Pseudohyperkalemia in capillary blood samples; haemolysis not the only culprit

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Primary objectives: • Establish that capillary plasma samples are unsuitable to evaluate the potassium status in patients.• Verify that pseudohyperkalemia in capillary samples is not only caused by haemolysis but also due to other potassium sources...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON36110

Source
ToetsingOnline

Brief title
Pseudohyperkalemia in capillary blood samples

Condition

- Other condition

Synonym
Falsely elevated plasma potassium concentration, Pseudohyperkalemia

Health condition

laboratorium diagnostiek, pseudohyperkalemie

Research involving
Human

Sponsors and support

Primary sponsor: Sint Franciscus Gasthuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Capillary blood samples, Hemolysis index, Potassium, Pseudohyperkalemia

Outcome measures

Primary outcome

The main study parameter is the comparison of the potassium and the free haemoglobulin (haemolysis index) concentration in corresponding venous- and capillary blood samples from the same patient.

Secondary outcome

Other parameters that will be measured are; lactate dehydrogenase (LDH), Aspartate aminotransferase (ASAT), creatinekinase (CK), phosphate, magnesium and sodium.

Study description

Background summary

In vitro haemolysis is the most important pre-analytical cause for interference in clinical laboratory blood tests1. Several parameters, like lactate dehydrogenase (LDH), Aspartate aminotransferase (ASAT) and potassium are spuriously elevated due to in vitro haemlysis.

Potassium is the major intracellular cation with roughly a 20-30 fold higher concentration inside the cell in comparison to the extracellular compartment. The sodium potassium ATP-ase is the major cellular enzyme responsible for maintaining this gradient. Due to this large difference in potassium concentration erythrolysis can have a substantial effect on the plasma potassium concentration (pseudohyperkalemia) in the clinical laboratory. Since both hyperkalemia and hypokalemia can cause dangerous cardiac arrest both pseudohyperkalemia and pseudonormokalemia (masking real hypokalemia), may cause

dangerous over- or under treatment respectively. This phenomenon is poorly understood by physicians, nurses and even laboratory technicians2.

Many modern laboratory analyzers have automated capability of measuring the free hemoglobine concentration spectrophotometrically, the haemolyses-index (H-index). The way the H-index is reported differs per manufacturer. For example Beckman analysers report the H-index in a scale from 1 to 10 whereby each level corresponds with a haemoglobin concentration range. Others (Roche Diagnostics, Cobas) report the H-index as a concentration in µmol/l. Based on the SKML external quality assessment of 2011, the Cobas Roche analyser is the most common platform for determining potassium concentrations in Dutch hospitals. Moreover a recent multicenter evaluation has shown that the H-index on the Cobas Roche analyzer is highly reproducible between laboratories.

There is ambiguity in dealing with in vitro haemolysis when reporting potassium results. Some laboratories add a qualitative remark (e.g. haemolysed sample) to the laboratory potassium result which varies with the H-index magnitude. When the H-index is beyond a predetermined threshold a *sample recollection* request is added as a comment and no potassium result is reported. On the other hand our laboratory and others use the H-index to correct potassium results with a correction factor. This correction factor is based on a whole blood in vitro lysate. This lysate is prepared by pooling whole blood which is then haemolysed by a freeze-thaw cycle and centrifuged. The supernatant is serially diluted in a non-haemolysed patient plasma sample. This will give a linear relation between the change in potassium concentration and the H-index. With regression analysis a slope is calculated and thus a correction factor determined. The reported potassium is calculated as such; K+reported = K+measured - (H-index *correction factor).

K+ = mmol/l
H-index = µmol/l hemoglobine
Correction factor = mmol K+/µmol hemoglobine

Using correction factors for estimating potassium concentration is controversial. One of the main reasons is the broad range of the correction factors proposed in literature. A significant part of this variability is attributable to the inter-individual variation in intracellular erythrocyte haemoglobin concentration. Another important argument against correction is that in vivo haemolysis (e.g. artificial heart valves, DIS, AIHA) will be seen as an in vitro haemolysed sample and unjustly corrected.

