

The Benefits and Limitations of Point of Care Testing for Patients with Diabetes Who are Acutely Unwell

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Abstract

Diabetic emergencies are associated with derangements in glucose and electrolytes with guidelines supporting treatment and serial monitoring. In clinical practice this is often achieved using a venous blood sample assessed using a blood gas analyzer (BGA), however their accuracy in measuring glucose, potassium and sodium in acutely unwell adults is unknown. Capillary blood tests can measure these parameters using a BGA and may be more acceptable to patients. We compared capillary and venous BGA results to gold standard venous laboratory sodium, potassium and glucose in acutely unwell diabetic patients and healthy controls to determine their accuracy and acceptability.

Methods: 48 acutely unwell diabetic patients and 23 healthy adults had consecutive bloods taken from arterialized ear lobe (EP) and finger prick (FP) (capillary bloods) and a standard venous sample. Venous samples were sent to an accredited NHS hospital biochemistry laboratory (VL) for reporting as well as being analyzed in a BGA (VBG). Results were compared to internationally agreed acceptability criteria using Bland-Altman limits of agreements. Patient preferences were recorded.

Results: VBG glucose met acceptability criteria (results within 20% of VL result) as did FP glucose when glucose values were ≥ 11.2 mmol/l but not when results were within the normoglycaemic range. Venous and capillary BGA potassium did not meet acceptability criteria (within 0.5 mmol/l of VL result) although capillary samples were more accurate than the VBG results ($p < 0.001$). FP, EP and VBG sodium all met acceptability criteria ($>95\%$ within 4 mmol/l of VL result). Participants found capillary tests less painful ($p < 0.001$) and preferred FP testing method to serial venous blood tests ($p = 0.002$).

Conclusion: Capillary and VBG samples can be used to guide acutely unwell diabetic patient treatment (with capillary testing preferred by patients) but caution is required as there is deviation from laboratory results, for potassium particularly.

Ethical approval was provided by NRES West Midlands (14/WM/1057).

Keywords: Diabetes; Hyperglycaemia; Hyperkalaemia; Potassium; Sodium; Point of care monitoring

Abbreviations: BGA: Blood gas analyzer; DKA: Diabetic ketoacidosis; EP: Ear lobe prick; FP: Finger prick; IQR: Interquartile range; ISO: International organization for standardization; ME: Measurement error; NHS: National health service (UK); NRES: National research ethics service committee; POCT: Point of care testing; UHBFT: University hospital Birmingham NHS foundation trust; UK: United Kingdom; US CLIA: United states clinical laboratory amendments; VL: Venous laboratory; VBG: Venous blood gas

Introduction

The prevalence of diabetes is increasing and is associated with significant health care utilisation. Diabetes currently accounts for up to

15% of bed occupancy in secondary care hospitals [1] with a high proportion being admitted with causes directly related to diabetes and diabetic complications [2]. Diabetic emergencies are frequently associated with derangements in blood glucose and electrolytes and close biochemical monitoring has been emphasized by international guidelines, where rapid correction has been shown to reduce morbidity as well as the length of hospital stay [3-8]. To achieve close biochemical monitoring, it is common to perform serial venepunctures during a single day to guide insulin and electrolyte replacement therapy [9,10]. However, there can be practical difficulties complying with international recommendations for serial testing. Venepuncture is painful and anxiety associated with venepuncture is common [11,12]. This anxiety can prevent a patient agreeing to repeat blood tests, which can affect their care [12]. Patients with acute illness can have poor venous access, and oedema and obesity can hinder serial testing. Furthermore, delirium associated with illness can also hamper the

ability to perform venepuncture and therefore impede compliance with treatment. Once a sample is taken, rapid correction of electrolyte abnormalities is limited by the speed at which clinical laboratories can process and report the biochemical analyses of venous samples, a process which can take several hours. Using blood gas analyzer (BGA) results may provide a rapid assessment of electrolyte disturbances, overcoming the delays associated with laboratory processing. However, since venepuncture is the most common method of blood sampling for this point of care testing (POCT), its compliance can be limited by the issues described above.

Capillary sampling provides an alternative means to gain a blood sample from a finger, heel or an ear lobe. While the validity of capillary blood glucose measurement by glucose meters is known [13-15], the accuracy of electrolyte and glucose measurements in either capillary heparinized samples or venous blood samples run through a blood gas analyzer are unknown in acutely unwell adult patients. This is important, as in routine clinical practice blood gas results are frequently used to guide clinical care in the acute setting. Indeed, only capillary pH, pO₂, pCO₂, has been validated when determined by a blood gas analyzer machine in adults [16].

