Desirée Perlee*, Klaas Henk van der Steege and Gijs den Besten

The effect of drone transport on the stability of biochemical, coagulation and hematological parameters in healthy individuals

https://doi.org/10.1515/cclm-2021-0513
Received April 29, 2021; accepted July 8, 2021;
published online July 21, 2021

Abstract

Objectives: Transport of blood tubes is mainly by car or pneumatic transport. The transportation of blood tubes by drones is a novel approach for rapid transportation of blood tubes over long distances. However, limited data on the stability of biochemical, coagulation and hematological parameters is available after transport of blood tubes by drone.
Methods: To investigate the effect of drone transport on the stability of blood parameters, four test flights were performed. Blood was drawn from 20 healthy individuals and 39 of the most frequently measured blood parameters were compared between 4 groups; immediate measurement (control), late measurement, transport by car and transport by drone. Total Allowable Error (TAE) of the EFLM Biological Variation Database was used to determine the clinical relevance of significant differences.
Results: The majority of blood parameters were not affected by drone transport. Eight of the measured parameters showed significant differences between all the groups; glucose, phosphate, potassium, chloride, hemoglobin, platelet count, APTT and Lactate dehydrogenase (LD). A clinically relevant increase for LD after transport and a decrease for glucose values in time and after transport compared with the control group was shown.
Conclusions: Transportation of blood tubes from healthy individuals by drones has a limited clinically relevant effect. From the 39 investigated blood parameters only LD and glucose showed a clinically relevant effect.

Keywords: biochemical; blood transport; clinical relevance; coagulation and hematological parameters; drone; stability.

***Corresponding author: Desirée Perlee,** PhD, Department of Clinical Chemistry, Isala Hospital, Dr. Van Heesweg 2, 8025 AB Zwolle, the Netherlands, Phone: +31 384247642, E-mail: d.perlee@isala.nl
Klaas Henk van der Steege and Gijs den Besten, Department of Clinical Chemistry, Isala Hospital, Zwolle, the Netherlands

Introduction

Pneumatic transport is the regular way of blood tube transportation within hospitals, allowing a speedy and reliable transportation to the central laboratory. This method is thoroughly validated in order to provide clinicians with quick and reliable results. Besides pneumatic transport, ground transportation by car is often used to transport blood tubes from the phlebotomy location to the laboratory.

Transportation of blood products and tubes over big distances by drones is a new way of blood sample transportation [1] which is currently not implemented in the Netherlands. Drones have been tested for a variety of functions as surveillance, entertainment and imaging, and could have a high potential in healthcare [2]. So far, drones have been used during disasters in multiple countries [3]. In addition, drones are being tested for the transport of blood products in Japan [4] and Canada [5], and are being used in Rwanda to transport blood products to rural areas [6].

With the drone as a novel way of timely and safe blood product transportation, we wondered if this method could be a suitable way to transport blood tubes in the Netherlands and in specific between the two separate hospital locations of the Isala Hospital. Since limited data is available on the effect of drone transport on the stability of biochemical, coagulation and hematological parameters, we assessed if the quality of the biological samples could be maintained in this controlled experimental setting.

Materials and methods

Study design

In this study, potassium EDTA-, sodium fluoride-, citrate-, and lithium heparin-anticoagulated (all BD vacutainer, STT II Advance, UK) venous blood was collected by a phlebotomist in the department of Clinical Chemistry at Isala Hospital in Zwolle, the Netherlands. In total 20 healthy volunteers were included in this study, 14 females and 6 males. Successive samples were obtained and divided over four groups; immediate measurement (control), late measurement, transport by car and transport by drone.

To examine the impact of drone (AVY, Amsterdam, the Netherlands) transport, one set of samples were flown in a loop flight for 30 min which resembles the distance between the two hospital locations of the Isala Hospital. A second set was driven to the flight site but not flown (car transport). Both sets were transported in isolating boxes. Temperature, speed and distance travelled by the drone were documented. In addition, sample temperature was continuously monitored using an Ebro EBI temperature data sensor (Xylem Inc., Rye Brook, NY). Control samples (immediate and late measurement) were stored in the laboratory at room temperature (20–23 °C) at all times.

