A new device to relieve venipuncture pain can affect haematology test results

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Background. *In vitro* diagnostic tests play a key role in patients' management (e.g., guiding red blood cell transfusions). The aim of this study was to evaluate the impact of an innovative device (Buzzy®) which is claimed to be able to relieve venipuncture pain by means of cold and vibration. This device was applied during collection of venous blood by venipuncture for conventional haematology testing.

Materials and methods. Blood was drawn from 100 volunteers by a single, expert phlebotomist. A vein was located in the left forearm without applying a tourniquet but using a subcutaneous tissue transilluminator device, so that venous stasis was avoided. Blood samples were collected with a 20G straight needle directly into 4mL K_3EDTA vacuum tubes. In sequence, external cold and vibration was established by Buzzy® on the right forearm -5 cm above the venipuncture site- for 1 minute before venipuncture and continued until the end of the same procedure already performed in the left forearm. Conventional haematological tests were performed using the same instrument (Sysmex® XE-2100D) in all cases.

Results. When Buzzy® was applied before drawing blood, erythrocyte counts and associated parameters (i.e., haemoglobin and haematocrit) were higher, whereas platelet number, leucocyte count and differential were lower. Statistically and clinically significant differences ($P < 0.001$) were observed for erythrocytes, haemoglobin and haematocrit.

Discussion. From a practical perspective, cold-induced haemoconcentration promotes the efflux of water, diffusible ions and low molecular weight molecules from the vessel, thus increasing the concentration of other blood analytes at the puncture site. These variations may influence test results, especially for erythrocytes, haemoglobin and haematocrit. The novel Buzzy® device should, therefore, be used with caution when collecting blood for conventional haematological testing because of the observed bias introduced in some parameters.

Keywords: blood specimen collection, laboratory error, phlebotomy, preanalytical variability, reproducibility of results

Introduction

In vitro diagnostic testing plays a crucial role in patients' management (e.g. for deciding whether red blood cell transfusion is necessary), provided that quality is ensured through the various phases of the testing process[1,2]. In agreement with the "brain-to-brain turnaround time loop" model[3], which was described more than four decades ago, laboratory testing entails nine crucial phases, i.e., ordering, identification, collection, transport, preparation, analysis, test reporting, interpretation and action[4]. These phases have also been grouped into five higher classes: (i) pre-pre-analytical, (ii) pre-analytical, (iii) analytical, (iv) post-analytical and (v) post-post-analytical phases[5]. There is now clear evidence that more than two-thirds of all errors arising from the testing process occur during the pre-pre- and pre-analytical phases[6-9]. The best approach for overcoming these problems is based on clinical governance and risk-management, which represent a set of complex actions put into act to guarantee the safety of patients and healthcare staff, and which contribute to defining the quality management system[10]. Unfortunately,

to the best of our knowledge there are so far only a few routine procedures for detecting non-conformities in the pre-pre- and pre-analytical phases[11,12]. In the pre-analytical phase, in particular, the processes involving blood drawing have been ignored by most studies that have addressed the leading sources of errors[13-15].

An innovative device called Buzzy® (MMJ Labs, Atlanta, GA, USA), which combines a cooling ice-pack and a vibrating motor, is currently marketed with the claim that it may be effective at attenuating venipuncture pain in adults and children, thus ultimately enhancing patients' compliance during venous blood collection[16-18]. The aim of this study was to assess the impact of using Buzzy® during blood sample collection on conventional haematology tests, since the combination of cold and vibration close to the venipuncture site may be a new and potential source of pre-analytical variability.

Materials and methods

Study design

A group of 100 healthy adults of both genders, who were volunteers for this study, were enrolled from a private laboratory (Bioanalise) in the city of Teresinay, Piaui, Brazil. Each volunteer provide informed consent to inclusion in this trial, which was performed in conformity with the Declaration of Helsinki and under the terms of relevant local legislation.