Capillary blood sampling offers several advantages in the acute setting. First, the relative ease of obtaining the samples compared to venepuncture. There are several collection sites on the body and these can be rotated (fingertips, earlobes). Second, testing can be performed with minimal training by medical, nursing and ancillary healthcare staff. Third, capillary sampling is believed to be less painful, and this may facilitate serial testing in the frail, anxious or those without capacity. Fourth, serial testing will not impact on venous access points which can then be used for intravenous medications and fluids and avoid cannulation in sites more prone to infection such as the lower limbs or the requirement of invasive central venous access.

Diabetic patients in hospital are already having frequent capillary blood taken for glucose and ketone monitoring. If the capillary blood could be taken for measurement of the other parameters at the same time, it would reduce the overall number of blood tests taken but also allow very close monitoring of these crucial biochemical tests. If capillary blood gas analyses were accurate enough to inform clinical decisions, these advantages would be of significant value to patient care. There are internationally agreed levels of accuracy for glucose, sodium, and potassium monitoring, as described in Table 1 [17,18].

Parameter	Accuracy Measure	Guideline
Sodium	95% of values within 4mmol/l of venous laboratory result	US CLIA (17)
Potassium	95% of values within 0.5mmol/l of venous laboratory result	US CLIA (17)
Glucose	95% of values within 20% of venous laboratory result	ISO (18)

The following published guidelines were used to determine venous and capillary BGA accuracy, the United States of America Clinical Laboratory Improvement Amendments (US CLIA) regulations and the European International Organisation for Standardisation (ISO), based in Geneva, Switzerland, that is responsible for defining the standards. 2013 guidelines.

Table 1: Test accuracy criteria used for comparisons across sample techniques.

We hypothesized that both venous blood and blood collected by capillary sampling analyzed using a BGA would provide results deemed accurate enough (by comparison to these international guidelines) to monitor glucose, sodium and potassium, both in healthy adults, and in acutely unwell diabetic patients admitted to a secondary care hospital. We further hypothesized that capillary sampling would be less painful and preferred by patients. The aim of this study was to determine the accuracy of venous blood and capillary samples, when measured using a BGA, compared to gold standard clinical laboratory processed venous blood tests in a cohort of acutely unwell diabetic patients and healthy controls.

Methods

This study was conducted according to the ethical principles set out in the Declaration of Helsinki [19]. All subject participation was supported by a favorable ethical review provided by the UK National Research Ethics Service Committee West Midlands (NRES reference 14/WM/1057) and by sponsorship agreed by the University Hospital Birmingham NHS Foundation Trust (UHBFT) Research and Development department.

Study design

This was an open study with participants recruited from a single secondary care NHS hospital (UHBFT, UK) in 2016.

Participants

Forty eight acutely unwell diabetic patients with capillary blood sugars of 10mmol/l or greater were recruited within 24 hours of admission. Inclusion criteria included a prior diagnosis of diabetes (type 1 or type 2), aged 18 years old or older, provision of signed informed consent or personal consultee and a glucose result of >10 mmol/l based on a POCT glucose result taken within 30 minutes prior to recruitment. Diabetic subjects were selected when capillary glucose meter readings were in the selected ranges, but clinical treatments were instigated for diabetic emergencies and therefore prone to change. Diabetic patients were stratified into those with glucose results of 10 mmol/l to 15 mmol/l or >15 mmol/l to determine if the accuracy of BGA results varied depending on glucose levels. All samples for the study were collected within 5 minutes of first sample collection and in a random order (as described below). Patients with hypoglycemia were deliberately excluded to avoid study participation delaying medical treatment. Twenty-three healthy volunteers were recruited from staff members of the UHBFT. Staff were included if they provided signed informed consent, were aged 18 years or older and had no significant past medical history and were not taking regular prescription medications.

