Activated Partial Thromboplastin Time Versus Antifactor Xa Heparin Assay in Monitoring Unfractionated Heparin by Continuous Intravenous Infusion

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BACKGROUND: Unfractionated heparin (UFH) has been used clinically for 5 decades. Despite being a cornerstone of anticoagulation, UFH is limited by its unpredictable pharmacokinetic profile, which makes close laboratory monitoring necessary. The most common methods for monitoring UFH are the activated partial thromboplastin time (aPTT) and antifactor Xa heparin assay (anti-Xa HA), but both present challenges, and the optimal method to monitor UFH remains unclear.

OBJECTIVE: To compare the performance of the aPTT with the anti-Xa HA for efficiency and safety of monitoring intravenous UFH infusions.

METHODS: This was a single-center, retrospective, observational cohort study conducted in an 852-bed academic medical center.

RESULTS: One hundred patients receiving intravenous UFH for a variety of indications were enrolled in the study; 50 were assigned to each group. The mean (SD) time to achieve therapeutic anticoagulation was significantly less in the anti-Xa HA group compared with the aPTT group (28 [16] vs 48 [26] hours, $p < 0.001$). In addition, a greater percentage of anti-Xa HA patients compared to aPTT patients achieved therapeutic anticoagulation at 24 hours (OR 3.5; 95% CI 1.5 to 8.7) and 48 hours (OR 10.9; 95% CI 3.3 to 44.2). Patients in the anti-Xa HA group also had more test values within the therapeutic range (66% vs 42%, $p < 0.0001$). A significant difference was seen between the 2 groups in the number of aPTT or anti-Xa HA tests performed per 24 hours ($p < 0.0001$) and number of infusion rate changes per 24 hours ($p < 0.01$), both favoring the anti-Xa HA group.

CONCLUSIONS: Monitoring intravenous UFH infusions with the anti-Xa HA, compared to the aPTT, achieves therapeutic anticoagulation more rapidly, maintains the values within the goal range for a longer time, and requires fewer adjustments in dosage and repeated tests.

KEY WORDS: activated partial thromboplastin time, antifactor Xa heparin assay, unfractionated heparin, venous thromboembolism.

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Unfractionated heparin (UFH) has been the mainstay of intravenous anticoagulant therapy for more than half a century. As a result, it has been extensively studied and used clinically for many indications, including treatment of venous thromboembolism (VTE).[1-4] Since its emergence, clinicians have struggled to overcome the challenge of maintaining a level of anticoagulation that provides optimal protection from thrombus extension or recurrence, while avoiding the risk of bleeding.[5-7] The narrow therapeutic index of UFH, as well as the intrapatient and interpatient variability, make close laboratory monitoring necessary.[8-14] The most common laboratory parameters used to monitor UFH are the activated partial thromboplastin time (aPTT) and heparin activity as measured by antifactor Xa (anti-Xa) analysis.[5,15] Of these 2 tests, the aPTT is most frequently used because of its relative accessibility, ease of automation, and cost.[15] Nevertheless, the test suffers from several limitations including, but not limited to, variation among the sensitivities of different aPTT reagents and susceptibility to factors that do not reflect intrinsic heparin activity.[5,8-9,15-20] Thus, patients may receive unnecessarily high or low heparin doses because of both physiologic and nonphysiologic influences on the aPTT. Although the anti-Xa heparin assay (HA) possesses its own limitations, it has demonstrated less variability and is not influenced by as many extraneous factors compared with the aPTT.[5,10,20,21] Anti-Xa HAs determine anticoagulant activity by measuring the ability of the heparin-antithrombin (AT) complex to inhibit activated coagulation factor X.[4] Since the anti-Xa HA measures the inhibition of a

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single enzyme, it is a more direct measure of UFH activity than the aPTT; consequently, it demonstrates less variability and exhibits minimal interference from the presence of biologic factors, such as lupus anticoagulants and elevated factor VIII, or simultaneous administration of oral anticoagulants.[4,5,9,14,22] Disadvantages of the anti-Xa HA are its relative expense and limited laboratory availability.[5,9]