The golden standard sample for laboratory blood diagnostics is a venous sample. In neonates capillary sampling is a very common technique to collect blood for routine laboratory diagnostics, including the potassium status. Capillary sampling is also performed in adults when venous sampling is problematic such as in obese patients and patients with fear of needles. In certain laboratories capillary samples are corrected for haemolysis in the method described above.

There is limited literature available which investigates potassium correction factors and pseudohyperkalemia in capillary blood samples. It was even addressed as one of the shortcomings in a recent study.

Our hypothesis is that pseudohyperkalemia in capillary samples is caused by:
1. Haemolysis. In lege artis capillary sampling mild pressure (squeezing) is used as the driving force for the expulsion of blood. This mild pressure will not only expel blood from the puncture opening but also induce haemolysis.
2. Tissue fluids. The puncture will cause tissue damage and thus leakage of intracellular fluids (high in potassium) which contaminate the sample. This contamination will have a large effect on capillary potassium concentration due to the small sample volume. With this leakage, unlike erythrolysis, no haemoglobin is released and therefore this cannot be corrected with a H-index. It is generally considered that this first drop contains the vast majority of tissue damage fluids. This contamination is neglectable in a venous blood sample due to the large volume drawn.
3. Shear stress. This is a phenomenon whereby the erythrocyte membrane is deformed but stays intact. Due to this deformation small electrolytes, unlike large proteins like haemoglobin, can pass through the cellular membrane. The mild force used in capillary sampling to expel blood out of the puncture site will cause shear stress in the erythrocytes.

In other words we believe that there are multiple sources of potassium, other than haemolysis, in capillary samples. Given the fact that these sources have no relation with a change in haemoglobin concentration, the H-index cannot be used to correct potassium results.

Study objective

Primary objectives:
• Establish that capillary plasma samples are unsuitable to evaluate the potassium status in patients.
• Verify that pseudohyperkalemia in capillary samples is not only caused by haemolysis but also due to other potassium sources e.g. tissue damage, shear stress. If true, this will make the use potassium correction factors, based on in-vitro haemolysis alone, invalid for capillary blood samples.

Secondary objective:
• Verify that the contribution of potassium from sources other than haemolysis in pseudohyperkalemia is more substantial in incorrect capillary sampling than with lege artis capillary sampling.

Study design

Cross-sectional study in twenty adult patients. From each volunteer we will

take four capillary samples.

The first sample will be performed correctly (lege artis).
A second capillary sample will be collected from another finger but now the first drop will not be wiped away.
A third capillary sample will be collected from another finger using a milking technique.
A fourth capillary sample will be collected from another finger wherby the first drop is not wiped away and a milking technique is applied.

Venous plasma (400 µl) will be taken from the vacutainer which will already be collected for routine laboratory diagnostics. This means no extra phlebotomy and no extra venous blood sample will be necessary from the volunteers.

All blood samples will be obtained by trained and certified phlebotomists from the Sint Franciscus Gasthuis. Sampling volunteers will be completed in a time frame of one month.

Study burden and risks

Burden and risk associated with a capillary blood sample out of a finger are neglectable. Futher, we like to stress that incorrect capillary sampling (not wiping first drop and/or milking the finger) will not increase the burden or risk for the patient.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adult patients visiting the out-clinic for bloodsampling on request of the physician.

Exclusion criteria

Patients with in vivo haemolysis, Patients with liver diseases, Patients with coagulation disorders, Patients receiving anti-coagulation medication, Cardiopulmonary comprised patients, Patients with skin lesions on their hands, Patients with thick callous skin on fingertips, Patients whom are unable to comprehend the informed consent, Patients unwilling to sign informed consent

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped

Start date (anticipated):	09-05-2012
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	01-12-2011
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL37343.101.11