Blood processing procedure

Four different areas of blood samples were taken consecutively from each participant, an earlobe prick (EP) and finger prick (FP) (both for capillary blood sampling) and standard venepuncture. One aliquot of blood from the venepuncture was used for BGA and one was sent to the clinical laboratories for standard processing. The order of testing was random, generated by the random list generator "random.org" (Randomness and Integrity Services Ltd, Dublin, Ireland). Blood gas analysis was performed within 2 minutes using a point of care testing Cobas® b 221 blood gas analyzer (Roche, Rotkreuz, Switzerland) in UHB hospital Clinical Decisions Unit. Laboratory samples were

delivered using SDS ac3000 pneumatic tube system (Aerocom, Vaughan, Canada) to avoid delay and were processed as per standard practice to reproduce usual clinical care.

For the EP samples the earlobe was cleaned with a PDI Sani-Cloth CHG 2% disinfectant wipe (PDI, Flint, UK) and the treated site was allowed to dry for 30 seconds. Following this procedure a thin film of transvasin® cream (Thornton & Ross Ltd, Huddersfield, UK) was placed on the earlobe to arterialise the ear lobe capillaries. Thereafter the earlobe was cleaned again with the PDI Sani-Cloth CHG 2% disinfectant wipe. The earlobe was then coated with a thin film of white soft paraffin prior to puncture with a Unitstix® 3 lancing device (Owen Mumford, Woodstock, UK) and the earlobe gently squeezed until a drop of blood was expressed. A heparinised RAPIDLyte® Multicap-S plastic capillary tube (Siemens, Erlangen, Germany) was filled with a 150µl column of blood which was analyzed using a point of care testing Cobas® b 221 blood gas analyzer. The same procedure occurred for the finger prick sample using the third or fourth finger of the non-dominant hand. Venous blood was collected into a RAPID Lyte Arterial Blood Sampling Syringe (Siemens, Erlangen, Germany) for BGA processing, and into a serum separating tube and sodium fluoride and potassium oxalate glucose blood tubes (both BD Vacutainer Systems, New Jersey, USA) for clinical laboratory processing for sodium, potassium and glucose.

Experience rating

Each patient had their experience of the 3 methods of taking blood (ear lobe prick, finger prick and standard venepuncture) documented via a visual analogue scale for assessing pain as previously described [20].

Analysis

Statistical evaluation used SPSS Statistics (Version 20, IBM, UK). Data distribution was assessed using the Kolmogorov-Smirnov or Shapiro-Wilk test and also using a Q-Q plot. Differences in the measurement error (ME) values for the samples (venous blood, finger prick and earlobe sample) were assessed using Friedman's test. Bland-Altman plots were used to plot the ME for capillary derived or venous BGA blood test results against the gold standard laboratory blood level. The proportion of patients within the acceptability criteria for each of the parameters was calculated from the data and was also estimated from the mean and standard deviation of the ME assuming a Normal distribution. As the acceptability criteria for glucose used percentage difference from the gold standard value, the percentage ME was calculated. When the percentage ME was not normally distributed, analysis used actual ME values. The experience rating was summarized by calculating the median values for pain scores as well as the quartiles. Comparisons between the sampling modalities was done using Friedman's analysis and post hoc analysis with pairwise comparisons. A p value of <0.05 was accepted as significant and all tests were two tailed.

Results

The demographics of all patients and healthy participants are shown in Table 1. Table 2 shows the median and ranges of results from all groups for each parameter. Complete testing was achieved in 83% of the 71 participants, as described in the modified consort diagram in Figure 1. Table 3 summarizes the laboratory gold standard results for glucose, sodium and potassium for each of the patient groups.

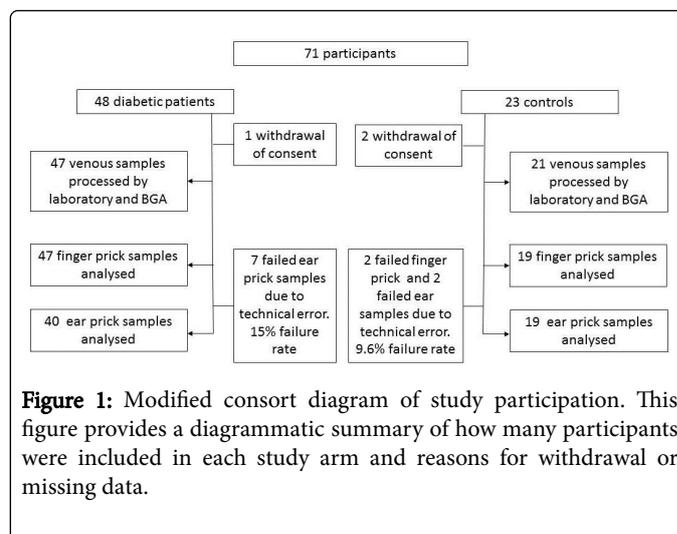


Figure 1: Modified consort diagram of study participation. This figure provides a diagrammatic summary of how many participants were included in each study arm and reasons for withdrawal or missing data.