Although randomized controlled trials comparing the aPTT test to the anti-Xa HA in a broad range of patients have yet to be reported, a study conducted by Levine et al. showed superiority of the anti-Xa HA in heparin-resistant patients, a population that requires more than 35,000 units of UFH per 24 hours to achieve therapeutic aPTT.[20] In the study, UFH was monitored by measuring either the anti-Xa HA or aPTT. The group monitored by anti-Xa HA, compared with the group monitored by aPTT, required significantly lower amounts of UFH, had a trend toward lower recurrent thromboembolic rates (4.6% vs 6.1% at 3 months) and incidence of major bleeding (1.5% vs 6.1%), but the differences did not reach statistical significance. Despite the documented advantages of the anti-Xa HA, most laboratories do not perform the test, citing the lack of clinical outcomes evidence and cost[8,16,23,24]; however, recent evidence suggests that the cost difference may be overestimated. A study evaluating the total costs associated with monitoring UFH concluded that the increase in dose changes and number of laboratory tests associated with aPTT-based monitoring negates the higher cost of the anti-Xa HA.[16]

In 2007, our institution made the decision to transition from aPTT to anti-Xa HA for monitoring intravenous UFH therapy, based on several factors. First, we encountered difficulty obtaining the aPTT reagent used at the time, and the alternative aPTT reagent had a large deviation from the previous therapeutic range of 60-90 seconds. Anti-Xa HA analysis performed using the new aPTT reagent showed that a therapeutic range of 75-105 seconds corresponded to a UFH concentration of approximately 0.3-0.7 units/mL. The dilemma of whether to use a new therapeutic aPTT range or start monitoring intravenous UFH using the anti-Xa HA was debated. Since our laboratory had recently acquired a coagulation analyzer that had the ability to perform a rapid anti-Xa HA, we decided to avoid the potential confusion of a new therapeutic aPTT range and convert to anti-Xa HA monitoring, using the STA-Rotachrom anti-Xa assay (Diagnostica Stago, Inc., Parsippany, NJ). Some of the anticipated benefits were improved anticoagulation and resource use secondary to a reduced need for laboratory monitoring, repeat bolus doses, and infusion rate changes.[9] The purpose of this study was to compare the performance of an aPTT-based protocol with an anti-Xa HA–based protocol for efficiency and safety of monitoring intravenous UFH infusions.

Methods

STUDY DESIGN

This was a single-center, observational cohort study conducted at an 852-bed academic medical center. The study involved a review of electronic and paper medical records of patients who received continuous intravenous UFH infusions, using the in-house standard UFH intravenous infusion protocol, between May 2005 and September 2009. All patients with standard UFH intravenous infusion protocol orders were identified through a query of the pharmacy information system; separate lower-dose protocols were available for patients considered at high-risk for bleeding and acute coronary syndrome indications, but those patients were not identified in the pharmacy query or included in this study. Of this population, 50 patients, before and after implementation of the anti-Xa testing, were selected through random number generation. The study protocol was reviewed and approved by the University of Florida Health Science Center Institutional Review Board, with waiver of informed consent.

PATIENTS

We categorized our cohort into 2 groups: patients who received intravenous UFH between May 1, 2005, and April 31, 2007 (aPTT group), and patients who received intravenous UFH between June 1, 2007, and September 1, 2009 (anti-Xa HA group). The first month of the new anti-Xa HA monitoring protocol, May 2007, was excluded from data collection to allow time for the nursing, laboratory, and medical staff to adjust to the new protocol.

Exclusion criteria included patient age younger than 18 or older than 89 years, UFH treatment for less than 24 hours, treatment interrupted for more than 10 hours, or inadequate compliance with protocol titration instructions. Inadequate protocol compliance was defined as deviation of more than 25% of the protocol elements during the total time of the patient's heparin treatment, (ie, failure to draw blood samples for laboratory tests within 1 hour of the indicated time, correctly adjust the heparin infusion rate, or administer the correct bolus dose when indicated).