Analysis

We tested the most frequent analyzed parameters in our laboratory. Blood samples were all processed according to standard laboratory instructions and paired samples were analyzed on the same system. In short; blood tubes for coagulation and biochemical analyses were centrifuged 2000 g for 10 min. Biochemical and coagulation parameters were subsequently analyzed with respectively the Roche Cobas 8000 analyzer (Roche Diagnostics, Basel, Switzerland) and the Sysmex CS-2500-analyzer (Sysmex Corporation, Kobe, Japan). Hematology parameters were determined with the Sysmex XN 9000 hematology analyzer (Sysmex Corporation, Kobe, Japan).

Statistical analysis

Comparisons between groups were done by two-way repeated measures ANOVA (Friedman test), if significant followed by Bonferroni post hoc analysis. The EFLM Biological Variation Database [7] was used to determine the clinical relevance of significant differences. Data are shown as percentage difference of paired samples and expressed as scatter dot plots with median (95% CI), showing the percentage difference of paired samples and the minimum and desirable total allowable error (TAE). Analysis were done using GraphPad Prism version 9.0 (Graphpad Software, San Diego, CA). A two-sided p-value <0.05 was considered significant for the Friedman test, a Bonferroni correction was used when appropriate.

Results

General parameters

In total, four drone flights were performed on two days. Outdoor temperature was respectively 14 °C and 10 °C. A decrease in temperature from 20–23 °C (indoor room temperature) to 14–17 °C in the transport boxes was reported during car and drone transport. No apparent differences between the transport groups were noted. During the flight, the drone covered a distance of 30 km with a speed of approximately 70 km/h at 100 m altitude.

To obtain insight into the effect of drone transport on a variety of analytes, we compared 39 parameters in four study groups; immediate measurement (control), late measurement and measurement after car transport and drone transport. Samples were checked for hemolysis, icterus and lipemia (HIL indices). No significant changes in HIL indices were seen between the groups (Supplemental Table 1). The majority of measured parameters showed no significant differences between all the groups determined by two-way repeated measures ANOVA. However, eight parameters showed significant results between the groups; glucose, phosphate, potassium, chloride, hemoglobin, platelet count, APTT and LD (Supplemental Tables 2 and 3). In order to show the significance between two individual groups, a Bonferroni post hoc test was used as multiple comparison test (Supplemental Table 2).

To investigate the clinical relevance of the significant differences, we used the minimum and desirable specification of TAE obtained from the EFLM database. For APTT no TAE was available and the CLIA proficiency testing criteria for acceptable analytical performance [8] was used.

We showed an increase in LD and potassium levels, both markers of hemolysis, after transport. Potassium levels increased significantly comparing late measurement with car transport. One sample exceeded the minimum level of TAE in the car transport group (Figure 1A). The other samples showed no clinically relevant differences. LD levels which indicate tissue damage showed multiple significant differences comparing individual groups (Supplemental Table 2). In total, 30% (6/20) of the samples in the car transport group and 45% (9/20) in the drone transport group showed a clinically relevant increase in LD value (Figure 1B).

Time and transport of blood tubes was associated with a decrease of glucose levels in all groups compared with the control (immediate measurement) group (Figure 1C). In total, 1 sample (5%) showed a clinically significant decrease in glucose after car transport and 6 samples (30%) showed a clinically significant decrease after drone transport.

Chloride and phosphate levels (Figure 1D and E) showed multiple significant comparisons between the groups (Supplemental Table 2). Extensive analysis of the clinical relevance revealed 1 sample (5%) exceeding the TAE for chloride in the drone transport group and 1 sample (5%) exceeding the TAE in the late measurement group for phosphate. Hemoglobin and platelet count, both critical hematological parameters, and APTT, a measurement essential for the interpretation of the coagulation state of the patient, showed no clinically relevant differences between the groups (Figure 1F–H).