	Group 1: Diabetic subjects (blood glucose 10-15 mmol/l)	Group 2: Diabetic subjects (blood glucose ≥ 15 mmol/l)
Healthy subjects		
N	23	25
Age	31 (24-49)*,†	72 (37-87)
Males	9 (39%)‡	14 (61%)‡
Ethnicity		
Caucasian	12 (52%)§	15 (60%)§
Asian	10 (43%)	6 (24%)
Afro-Caribbean	0	4 (16%)
Other	1 (4%)	0
Type 2: Diabetes	1	23:2
Arterial pH<7.35	0	1 (4%)

Age is the median and range in parentheses. Male and ethnicity is the number and percentage in parentheses. Type 2:1 diabetes is numbers of participants with either type 2 or 1 diabetes in this cohort. Arterial pH is number (and percentage) of patients with a pH below the normal range on initial recruitment. * = significantly different from group 1 diabetic subjects (p<0.05). † = significantly different from group 2 diabetic subjects (p<0.05) compared using Kruskal-Wallis test followed by Dunn's test. ‡, §, || = No significant difference between all groups using Fishers exact test (p<0.05). || = No significant difference compared to group 2 diabetic subjects by Fishers exact test (p<0.05).

Table 2: Demographics for healthy participants and acutely unwell diabetic patients.

Glucose

The acceptability criteria for glucose were derived from the International organization of standardisation (ISO) guidelines which state 95% of results should fall within 20% of a plasma laboratory sample [18]. Table 4 shows the results of the estimated and observed proportion of tests meeting the acceptability criteria. When comparing all groups together, 97% of venous BGA met this guideline, with the largest deviation of 2.3 mmol/l higher than the reported VL result.

Eight seven percent of finger prick samples analysed through the BGA met the ISO guideline, with the largest deviation of 4.6 mmol/l higher than the reported VL result. Sixty eight percent of ear prick samples analysed through the BGA met ISO guidelines with the largest deviation of 3.4 mmol/l higher than the reported VL results.

Healthy subjects		Group 1: Diabetic subjects (blood glucose 10-15 mmol/l)	Group 2: Diabetic subjects (blood glucose ≥ 15 mmol/l)
Glucose (mmol/l)	5.1 [†] (4.4-7.7)	12.55 [†] (6.1-28.2)	19.7 (5.6-39)
Potassium (mmol/l)	4.3 [‡] (3.7-4.8)	4.3 (3.5-5.7)	4.4 (3.7-5.1)
Sodium (mmol/l)	139 (135-142)	137 (118-143)	135 (125-143)

Results are from the venous blood sample processed in standard clinical laboratories, and as such represent the gold standard test. The given results were taken within 30 minutes of the screening POCT glucose. Data are median with range in parentheses. * = significantly different from group 1 diabetic subjects, (p<0.05). † = significantly different from group 2 diabetic subjects (p<0.05). ‡ = Not significantly different to group 1 or group 2 diabetic subjects. || = significantly different compared to group 1 and group 2 diabetic subjects. All compared using Kruskal-Wallis test followed by Dunn's test.

Table 3: Median and ranges of results by parameter and patient group (from gold standard laboratory result).

Sampling method		Estimated* % Meeting Acceptability Criteria	Observed Numbers Meeting Acceptability Criteria	Observed % Meeting Acceptability Criteria (95% CI)
Glucose	Finger prick	<95 for values ≤11.1	24/31	77 (59-90)
		>95 for values >=11.2	38/38	100 (91-100)
	Ear Prick	79	51/59	86 (75-94)
	Venous BGA	97	66/69	96 (88-99)
Sodium	Finger prick	95	66/67	99 (92-100)
	Ear Prick	97	57/61	93 (84-98)
	Venous BGA	98	68/69	99 (92-100)
Potassium	Finger prick	88	60/69	87 (77-94)
	Ear Prick	81	51/61	84 (72-92)
	Venous BGA	70	51/69	74 (62-84)

The estimated and observed proportion of tests meeting the acceptability criteria. Glucose is divided into results above or equal to 11.2mmol/L and below this value, as differences were seen in the percentage of results meeting acceptability criteria in the hyperglycaemic and normoglycaemic range. Data is presented as the numbers and observed percentage (with 95% confidence intervals (CI)). *Estimated assuming the measurement error is Normally distributed (means and standard deviations are those used in calculation of limits of agreement).

