main diagnoses of the patients were non-Hodgkin's lymphoma (18.5%), acute lymphoblastic leukaemia (14.1%), chronic myelogenous leukaemia (14.1%), immune thrombocytopenia (7.0%) and Hodgkin's lymphoma (7.0%). A single technician procured most samples (54.3%); two others performed 32.6% and 13.1% of the procedures, respectively. CBC analysis was performed successfully in all 184 samples obtained. No infection was observed at the puncture site of any patient, including neutropenic patients. Statistical significant differences were seen between capillary and venous measurements. However, a good concordance was seen; at least a 0.7 Cohen's kappa was observed in all blood counts. Tables 1 and 2 summarize the main results.

A higher number of leucocytes was measured in the capillary blood samples than in the venous blood samples $0.6 \times 10^3/\mu L$ (standard deviation (SD) $\pm 0.8 \times 10^3/\mu L$), which was also observed in the different subtypes of white blood cells; however, there is a poor reproducibility of the differential and should be further studied. The greatest differences were found for monocytes ($+0.4 \times 10^3/\mu L$, SD $\pm 3.6 \times 10^3/\mu L$), while basophils had the lowest difference ($+0.01 \times 10^3/\mu L$, SD $\pm 0.09 \times 10^3/\mu L$) between both samples. The mean cytometry results for all variables can be found in Table 1. Repeated sample analysis revealed statistically significant differences between measurements across the leucocyte differential ($P < 0.001$). In spite of these differences, good correlations were found, as the correlation coefficients ranged from 0.8 to 0.9 ($P < 0.001$).

Most patients had a normal leucocyte count in both venous (64.1%) and capillary (68.5%) samples. Overall diagnostic concordance occurred in 93.5% of samples ($\kappa = 0.87$, $P < 0.001$), with a sensitivity of 79.2% and specificity of 100% for diagnosing leukopenia. Slight tendency to overestimate cell counts occurred in neutrophils as well, as 14.1% of patients were considered neutropenic *vs.* 12.0% of patients in the venous and capillary samples, respectively, with an overall diagnostic concordance rate of 96.4% ($\kappa = 0.87$, $P < 0.001$). Sensitivity for the diagnosis of neutropenia was 84.6% while specificity was 100%.

The capillary-measured haemoglobin (Hb) *vs.* venous mean difference was +0.2 g/dL (SD ±0.2 g/dL, $P \leq 0.001$, $r = 0.99$), while the difference for haematocrit (Hto) was +0.5% (SD ±0.7%, $P \leq 0.001$, $r = 0.99$), for mean corpuscular haemoglobin concentration (MCHC) was

Table 1. Comparison between capillary and venous blood cytometry results in 92 haematological patients

		Venous		Capillary		Change in mean*		
	Units	Mean	±SD	Mean	±SD	Mean	±SD	*P* value
Leucocytes	$\times 10^3/\mu L$	10.5	28.6	11.2	29.2	+0.6	0.8	<0.001
Neutrophils	$\times 10^3/\mu L$	5.5	18.1	5.7	17.7	+0.2	0.5	<0.001
Lymphocytes	$\times 10^3/\mu L$	3.3	8.0	3.6	8.6	+0.2	0.7	<0.001
Monocytes	$\times 10^3/\mu L$	0.7	1.5	1.2	4.9	+0.4	3.6	<0.001
Eosinophils	$\times 10^3/\mu L$	0.2	0.8	0.2	0.8	+0.0	0.0	<0.001
Basophils	$\times 10^3/\mu L$	0.3	2.9	0.3	2.9	+0.0	0.0	<0.001
RBCs	$\times 10^6/\mu L$	4.1	0.9	4.2	0.9	+0.1	0.0	<0.001
Haemoglobin	g/dL	12.4	2.2	12.7	2.3	+0.2	0.2	<0.001
Haematocrit	%	36.6	6.2	37.1	6.3	+0.5	0.7	<0.001
MCV	fL	90.6	8.6	89.9	8.5	−0.7	0.3	<0.001
MCH	pg	30.8	3.4	30.8	3.3	+0.0	0.4	0.53
MCHC	pg	33.9	1.5	34.3	1.4	+0.3	0.5	<0.001
RDW	%	15.5	3.3	15.5	3.3	+0.0	0.1	0.376
Platelets	$\times 10^3/\mu L$	195.3	130.3	190.4	124.9	−4.9	19.1	0.015
MPV	fL	9.4	2.7	10.0	2.4	+0.5	1.9	<0.001

Abbreviations and cut-off values for leucocytes: high leucocytes: $>10 \times 10^3/\mu L$, normal leucocytes $\geq 4 \times 10^3/\mu L$ and $<10 \times 10^3/\mu L$, low leucocytes $<4 \times 10^3/\mu L$. High neutrophils $>6 \times 10^3/\mu L$, normal neutrophils $\geq 1.5 \times 10^3/\mu L$ and $<6 \times 10^3/\mu L$, low neutrophils $<1.5 \times 10^3/\mu L$. High lymphocytes $>4.5 \times 10^3/\mu L$, normal lymphocytes $>1.5 \times 10^3/\mu L$ and $<4.5 \times 10^3/\mu L$, low lymphocytes $<1.5 \times 10^3/\mu L$. RBCs, red blood cells; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; RDW, red blood cell distribution width; MPV, mean platelet volume.
*The venous sample was the reference for calculating this value.