Collection of diagnostic blood specimens

The blood specimens was collected in only one working day by a single, expert phlebotomist, according to established phlebotomy guidelines[14,19]. All subjects respected a 12-hour fast and remained seated for at least 15 minutes prior to phlebotomy, so that possible interferences of blood distribution due to the posture could be prevented[20]. A suitable vein was identified in the left forearm using a subcutaneous tissue transilluminator device (Venoscópio IV plus, Duan do Brasil, Sao Paulo, Brazil) without the application of a tourniquet[21-23]. Blood samples were collected with 20G straight needles into 3 mL Venosafe® K_2EDTA vacuum tubes (5.9 mg K2EDTA, ref. VF-053SDK06; Terumo, Leuven, Belgium). Nearly 2 mL of blood were preliminarily collected into a discard tube without additive (Vacuette®, Greiner Bio-One GmbH, Kremsmünster, Austria) to exclude potential interference from contact phase activation of blood, or tissue factor. In sequence, external cold and vibration was applied by Buzzy® on the right forearm, 5 cm above the puncture site, for 1 minute before venipuncture and maintained until the end of the same procedure performed in the left forearm. Buzzy® is a reusable 8×5×2.5 cm plastic device that resembles a bee and contains a battery-powered vibrating motor with an 18 g solid frozen ice-pack underneath. All blood collection steps were appropriately standardised (e.g., use of needles and vacuum tubes of the same lot).

Laboratory tests

All samples were processed in triplicate for conventional haematological testing immediately after collection (i.e., within 15 minutes). All specimens were analysed in the same Sysmex® XE-2100D, automated haematology analyser (Sysmex Corporation®, Kobe, Japan). The parameters tested included red blood cell (RBC) count, haematocrit (Hct), haemoglobin (Hb) concentration, mean corpuscular volume, mean corpuscular haemoglobin content, RBC distribution width, white blood cell (WBC) count and differential, including lymphocytes, monocytes, neutrophils, eosinophils and basophils, platelet count and mean platelet volume. The instrument was previously calibrated against appropriate proprietary reference standard material and verified with the use of appropriate controls. Our internal quality control evaluation of the within-run precision of the Sysmex® XE-2100D showed low coefficients of variation (Table I).

Statistical analysis

The significance of differences between samples was assessed by using a Student's paired *t*-test after the normal distribution of values had been verified with the D'Agostino-Pearson omnibus test. A non-normal distribution was found only for mean corpuscular volume: in this case, results were assessed by the Wilcoxon's ranked-pairs test. The level of statistical significance was set at $P < 0.001$. The bias from conventional and Buzzy-assisted venipuncture was assessed according to the current desirable quality specifications for bias (B), derived from biological variation[24].

Results

When cold and vibration were established by Buzzy® before collection of blood samples, RBC count and associated parameters (Hb and Hct) showed significantly increased values, whereas the platelet count, WBC count and differential counts were decreased (Table I). The differences were statistically ($P < 0.001$) and clinically significant only for RBC count, Hb concentration and Hct.

Discussion

It has recently been shown that direct-to-consumer testing presents more risks than real opportunities for patients and healthcare systems[4]. Our study group also previously demonstrated that changes of brand of *in vitro* diagnostic devices (e.g. vacuum tubes[25-28] and syringes[29])

Table I - Impact of Buzzy® on routine haematology tests.

Tests	Units	Desirable bias (%)	CVa	Buzzy®	Gold standard	Mean % difference	P-value
RBC**	(10^{12}/L)	1.7	1.5	4.90±0.55	4.80±0.55	**2.0**	**0.0006**
Hb**	(g/L)	1.8	1.0	141.4±13.2	137.9±12.7	**2.5**	**0.0002**
Hct**	(%)	1.7	1.5	41.5±4.0	40.6±4.0	**2.2**	**0.0005**
MCV*	(fL)	1.2	1.0	84.6 (81.9-88.1)	84.4 (81.8-88.3)	0.2	0.6245
RDW**	(%)	1.7	2.0	12.7±0.6	12.7±0.5	0.0	0.3343
WBC**	(10^9/L)	5.6	3.0	7.10±1.89	7.35±1.94	–3.5	0.0099
NEU**	(10^6/L)	9.1	8.0	4.15±1.49	4.27±1.57	–2.9	0.0256
LYMP**	(10^6/L)	7.4	8.0	2.32±0.80	2.41±0.80	–3.9	0.0425
MONO**	(10^6/L)	13.2	9.8	0.28±0.05	0.29±0.08	–3.6	0.4431
EOS**	(10^6/L)	19.8	15.5	0.16±0.07	0.16±0.08	0.0	0.6165
BASO**	(10^6/L)	15.4	9.7	0.041±0.02	0.046±0.02	–12.2	0.0894
PLT**	(10^9/L)	5.9	4.0	272±66	274±66	–0.7	0.3705
MPV**	(fL)	2.3	1.2	9.09±0.71	9.12±0.81	–0.3	0.7116