Table 4: Estimated and observed proportions of tests meeting the acceptability criteria by parameter and sampling method.

The mean bias was positive (on average values were higher than the gold standard results) for all modalities. Mean bias, Finger prick; 0.26mmol/l (3.8%); Ear prick, 0.46 mmol/l (9.1%) and Venous BGA, 0.23 mmol/l (3.1%). Finger prick samples met the acceptability criteria when in the hyperglycemic range of greater than or equal to 11.2 mmol/l but not in the normoglycaemic range. Both the finger prick and venous BGA glucose were significantly more accurate than the ear prick samples (p=0.002 and <0.001 respectively, pairwise comparisons following Friedman's test).

Figure 2 presents the Bland Altman plots for glucose comparing venous blood gas samples (A), ear (B) and finger (C) capillary results to the laboratory glucose result.

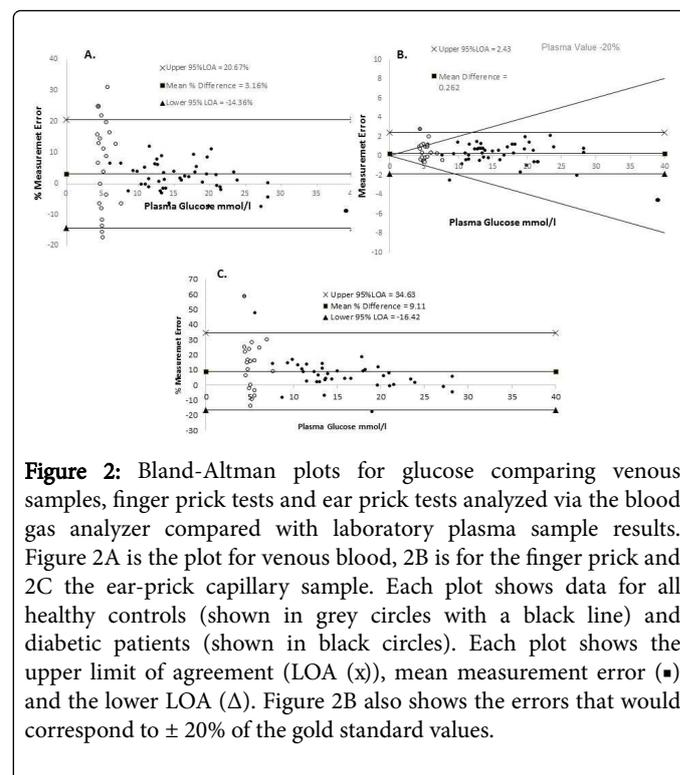


Figure 2: Bland-Altman plots for glucose comparing venous samples, finger prick tests and ear prick tests analyzed via the blood gas analyzer compared with laboratory plasma sample results. Figure 2A is the plot for venous blood, 2B is for the finger prick and 2C the ear-prick capillary sample. Each plot shows data for all healthy controls (shown in grey circles with a black line) and diabetic patients (shown in black circles). Each plot shows the upper limit of agreement (LOA (x)), mean measurement error (●) and the lower LOA (Δ). Figure 2B also shows the errors that would correspond to ± 20% of the gold standard values.

Potassium

The acceptability criteria for Potassium were derived from the US CLIA guidelines which state that 95% of results should fall within 0.5 mmol/l of a serum sample [17]. When comparing all groups together, 70% of venous BGA results met this guideline (See Table 4), with the largest deviation of 1.01 mmol/l lower than the reported VL result. Eight seven percent of finger prick samples analyzed through the BGA met the US CLIA guideline, with the largest deviation of 1.03 mmol/l lower than the reported VL result. Eighty percent of ear prick samples analyzed through the BGA met US CLIA guidelines with the largest deviation of 0.88 mmol/l lower than the reported VL results.

