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Effect of Heparin Flush in Blood Drawn from Arterial Line on Activated Clotting Time and Thromboelastogram

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Abstract

The usage of low dose heparin as an additive to normal saline is a very acceptable medical practice for the maintenance of arterial line. However, heparin potentially may affect the exactness of coagulation studies carried out on blood sampled from a heparin flushed arterial line. This prospective, comparative observational study was designed to evaluate the effect of blood sampling through a heparin flushed arterial catheter on the validity of common and advanced coagulation tests including activated clotting time (ACT) and thromboelastogram (TEG). Whereas heparin flush did not affect international normalized ratio (INR) and activated partial thromboplastin time (aPTT), it significantly prolonged ACT together with the R-time and K-time components of TEG. This advocated being cautious when measuring ACT and some TEG parameters from a heparin flushed arterial line in a clinical setting.

Abbreviations

INR: International Normalized Ratio; aPTT: Activated Partial Thromboplastin Time; ACT: Activated Clotting Time; TEG: Thromboelastogram; R: Reaction time (time from the start of a sample run until the first significant levels of detectable clot formation); K: Time from the measurement of R until a fixed level of clot firmness is reached; MA: Maximal Amplitude; CPB: Cardiopulmonary Bypass

Introduction

An arterial catheter is commonly inserted to allow a direct line access to the arterial tree of the vascular system for many indications including continuous accurate measurement of blood pressure and blood sampling for chemistry, gas and the coagulation status. The usage of a low dose heparin as an additive to normal saline is a very acceptable medical practice for the maintenance of arterial line. Whereas heparin does not affect the exactness of blood gas and chemistry tests, it may have a significant impact on the quality of the coagulation status examination, being involved in the blood clotting cascade. Although past publications had found that clotting studies carried out on blood sampled from an arterial line correlate well with those obtained from a venipuncture, except for some effect on activated partial thromboplastin time (aPTT) [1], more recent observation challenged these findings [2]. A literature search revealed very few articles comparing activated clotting time (ACT) sampled from an arterial heparin-flushed line with venous heparin-free line [3,4] and only one which mentions Thromboelastogram (TEG) in the context of reliance on clotting profile assessment and heparinized arterial line [2]. Since our hypothesis is the presence of even very low dose heparin may have a significant effect on more sensitive clotting measurements, and as the accurate assessment of blood clotting is crucial for patient safety, this prospective, comparative observational study was designed to evaluate the effect of blood sampling through a heparin flushed arterial catheter on the validity of common and advanced coagulation tests, including ACT and TEG.

Methods

The study was designed as a prospective, comparative observational study, and performed in the Cardiothoracic Anesthesia Unit of the Department of Anesthesiology in Rambam Healthcare Campus in Haifa, Israel A tertiary, university affiliated teaching hospital.

Following approval from the hospital's ethics committee and obtaining written informed consent, patients scheduled for elective cardiac or thoracic surgery requiring invasive blood pressure monitoring were enrolled to the study. Patients with known coagulation disorders were excluded from the study. The age, height, weight and European system for cardiac operative risk evaluation (EuroSCORE) risk assessment grading were recorded, as well as pre-operative hemoglobin concentration, platelet count, aPTT and international normalized ratio (INR) studies.

Aiming to evaluate the differences in coagulation studies in patients with near normal coagulation system, all blood samples were withdrawn prior to the commencement of surgery, and prior to administration of high dose heparin for cardiopulmonary bypass (CPB).

An 18G arterial catheter (BD Venflon, BD, Becton Drive, Franklin Lakes, NJ, USA) was inserted into a radial artery. Following the arterial line insertion, the catheter was flushed with 10 ml of the heparin containing solution and then connected to a flushing system (Art-Line, BioMetrix, Kiryat Mada, Jerusalem, Israel) containing a standard flush solution constituted of heparin 2 units/ml, sodium chloride 0.9%, 1.9 microgram/ml citric acid, and 8.7 microgram/sodium phosphate (Teva Pharmaceutical Industries LTD, Israel). The flushing system had been operated for at least 30 minutes prior to connecting to the patient.

Once a peripheral venous catheter or a second large bore peripheral venous catheter were installed, a blood sample was drawn and marked as "Venous blood", In parallel, 10 ml dead space blood [1,2] was aspirated from the catheter and discarded, immediately followed by another blood sample marked as "Arterial blood". Both the "Venous

blood" and the "Arterial blood" samples were processed for coagulation tests in the same fashion using the same measurement equipment.

Activated clotting time (ACT) measuring the time of formation of a stable clot in activated blood , aPTT quantifying the intrinsic coagulation pathway, and international normalized ratio (INR) quantifying the extrinsic coagulation pathway, as well as Thromboelastographic values (R,K, Alpha Angel and MA) were measured. Blood for INR and aPTT studies was sent in a sodium citrate containing glass vial (Vaacuette®,Greiner Bio One International GmbH, Frickenhausen, Germany) to the hospital laboratory, and tests were performed using an automated equipment (Sysmex CA-1500, Siemens AG, Erlangen, Germany). Normal INR and aPTT ranges in our institution laboratory were 0.8-1.2 and 30-50 seconds, respectively.

ACT was determined using an ACT-II Coagulation timer (Medtronics Inc., Minneapolis, USA) using a HR-ACT kit in a temperature of 37°C. Two separate blood vials were used for each test, and their average was regarded as the ACT final value.