Discussion

Drone transport could be a novel transport method for blood tubes, however limited data is available on the

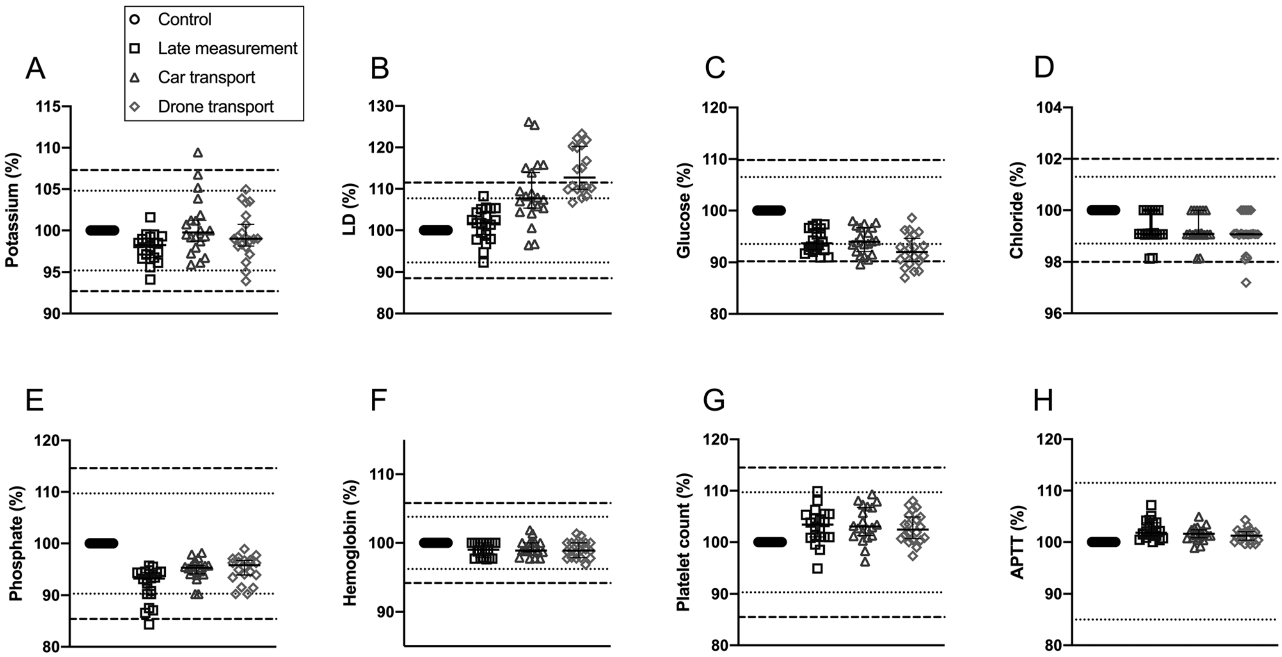

Figure 1: The clinical relevance of the effects of drone transport on biochemical, coagulation and hematological parameters.
Dot plots and median (95 % CI) depicting the clinically relevant differences of potassium (A), LD (B), glucose (C), chloride (D), phosphate (E), hemoglobin (F), platelet count (G) and APTT (H).
n=20 samples per group. Minimum (—) and desirable (·····) total allowable error are shown.

stability of blood under these specific circumstances. Drones can improve the current transport of blood tubes and products as they are able to deliver the products more rapidly and can access rural areas. However, legal regulations differ between countries and safety aspects should be investigated thoroughly before use. For example, protocols should be developed in case of drone failure to ensure transport is guaranteed.

To our knowledge, this study is the first large study in the Netherlands were we assessed the effect of drone transport on the stability of a broad spectrum of analytes.

Comprehensive analysis of 39 routinely measured biochemical, coagulation and hematological parameters showed that the majority of the analytes was not influenced by drone transport.