The mean bias was negative (on average samples were lower than the serum value) for all testing methods. Mean bias, Finger prick; -0.191 mol/l; Ear prick, -0.011 mmol/l and Venous BGA, -0.394 mmol/l. None of the modalities met the acceptability criteria, but venous BGA samples were significantly less accurate than both the capillary sampling methods (p=0.001 and p<0.001, pairwise comparisons following Friedman's test).

Figure 3 presents the Bland Altman plots for potassium comparing venous blood gas samples (A), ear (B) and finger (C) capillary results to the laboratory potassium result.

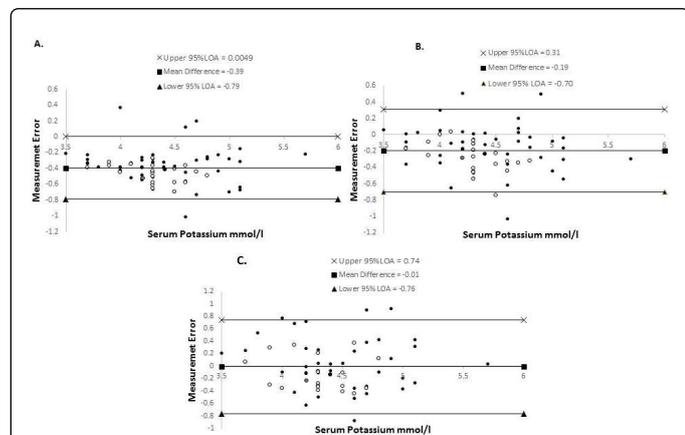


Figure 3: Bland-Altman plots for potassium comparing venous samples, finger prick tests and ear prick tests analysed via the blood gas analyzer compared with laboratory plasma sample results. Legend. Figure 3A is the plot for venous blood, 3B is for the finger prick and 3C the ear-prick capillary sample. Each plot shows data for all healthy controls (shown in grey circles with a black line) and diabetic patients (shown in black circles). Each plot shows the upper limit of agreement (LOA (x)), mean measurement error (■) and the lower LOA (Δ).

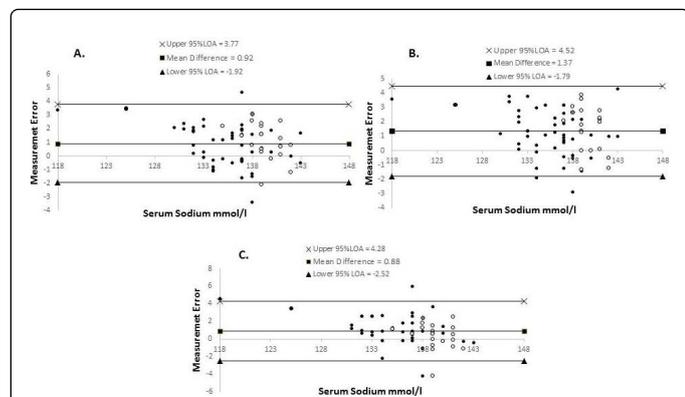


Figure 4: Bland-Altman plots for sodium comparing venous samples, finger prick tests and ear prick tests analyzed via the blood gas analyzer compared with laboratory plasma sample results. Legend. Figure 4A is the plot for venous blood, 4B is for the finger prick and 4C the ear-prick capillary sample. Each plot shows data for all healthy controls (shown in grey circles with a black line) and diabetic patients (shown in black circles). Each plot shows the upper limit of agreement (LOA (x)), mean measurement error (■) and the lower LOA (Δ).

Sodium

The acceptability criteria for sodium were derived from the US CLIA guidelines which state that 95% of results should fall within 4 mmol/l of a serum sample [17]. When comparing all groups together,

98% of venous BGA met this guideline (Table 4), with the largest deviation of 4.7 mmol/l higher than the reported VL result. Ninety five percent of finger prick samples analyzed through the BGA met the ISO guideline, with the largest deviation of 4.3 mmol/l higher than the reported VL result. Ninety seven of ear prick samples analyzed through the BGA met ISO guidelines with the largest deviation of 4.6 mmol/l higher than the reported VL results.

The mean bias was positive (results were higher than gold standard laboratory samples) for all testing modalities but all sampling modalities met the acceptability criteria. Mean bias, Finger prick; 1.37 mol/l; Ear prick, 0.88 mmol/l and Venous BGA, 0.92 mmol/l. Finger prick sampling was significantly less accurate than both the ear prick and venous BGA methods (p values 0.015 and 0.008, respectively, pairwise comparisons following Friedman's test). Figure 4 presents the Bland-Altman plots for venous blood gas (A) finger prick (B), ear (C) capillary sodium results compared to the venous serum gold standard.