*Non-normal distribution; the values are presented as median (interquartile range); P-value represents the significance by Wilcoxon ranked-pairs test. **Normal distribution; the values are presented as mean ± standard deviation; P-value represents the significance by paired Student's *t*-test. The P-values in bold are statistically significant (P <0.001) and bold mean % differences represent clinically significant variations, when compared with desirable bias[24]. RBC: red blood cell count; Hct: haematocrit; Hb: haemoglobin concentration, MCV: mean corpuscular volume; RDW: red blood cell distribution width; WBC: white blood cell count; NEU: neutrophil count; LYMP: lymphocyte count; MONO: monocyte count; EOS: eosinophil count; BASO: basophil count; PLT: platelet count; MPV: mean platelet volume.

represent a new source of pre-analytical variability. It is also noteworthy that the most important guideline on diagnostic blood specimen collection by venipuncture recommends procedures that may generate venous stasis[14]. Inal and Kelleci, and Baxter *et al.* recently showed that Buzzy® is effective at relieving needle pain during venipuncture[16-18]. Obviously, the ability of phlebotomists to put patients at ease is considered a very important issue by outpatients[30]. Oatey and Stiller showed that 28% of inpatients shared the opinion that venipuncture is indeed a painful medical procedure[31]. As such, the Buzzy® device may be viewed as an attractive novelty to overcome this important clinical issue. Indeed, as suggested by the manufacturer of Buzzy®[32] the phlebotomist should distract the patients for a while (15 sec) after placing the device. We measured that the time lap needed to perform this pre-phlebotomy operation was 55±10 sec (mean ± SD for 8 plebotomists); we, therefore, adopted 1 minute as our standardised time. A previous assessment of Buzzy® use during diagnostic specimen collection by venipuncture for routine immunochemistry testing showed negligible variations, with significant bias only reported for total protein and albumin concentrations out of the 34 analytes tested[33]. Nevertheless, it is important to focus on RBC count, Hb concentration and Hct (Table I), since these parameters are often and misleadingly considered very solid and relatively insensitive to pre-analytical variables. Obviously the quality specifications for bias derived from biological variation (Table I)[24] are considered both very important and useful in daily practice by quality managers of medical laboratories[34-37]. According to our results, there is a tangible risk that some physicians could make inappropriate clinical decisions (e.g., delay or avoid RBC transfusions[38-40]) as a consequence of biased[24] haematological results due to the use of the new Buzzy® device. The most reasonable explanation for the bias is vasoconstriction due to direct skin cooling[41,42]. From a practical perspective, the cold-induced haemoconcentration[43] promotes efflux of water, diffusible ions and low molecular weight molecules from the vessel and may, therefore, increase the concentration of various analytes in close proximity to the venipuncture site. These variations could potentially impair the reliability of test results, especially RBC count, Hb concentration and Hct. In a systematic review Fuller *et al.* showed that vibration increases muscle perfusion, with the magnitude of the increase being positively related to the vibratory load applied[44]. The finding of a decreased WBC count is consistent with the hypothesis that the external vibration may trigger leucocyte recruitment.

It is well established that the sampling process is a crucial step in research[45]. One strength of our study was the accurate standardisation of all steps (i.e., all diagnostic blood specimens were collected by a single

expert phlebotomy in one working day and all *in vitro* equipment was from the same lot), which minimised potential biases.

In conclusion the novel Buzzy® device should be used with caution when collecting blood for conventional haematological testing because of the observed bias introduced in some parameters. Another important issue that may argue against the use of this device is the risk of triggering precipitation of cold agglutinins as a consequence of prolonged contact of ice with the skin. This aspect deserves scrutiny in further investigations.

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Disclosure

All authors confirm that they contributed to the intellectual content of this paper and met the following three requirements: (i) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (ii) drafting or revising the article for intellectual content; and (iii) final approval of the published article.

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