Table 2. Concordance in the diagnosis of high, normal and low haemoglobin, leucocytes and platelets between capillary and venous peripheral blood cytometry

		Venous		Capillary		Concordance			
	Finding	*n*	%	*n*	%	%	All*	κ	*P* value
Leucocytes	Low	24	26.1	19	20.7	79.2	93.5% (86/92)	0.8	<0.001
	Normal	59	64.1	63	68.5	98.3			
	High	9	9.8	10	10.9	100			
Neutrophils	Low	13	14.1	11	12	84.6	94.6% (87/92)	0.8	<0.001
	Normal	67	72.8	66	71.7	95.5			
	High	12	13	15	16.3	100			
Lymphocytes	Low	42	45.7	37	40.2	88.1	94.6% (87/92)	0.9	<0.001
	Normal	44	47.8	49	53.3	100			
	High	6	6.5	6	6.5	100			
Haemoglobin	Low	47	51.1	42	45.7	89.4	85.9% (79/92)	0.7	<0.001
	Normal	41	44.6	38	41.3	80.5			
	High	4	4.3	12	13	100			
Platelets	Low	37	40.2	39	42.4	100	97.8% (90/92)	0.9	<0.001
	Normal	52	56.5	50	54.3	96.2			
	High	3	3.3	3	3.3	100			

High leucocytes: $>10 \times 10^3/\mu L$, normal leucocytes $\geq 4 \times 10^3/\mu L$ and $<10 \times 10^3/\mu L$, low leucocytes $<4 \times 10^3/\mu L$. High neutrophils $>6 \times 10^3/\mu L$, normal neutrophils $\geq 1.5 \times 10^3/\mu L$ and $<6 \times 10^3/\mu L$, low neutrophils $<1.5 \times 10^3/\mu L$. High lymphocytes $>4.5 \times 10^3/\mu L$, normal lymphocytes $>1.5 \times 10^3/\mu L$ and $<4.5 \times 10^3/\mu L$, low lymphocytes $<1.5 \times 10^3/\mu L$. High haemoglobin >18 g/dL, normal haemoglobin for men ≥13 g/dL and <18 g/dL, for women ≥12 g/dL and <16 g/dL, low haemoglobin for men <13 g/dL and for women <12 g/dL. High platelets $>450 \times 10^3/\mu L$, normal platelets $\geq 150 \times 10^3/\mu L$ and $<450 \times 10^3/\mu L$, low platelets $<150 \times 10^3/\mu L$.
*Concordance in diagnosis of pooled findings; including high, normal and low values.

+0.3 pg (SD ±0.5 pg, $P \leq 0.001$) and for mean cospuscular haemoglobin MCH was +0.03 pg (SD ±0.4, $P \leq 0.53$). The capillary-measured erythrocytes (RBC) *vs.* venous difference was $0.1 \times 10^6/\mu L$ (SD ±0.09, $P \leq 0.001$), while the difference for mean corpuscular volume (MCV) was −0.7 fl (SD ±0.3, $P \leq 0.001$). Using capillary values, we could detect anaemia with a sensitivity of 89.4% and a specificity of 100% and polyglobulia with a sensitivity of 100% and a specificity of 90.9%.

Capillary-measured platelets *vs.* venous showed a difference of -4.9×10^9/L (SD $\pm 19.1 \times 10^3/\mu L$, $P \leq 0.015$, $r = 0.99$); for thrombocytopenia, a difference of $<30 \times 10^9$/L (kappa 0.9, $P \leq 0.001$) was found, and for thrombocytosis, a difference of $>450 \times 10^9$/L (kappa 0.9, $P \leq 0.001$) was found. The sensitivity for diagnosing thrombocytopenia was 100% and the specificity was 96.4%.

Clinical therapeutic decision-making in haematological patients is often based on CBC values. Some differences have been found between capillary and venous blood samples. Daee *et al.* [4] reported more than 20 years ago that neutrophil counts were higher by 8.1% in capillary samples in a cohort of 40 adult healthy subjects. In the case of infants and children up to 14 years of age, increases of 17.2% in capillary samples were observed [5], whereas Schalk *et al.* [6] reported no statistically significant differences in adult haematological patients when compared to healthy subjects. It is important to emphasize that some of these studies were performed in the 1980s, when analyser technology was different. With the use of new-generation analysers, no significant differences were found when comparing venous *vs.* capillary blood in a study performed using a similar analyser to ours (Sysmex XT-2000i) [7]. Previous studies have demonstrated that there is a statistically significant difference in venous *vs.* capillary peripheral blood samples; however, these differences were greater in children than in adults [8] and do not have clinical importance nor do they play a defining role in changing diagnostic or therapeutic decisions. Studies performed before now included cohorts of patients suffering from several advanced haematological diseases, similar to the cohort presented herein, albeit important differences were the use of a nonautomated lancet and the fact that three different operators were imitating a real-life setting. Although the values obtained for leucocytes were slightly

higher in capillary samples (+0.6 × $10^3/\mu$L mean increase in neutrophils and +0.2 × $10^3/\mu$L mean increase in lymphocytes), they were comparable to those obtained in a venous CBC, with an acceptable sensitivity and specificity. The costs of 1000 automated and nonautomated lancets are $384.0 and $53.0 USD, respectively.

The limitations of our study include a small sample size between operators and the lack of a comparative randomized design. It is also important to note that patient comfort was not analysed.

Our results suggest that the use of automated lancets may not make a real difference and therefore could be unnecessary. In summary, this study confirms that the results obtained employing regular inexpensive lancets handled by experienced laboratory personnel are comparable with those reported using automated puncture depth-standardized lancets.

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Presented in poster form at the 55th meeting of the Agrupación Mexicana para el studio de la Hematología (AMEH), Guadalajara, México, May 2014. (Abstract No. A1155)

doi: 10.1111/ijlh.12340

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