Experience rating

There were no differences in pain scores (rated 0-10) in the healthy group between the finger prick (median (IQR)) 1.2 (0.5-1.9) and the ear prick 0.8 (0.5-1.9) compared to the venepuncture sample 1.3 (0.4-1.8) (p=0.295 and 0.058 respectively). In the patient group, finger prick (median (IQR)) 0.5 (0-1.5)) and ear prick (0.4 (0-1.7)) pain scores were both significantly lower than for the venepuncture blood tests (1.4 (0-3.5), p<0.001) (Friedman's test).

The diabetic patient group was also asked which sampling modality they preferred. 60% preferred the finger prick sampling method (95% confidence interval (CI) of 46.3-73.0%), compared to 17% (CI 8.4-29.9%) who preferred ear prick, 13% (CI 5.48-25.1%) who preferred venous sampling and 2% (CI 0-11.9%) who had no preference. Four patients (8%) were unable to comment due to illness severity.

Discussion

Finger prick blood assessment of glucose is commonly used to assess glycaemia in both the acute and chronic setting in diabetic patients. However, during diabetic emergencies it is common to diagnose and have to manage other biochemical abnormalities concurrently, such as hypo or hyperkalemia and hypo and hypernatremia [21]. Clinically, it would be advantageous to be able to monitor these parameters using the same capillary sample used to monitor blood glucose levels, as opposed to a separate venous blood sample. This is the first study to assess the accuracy and acceptability of capillary blood tests when assessed in a blood gas analyzer for glucose, sodium and potassium in an acutely unwell diabetic population, as well as in healthy controls.

All glucose BGA samples tended to overestimate the plasma glucose by approximately 3-7%. During hyperglycemia, the finger prick and venous BGA samples were sufficiently accurate and met acceptability criteria, suggesting they could be used to manage patients during hyperglycemic episodes; a time when most frequent monitoring is clinically indicated. However, FP samples did not meet accuracy criteria when samples returned to the normoglycaemic range and ear pricks samples did not meet acceptability criteria at any point. The dichotomy of results for BGA and FP reflects the use of a percentage cut off for acceptability criteria. The largest difference using FP testing was 4.6 mmol/l greater than the laboratory result during hyperglycemia and 1.7 mmol/l during normoglycaemia (FP). For BGA

these differences were 2.3 mmol/l and 0.4 mmol/l respectively. While these differences from the gold standard results are unlikely to impact on clinical care during hyperglycemia, the FP differences could be clinically important when patients were approaching normoglycaemia, which could limit the usefulness of FP testing using a BGA in this group.

BGA, FP and EP sampling all met acceptability criteria for sodium, both in patients and healthy participants, suggesting all of these monitoring modalities could be used with confidence in conditions where sodium levels require monitoring.

Neither FP nor EP capillary nor venous BGA samples met the US CLIA guidelines for potassium of 95% of the samples within 0.5 mmol/l of the gold standard [17]. All testing modalities underestimated the potassium concentration when compared to the laboratory result by an average (mean bias) of -0.01 mmol/l to -0.39 mmol/l, with the largest difference from the laboratory gold standard being 1.03 mmol/l, a difference which could be clinically significant when treating derangements in potassium.

These results suggest that a venous sample and FP sample run through a BGA can guide clinical care during hyperglycemia (but not normoglycaemia, where results from the POCT testing were higher than those reported from laboratory tests); a venous sample, FP or EP sample run through a BGA can be used to guide clinical care for assessment of serum sodium and none of these modalities can be used to accurately assess serum potassium, when compared to their laboratory gold standard tests. However, there are questions as to whether the reported gold standard reflects the physiological state at the time of testing [22].

Ex-vivo blood cells metabolize glucose via glycolysis, and can lower glucose concentration in whole blood by as much as 0.4 mmol/l per hour [23]. Glucose is routinely collected in "Grey top" tubes containing potassium oxalate (as an anticoagulant) and sodium fluoride (to inhibit glycolysis). However, this system is not fully effective; fluoride blocks glycolysis by the inhibition of enolase in the glycolytic pathway, so although lactate production is strongly inhibited, glucose is still metabolized until a significant depletion of ATP occurs, usually after the first hour of sample collection [22]. Hence glucose is still metabolized at approximately 5% to 7% per hour at room temperature in ex-vivo samples, because upstream enzymes continue to convert it to glucose-6-phosphate [24].