Thromboelastography was performed using a TEG® 5000 Thrombelastograph® Hemostasis Analyzer System (Haemoscope, Niles, IL, USA) Using citrated whole blood as per standard manufacturer operating instructions.

Sample size was calculated using retrospective patient chart review. All the variables were recorded on a computerized spreadsheet and assigned to each study subject by name and identification number. Data was evaluated by statistical package for the social sciences (SPSS) software, version 17 (SPSS Inc. Chicago, IL, USA). Descriptive statistic studies, including mean and standard deviation ware used. A paired T-Test was used to determine statistical significance. Normal distribution was assessed by both Back-of-the-envelope test and Kullback–Leibler divergences.

Results

Thirty six patients were enrolled to the study between 11 March 2010 and 8 August 2013 (20 males and 16 females). The average age was 68 ± 11 years, the average height 163 ± 11 cm and the average weight 73 ± 15 kg.

In pre-operative blood tests performed one to three days prior to the operation, the average hemoglobin concentration was 12.5 ± 19 g/dL, average platelet count 206 ± 65 X 109/L, average INR 1 ± 0.1 and average aPTT 28 ± 5 seconds.

Average INR of Arterial blood was the same as for venous blood. Similarly, aPTT for Arterial blood was 29 ± 5 seconds - prolonged by one second compared with venous blood (P<0.01).

Average ACT of Arterial blood sampled was 10 seconds [8.1%, (P<0.01)] longer compared with Venous blood.

Average R, defined as R-time (reaction time)- the time from the start of a sample run until the first significant levels of detectable clot formation (amplitude=2 mm in the TEG tracing) for Arterial blood was 1.2 second longer [12%, (P<0.01)] compared with Venous blood, Similar effect was found with average K, defined as K-time - the time from the measurement of R until a fixed level of clot firmness is reached (amplitude=20 mm in the TEG tracing), namely 0.3 second [16%, (P=0.03] prolongation for Arterial blood compared with venous blood. Neither Average TEG angle alpha (the kinetics of clot development of blood) nor average TEG MA [maximum amplitude a measurement of maximum strength or stiffness (maximum shear modulus) of the developed clot] showed insignificant difference between Arterial and Venous blood (Table 1).

Coagulation study	Venous blood	Arterial blood	Normal values	P*
INR	1.1 ± 0.1	1.1 ± 0.1	0.8-1.2	0.12
aPTT (Seconds)	28 ± 4	29 ± 5	25-35	<0.01
ACT (seconds)	122 ± 16	132 ± 14	80-160	<0.01
TEG R (seconds)	6.6 ± 2.1	7.8 ± 2.1	4-8	<0.01
TEG K (seconds)	1.9 ± 0.7	2.2 ± 0.8	1-4	0.03
Alpha Angle (degrees)	67 ± 7	69 ± 7	47-74	0.06
TEG MA (mm)	65 ± 7	65 ± 8	55-73	0.63

Table 1: Effect of blood sampled from venous blood or from Arterial line flushed with heparin on coagulation studies (Arterial blood).

Discussion

There is a heated debate in the literature if there is any real need to use heparin for arterial line maintenance. On the one hand, some studies present unequivocally approach that no significant difference in duration of patency exists between intravascular catheters flushed with saline or with a heparinized solution [5-7]. This position has important practical implications with regards to avoidance of exposure to heparin-associated risks [8] including inadvertent flow of extra fluid volume and unintended overdose from a pressurized bag of heparin solution together with additional costs associated with the use of a unique solution and a potential for heparin induced thrombocytopenia (HIT) [9-11]. Yet, others encourage heparin usage because of longer duration of patency compared with saline, and do not fear either the higher costs, overdose or the not proven risk of HIT [11,12].

Indeed, there are recommendations to aspirate from the intravascular indwelled catheter a dead space volume of at least 5 mL comprising of flushing solution and blood, discard it and then redraw a certain volume of blood necessary to conduct the necessary test on it [13]. This action provides the operator with a sense of assurance that the tested sample is free of any contamination. With respect to INR

and aPTT, our findings coincide with the literature [2,14]. However, apparently according to our study this feeling is baseless when it comes to more specific measurements which in our case are the advanced coagulation test of ACT and some TEG parameters. The differences, despite being small, may raises critical questions pertaining to the use of heparin flush in arterial line and the reliability of clotting functions tests which are nowadays more available, accessible and widespread as a means of monitoring and managing of many situations including heart, vascular, and transplantation surgery, major trauma, severe bleeding and more. Prolonged ACT may indicate a deficiency in coagulation factors, thrombocytopenia and aprotinin use [15-17]. Inasmuch R, the point at which most traditional coagulation assays reach their end-points is prolonged by anticoagulants and factor deficiencies and K, a measure of the speed to reach a certain level of clot strength and is prolonged by anticoagulants may be affected by heparin flush.

Conclusion

Due to the small sample size and limited clinical settings, we refrain from taking a position pro or against the use of heparin flush versus saline for arterial line maintenance, but suggest to be cautious when measurements such as ACT and some TEG parameters in a clinical setting has a potential to become affected by heparin contamination. Despite the relatively low clinical significance, it may be wise to compare blood samples drawn from a single site when evaluating coagulation changes over time.

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