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Activated clotting time or activated partial thromboplastin time as the method of choice for patients undergoing neuroradiological intervention

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Abstract We evaluated the role of the activated clotting time (ACT) and activated partial thromboplastin time (APTT), both currently available as bedside tests, for monitoring anticoagulation following bolus injection of 2500 or 5000 IU heparin in 21 patients undergoing neuroradiological procedures. APTT was measured using the CoaguChek Pro device compared to the laboratory standard measurement and ACT comparing CoaguChek Pro to Hemochron Celite and Kaolin. Statistical analysis was performed using Bablok-Passing regression. Despite heparin doses of 2500–5000 IU APTT measurements were out of range in 67% of patients using CoaguChek Pro and in 76.5% of patients using the laboratory measurement. ACT was reliably determined in all patients. The correlation between the different devices (CoaguChek Pro vs. Hemochron Celite r = 0.69, Kaolin r = 0.78) and assays (Hemochron Celite/Kaolin r = 0.85) was good. ACT ranged from 141–417 s measured by CoaguChek Pro and 138–320 s measured by Hemochron Celite and 172–381 s using Hemochron Kaolin. These results indicate that ACT is the method of choice for monitoring anticoagulation in neuroangiographic procedures.

Keywords Activated clotting time · Activated partial thromboplastin time · Neuroradiology

Introduction

Heparin is routinely given intravenously to reduce the risk of thromboembolic complications in neuroangiography [1, 2, 3]. There are generally two ways of monitoring anticoagulation: the activated partial thromboplastin time (APTT) and the activated clotting time (ACT). The former is currently the most commonly used to monitor clinical heparin therapy despite its log-linear relationship to heparin dose and individual patient variations [4, 5, 6]. ACT is used to monitor anticoagulation during cardiopulmonary bypass and cardiac catheterisation procedures requiring large (≥10000 IU) bolus injections of heparin, since it provides reliable data at higher heparin doses, with a linear

relationship [7, 8, 9, 10, 11]. In the past, determination of the APTT required a laboratory assessment with a turn-around time of 1–4 h [4, 10], rendering it useless during procedures, when adjustments of anticoagulation have to be made within minutes. New point-of-care devices have been developed offering instant APTT measurements using one drop of blood, comparable to ACT techniques.

Since there is a higher risk of intracerebral bleeding in neuroradiological interventional procedures the boluses of heparin are in the range 2500–7500 IU aiming for an ACT >200 s, or 1.5–2.5 times the initial value [1, 2], compared with 300–400 s for cardiac interventions [8, 9, 11, 12, 13, 14], the question arose whether APTT or ACT is better for monitoring the efficacy of anticoagulation at lower heparin doses.

Materials and methods

We prospectively studied 21 consecutive patients, ten men and 11 women aged 19–74 years (mean 54 years), undergoing neuro-radiological interventions such as embolisation of an arteriovenous malformation, coiling of an aneurysm, placement of a carotid stent or temporary occlusion of a carotid artery, from whom informed consent could be obtained. The study was approved by the local ethics committee. Heparin was given as a bolus of 2500 IU (in seven patients) or 5000 IU (in 14). Four patients received an additional bolus of 2500 IU on the decision of the interventionalist when the ACT level measured on Kaolin was < 200 s, so that the total dose of heparin was 7500 IU in two patients. The blood samples were taken before and 2–10 minutes after administration of heparin, then between 50–160 minutes after the first injection; on each occasion 9 ml blood was withdrawn via the arterial sheath and distributed onto the different devices.

ACT was measured with two independent CoaguChek Pro devices (Roche Diagnostics GmbH) and an Automated Coagulation Timer Hemochron 801 (International Technidyne Corporation) with two channels. One channel was used for Celite and the other channel for Kaolin test tubes, respectively. APTT was measured from whole blood with a CoaguChek Pro device (Roche Diagnostics GmbH) and from a citrate blood sample in the hospital laboratory using the Patrontin kit (Behring). In four patients no laboratory APTT could be obtained due to a failure in blood sampling.

The statistical analysis of correlation between the different devices and the assays was carried out using the Bablok-Passing regression.

Results

Prior to the intravenous bolus of heparin the APTT measured by the CoaguChek Pro device was < 18–35.7 s (mean 27.4 ± 4.7 s); the laboratory measurements were 26–38 s (mean 31.3 ± 3.6 s), with one failure in blood sampling. The baseline ACT measured with CoaguChek Pro was < 100–129 s (mean 112 ± 9 s), compared to 92–158 s measured with Hemochron Celite (mean 124 ± 16 s) and 97–148 s with Hemochron Kaolin (mean 120 ± 13 s).