All POCT testing modalities reported lower potassium concentrations than measured in the gold standard laboratory test, but this might also be reflective of ex-vivo changes in potassium rather than true differences in the accuracy of POCT measures. 98% of body potassium is intracellular, and therefore a small release of potassium from cells can significantly affect the concentration of measured (extracellular) potassium. The ratio between intracellular and extracellular potassium is approximately 40:1 and studies report a change in the ratio as small as 2.5% leading to increases in the potassium concentration by 0.1 mmol/l [25]. Phlebotomy technique has been shown to alter potassium readings due to increased hemolysis [26]. Furthermore, serum samples have been reported to have higher potassium concentrations (by 0.36 ± 0.18 mmol/l) compared with plasma samples due to clotting-associated potassium release from platelets [20]. Hemolysis is less relevant for the measurement of Sodium, with studies suggesting moderate hemolysis was associated with less than a 1% change in sodium measurements [27]. These physiological changes in ex-vivo blood tests (glycolysis and hemolysis)

might explain the discordance (glucose and potassium) and concordance (sodium) between the gold standard and POCT measurements in the current study.

Recent DKA guidelines suggest using serial samples analyzed by BGA to assess hyperkalemia with intermittent laboratory confirmation [28]. Our study suggests there will be differences between the two modalities, which should be recognized, and that a finger prick capillary test may be more accurate than a venous sample when analyzed using a BGA.

Furthermore, this method of sampling was preferred by 60% of patients with diabetes. Ear prick capillary samples were generally less accurate and less preferred by patients.

The study has potential limitations. The three different sampling modalities were taken sequentially over approximately 10 minutes. The order of sampling was randomly assigned throughout the study, to reduce collection bias. It is possible that variability in the measured results may reflect true physiological changes in parameters over this period. During an acute admission, patients often receive rapid intravenous infusions of therapies that may alter concentrations of blood constituents. This is particularly relevant to glucose where delays of 15 min or more have been shown to reduce clinical accuracy to below the ISO standards [29]. The effect of the timing of the samples, however, is unlikely to be as significant for sodium or potassium as they do not have the same degree of post-prandial peaks and troughs as glucose and have a more stable diurnal variation [30]. The venous BGA and laboratory sample were taken from the same venepuncture sample, which might explain the increased level of agreement noted.

A further potential limitation of this study is that the full range of pathological results were not included. Glucose results included those patients with hyperglycemic ranges up to levels which may be expected for acutely unwell adults, however, patients were not studied in the hypoglycemic range due to the speed of response required for treatment in this group. As the current study suggests decreased accuracy at lower glucose level, the results cannot be extrapolated to hypoglycemic levels. No samples were within the hypernatremic range and therefore these results cannot be extrapolated to include hypernatremia. The current study also did not include patients with significantly deranged potassium concentrations, and therefore results cannot be extrapolated to hypo or hyperkalemia. This would be of particular importance as previous studies of arterial samples taken out of the normal range have showed poor agreement when potassium is less than 3 mmol/l and greater than 5 mmol/l [31,32].

Conclusion

In acutely unwell diabetic patients it is desirable to measure glucose, sodium and potassium at regular intervals with the minimal patient discomfort and with the least delay in gaining results. A venous BGA or FP capillary assessment is able to accurately measure glucose in the hyperglycemic patient, and sodium, although there is discordance between POCT and laboratory glucose and potassium measurements. A capillary blood test provides a method which is preferred by patients and less painful but with similar levels of accuracy to a venous sample analyzed by BGA. This could be used as an alternative for regular testing but with intermittent laboratory confirmation or confirmation when electrolytes fall outside of the normal range.

Declarations

Ethics approval and consent to participate

This study was conducted with appropriate ethical approval granted from the National Research Ethics Service Committee West Midlands (14/WM/1057) with all participants providing informed written consent or personal consultee consent to take part.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no competing interests in relation to this study.

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Authors' contributions

TL designed the study, collected data, analyzed data and prepared the manuscript. PN oversaw statistical analysis. VRK designed the study and assisted with manuscript preparation. ES designed the study, oversaw patient recruitment and prepared the manuscript.

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