To draw conclusions on the effect of drone transport on hemolysis, we included LD, potassium and bilirubin in this study which are all sensitive to hemolysis. As samples in our study are subjected to movement and during drone transport additionally to atmospheric pressure, we expected more cell damage and therefore more hemolysis in both transport groups. Furthermore, leakage of potassium from red blood cells in time and at low temperature, which was reported during car and drone transport, are well-known phenomenons [9, 10]. Previous reports showed that LD and potassium levels did not increase in blood products (RBC solution) after drone transport [4]. In our study, no significant differences in bilirubin levels and hemolysis index were noted and the effect on potassium was limited to one clinically significant sample. However, LD levels showed a clinically significant increase, which could potentially be the result of movement during transport and therefor improved by optimization of the stabilization of blood tubes in the transport box. These results show that drone transport has besides the reported increase in LD levels no clinical relevant effects on hemolytic parameters measured in healthy individuals.

Drone transport was compared with immediate measurement, as this reflects the clinical situation *in vivo* the most accurate. Nevertheless, blood tubes are in general transferred with pneumatic or car transport to the central laboratory. It is described that the pneumatic transport system can cause hemolysis because of the movement of the tubes [11]. In addition, multiple studies compared manual transport with pneumatic transport, showing an increase in hemolysis [12] and in specific an increase in potassium and LD level after pneumatic transport [13]. Since pneumatic transport was not included as study group, it is difficult to compare drone transport with pneumatic transport.

Glucose concentrations showed a clinically relevant decrease in all groups compared with the control (immediate measurement) group, which can be explained by both the sodium fluoride (NaF) tube and the study population. The difference between the drone and car group was not clinically relevant.

NaF blood tubes are commonly used in the clinic as NaF is a well-known glycolysis inhibitor. The inhibition of glycolysis takes 1–2 h [14] in which the cells are still able to use glucose. This could explain the difference in glucose results with the immediately measured control group. Previous investigations have documented a time-dependent decrease of glucose levels in NaF blood tubes [15, 16], which could be prevented by the use of liquid citrate buffer [17]. On the contrary, Ling et al. described an increase in glucose and potassium levels after drone transport of blood products, though these results were explained by the higher temperature exposure of the samples [6]. This could be a possible explanation in our study as well since we measured decreased glucose concentrations in the drone and car group and the temperature in these groups was temporary lowered compared with the immediate measurement group. In addition, the study samples exceeding the minimum TAE were all located in the low measurement area with absolute glucose levels ranging 3.6–5.4 mmol/L. Hence explaining the multiple clinically relevant samples, as it is in this low area more difficult to pass the TAE criteria.

Recently**,** Johannessen et al. showed the effect of drone transport on pathological samples [18]. In this study they showed that turbulence exposure up to 30 G had no significant effect on hematological and most biochemical analytes they measured in pathological samples. However, AST, LD and lipid index changed significantly in plasma samples, which was possibly prevented by not centrifuging samples before the flight. It was hypothesized that separator gels that remain at the bottom of the tube before centrifugation may be less prone to damage than gels after transformation during centrifugation and then located higher in the tube. When blood tubes are centrifuged before g-force exposure the gel can become more porous and probably be more prone to disintegration during vibration and turbulence potentially resulting in leakage of analytes. In our study we centrifuged the samples afterwards, which could have a beneficial effect on the stability.

Although the presented results look very promising we should be careful by drawing conclusions. In this study only healthy individuals were included and thereby lacking pathological samples outside the reference intervals. More research is required to study the effect of drone transport on pathological patient samples. An additional study is planned in which we will include g-force measurement and in which we will use temperature controlled boxes.

Conclusions

Drone transport of blood tubes from healthy individuals has limited clinically relevant effects on biochemical, coagulation and hematological parameters. From the 39 investigated blood parameters only LD and glucose showed a clinically relevant effect.

Acknowledgments: The authors would like to thank Medical Drone Service for the technical assistance with the drone, all volunteers who participated in this study and Erna Lenters-Westra, Jan van der Kolk and Mireille Edens for their advice.
Research funding: None declared.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Competing interests: Authors state no conflict of interest.
Informed consent: Informed consent was obtained from all individuals included in this study.
Ethical approval: The local Institutional Review Board deemed the study exempt from review.