After the 2500 or 5000 IU heparin bolus a useful APTT measurement was obtained in only seven (33%) of the 21 patients using CoaguChek Pro; the remainder had an APTT > 150 s. In the laboratory a definite APTT was obtained in four (23.5%) of 17 patients, the value in the other 13 cases being > 160 s. In four patients no result was obtained due to a failure of the blood sample. ACT after the heparin bolus were 141–417 s (mean 222 ± 67 s) measured with CoaguChek Pro, 138–320 s (mean 199 ± 43 s) using Hemochron Celite and 172–381 s (mean 229 ± 52 s) with Hemochron Kaolin.

Samples taken at the end of the procedure showed an APTT > 160 s in eight (38.1%) of the 21 patients when measured with CoaguChek Pro; the others were 20.3–137.2 s. Laboratory measurements yielded an APTT > 160 s in nine (45%) of 20 patients (one sample being inadequate), the others being 27–88 s. ACT at this stage was 104–233 s (mean 157 ± 36 s) measured with the CoaguChek Pro, 72–256 s (mean 164 ± 46 s) using the Hemochron Celite and 114–255 s (mean 167 ± 38 s) with Kaolin.

Correlation between the different devices and assays was good: that correlation between the APTT measured by CoaguChek Pro and the standard laboratory measurement was $r = 0.87$ (slope = 0.94). The correlation of the ACT obtained with CoaguChek Pro and with Hemochron Celite was $r = 0.69$ (slope 1.19) and with Hemochron Kaolin it was $r = 0.78$ (slope 1.04). The correlation of Celite and Kaolin was $r = 0.85$ (slope 1.14).

Discussion

The risk of neurological complications in diagnostic cerebral angiography is 0.09–1%, increasing with the age of the patient, atherosclerotic plaques, prior stroke and longer procedures [15, 16, 17, 18, 19, 20]. To minimise the risk of interventional procedures heparin is given intravenously, since the risk is known to be substantially increased, up to 5.7% in endovascular coil embolisation, for example [21]. Monitoring of heparin-induced anticoagulation is crucial to ensure its efficacy, to minimise complications and to reveal any lack of response.

The use of ACT during percutaneous angioplasty in cardiac laboratories is well established and it has been found to be superior to APTT, which tends to run out of the measurable range [5, 7, 10, 11]. This is due to the large (≥ 10000 IU) doses of heparin given, since an ACT 300–350 s is aimed for, to prevent formation of thrombus and ensure a safe procedure [8].

In neuroangiography the heparin boluses are mainly 2500–7500 IU, since there is a fear of cerebral haemorrhage [1, 2]. The use of ACT for monitoring anticoagulation in these procedures was adopted slowly, despite the fact that the need for continuous monitoring is obvious. In the recent guidelines of the American Society of Interventional and Therapeutic Neuroradiology [22] ACT measurements are recommended for all endovascular neuroradiological procedures when heparin is given, but to date only three publications [1, 2, 3] deal with this. The speed and ready availability of ACT compared to APTT have been emphasised in the past; the latter was unsuitable for neuroradiological procedures because of the time it took [1, 10, 11]. Since bedside measurements of APTT became available, we thought we should study the usefulness of both techniques at the lower heparin doses used in neuroradiology.

Both during and at the end of our procedures, the APTT could not be used to assess anticoagulation since in several patients the upper limit was exceeded in both

bedside and laboratory testing. ACT was useful in the whole group. Our quantitative ACT findings detailed above are in good agreement with those of Kaluski et al. [13], who found a mean ACT of 185 ± 19 s (range 157–238 s) after a single bolus of 2500 IU heparin.

We found a good correlation between bedside and laboratory testing for APTT, our r value of 0.87 being in agreement with the 0.89 found by Reiner et al. [5]. The bedside test has the advantage that it is easy to perform and there were no missing values due to failed blood sampling.

Correlation between the different ACT methods was moderate. However, the differences are easily explained by the different activators used in the assays and the different techniques of the devices. This has been shown, for example, by comparing the Hemochron and Hemo Tec (Medtronic) devices. The activators are also known to have a different potential at low doses of heparin [7, 12, 23]. Our results underline the importance of considering which device is used, when trying to establish a threshold ACT for neuroangiographic procedures, something which has not been done so far.

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