References

1. Patel MK, El-Khoury JM, Simundic EA, Farnsworth CW, Broell F, Genzen JR, et al. Evolution of blood sample transportation and monitoring technologies. Clin Chem 2021;67:812–9.
2. Lippi G, Mattiuzzi C. Biological samples transportation by drones: ready for prime time? Ann Transl Med 2016;4:92.
3. Zailani MAH, Sabudin RZAR, Rahman RA, Saiboon IM, Ismail A, Mahdy ZA. Drone for medical products transportation in maternal healthcare: a systematic review and framework for future research. Medicine (Baltim) 2020;99:e21967.
4. Yakushiji F, Yakushiji K, Murata M, Hiroi N, Takeda K, Fujita H. The quality of blood is not affected by drone transport: an evidential study of the unmanned aerial vehicle conveyance of transfusion material in Japan. Drones 2020;4:4.
5. Homier V, Brouard D, Nolan M, Roy MA, Pelletier P, McDonald M, et al. Drone versus ground delivery of simulated blood products to an urban trauma center: the Montreal medi-drone pilot study. J Trauma Acute Care Surg 2021;90:515–21.
6. Ling G, Draghic N. Aerial drones for blood delivery. Transfusion 2019;59:1608–11.
7. Aarsand AK, Fernandez-Calle P, Webster C, Coskun A, Gonzales-Lao E, Diaz-Garzon J, et al. The EFLM biological variation atabase [online]. Available from: https://biologicalvariation.eu/ [Accessed 12 Mar 2021].
8. Westgard J. CLIA proposed acceptance limits for proficiency testing [online]; 2019. Available from: https://www.westgard.com/2019-clia-requirements.htm [Accessed 12 Mar 2021].
9. Asirvatham JR, Moses V, Bjornson L. Errors in potassium measurement: a laboratory perspective for the clinician. N Am J Med Sci 2013;5:255–9.

10. Stankovic AK, Smith S. Elevated serum potassium values: the role of preanalytic variables. Am J Clin Pathol 2004;121:105.
11. Kara H, Bayir A, Ak A, Degirmenci S, Akinci M, Agacayak A, et al. Hemolysis associated with pneumatic tube system transport for blood samples. Pak J Med Sci 2014;30:50–8.
12. Ellis G. An episode of increased hemolysis due to a defective pneumatic air tube delivery system. Clin Biochem 2009;42:1265–9.
13. Weaver DK, Miller D, Leventhal EA, Tropeano V. Evaluation of a computer-directed pneumatic-tube system for pneumatic transport of blood specimens. Am J Clin Pathol 1978;70:400–5.
14. Gambino R, Piscitelli J, Ackattupathil TA, Theriault JL, Andrin RD, Sanfilippo ML, et al. Acidification of blood is superior to sodium fluoride alone as an inhibitor of glycolysis. Clin Chem 2009;55: 1019–21.
15. Lippi G, Nybo M, Cadamuro J, Guimaraes JT, van Dongen-Lases E, Simundic AM. Blood glucose determination: effect of tube additives. Adv Clin Chem 2018;84:101–23.
16. Waring WS, Evans LE, Kirkpatrick CT. Glycolysis inhibitors negatively bias blood glucose measurements: potential impact on the reported prevalence of diabetes mellitus. J Clin Pathol 2007;60:820–3.
17. Juricic G, Bakliza A, Saracevic A, Kopcinovic LM, Dobrijevic S, Drmic S, et al. Glucose is stable during prolonged storage in un-centrifuged Greiner tubes with liquid citrate buffer, but not in serum and NaF/KOx tubes. Clin Chem Lab Med 2016;54:411–8.
18. Johannessen KA, Wear NKS, Toska K, Hansbo M, Berg JP, Fosse E. Pathologic blood samples tolerate exposure to vibration and high turbulence in simulated drone flights, but plasma samples should be centrifuged after flight. IEEE J Transl Eng Health Med 2021;9: 4000110.

Supplementary Material: The online version of this article offers supplementary material (https://doi.org/10.1515/cclm-2021-0513).