PROTOCOLS

According to the standard UFH aPTT and anti-Xa HA protocols at our institution (Tables 1 and 2), an intravenous bolus dose (80 units/kg) was immediately followed by an initial infusion at a rate of 18 units/kg/h. All doses and rates were calculated based on total body weight (TBW), except for patients weighing more than 125 kg; adjusted body weight (ABW) was used in that population.[25] Monitoring tests were to be conducted at 6-hour intervals after initiation and subsequent rate adjustments until therapeutic anticoagulation was achieved. Our hospital's protocol defines therapeu-

tic anticoagulation as 2 consecutive laboratory test values within the therapeutic range. Thereafter, the monitoring frequency was changed to once daily. Because our hospital's protocol defines therapeutic anticoagulation as 2 consecutive laboratory test results within the therapeutic range, this definition of therapeutic anticoagulation was also used for our study. The anti-Xa HA can be performed with or without addition of exogenous AT.[4] During the study period, the tests were performed without excess AT, so the reaction relied upon existing AT in patient plasma. Both protocols were developed based on previously published weight-based heparin dosing nomograms and recommendations of clinical practice guidelines at the time of implementation.[2,8,14,26-31]

DATA COLLECTION AND OUTCOMES

We collected data on sex, age, height, TBW, ideal body weight (IBW) (calculated using the Devine method), ABW (IBW plus 40% of the difference between TBW and IBW), concomitant medications, creatinine clearance according to the Cockcroft-Gault formula, and whether the patient required an intensive care unit (ICU) admission during UFH treatment.[32,33] Heparin-specific data collected included the initial infusion rate, bolus doses, time and results of aPTT or anti-Xa HA tests, and time and dose of UFH infusion rate adjustments.

The primary outcome in this study was the time to achieve therapeutic anticoagulation. For this analysis, data were truncated at the time therapeutic anticoagulation was achieved or the first 96 hours of therapy, whichever came first. Times to therapeutic anticoagulation in the anti-Xa HA and aPTT groups were organized within a discrete time survival analysis framework into binomial events occurring within each of four 24-hour intervals after the initiation of treatment (0-24, 25-48, 49-72, and 73-96 hours).[34]

The principal secondary outcome was the percentage of monitoring test results below, within, and above the therapeutic range. These variables were collected to assess the ability of aPTT- and anti-Xa HA–based protocols to sustain laboratory values within the therapeutic range pre- and posttherapeutic anticoagulation. Unlike the primary outcome, this analysis was performed without truncation, so the aPTT and anti-Xa HA results were collected until therapeutic anticoagulation was achieved, even if it occurred after the first 96 hours of therapy.

Other secondary outcomes included the number of monitoring tests and heparin infusion rate adjustments per 24 hours averaged across the entire follow-up period of each patient, duration of treatment, length of stay, mortality related to bleeding or VTE, and major hemorrhage during UFH treatment. A major hemorrhage was defined as overt bleeding with at least 1 of the following: a drop in the hemoglobin level of at least 2.0 g/dL, transfusion of at least 2 units of blood, requirement of surgical intervention, or symptomatic intracranial hemorrhage.[27]

Table 1. aPTT Dosage Adjustment Protocol

aPTT (sec)	Bolus Dose (units/kg)	Stop Infusion (min)	Rate Change
Initial dose	80		18 units/kg/h (initial rate)
≤34	80		Increase by 4 units/kg/h
35-59	40		Increase by 2 units/kg/h
60-90	No		No change
91-110	No		Decrease by 1 unit/kg/h
111-212	No		Decrease by 2 units/kg/h
>212	No	60	Decrease by 3 units/kg/h

aPTT = activated partial thromboplastin time.

Table 2. Anti-Xa HA Dosage Adjustment Protocol

Anti-Xa HA (units/mL)	Bolus Dose (units/kg)	Stop Infusion (min)	Rate Change
Initial dose	80		18 units/kg/h (initial rate)
<0.2	80		Increase by 4 units/kg/h
0.2-0.29	40		Increase by 2 units/kg/h
0.3-0.7	No		No change
0.71-0.8	No		Decrease by 1 unit/kg/h
0.81-0.9	No	30	Decrease by 2 units/kg/h
>0.9	No	60	Decrease by 3 units/kg/h

Anti-Xa HA = antifactor Xa heparin assay.

STATISTICAL ANALYSIS

Data were entered and analyzed using Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA); statistical analysis was conducted with Statistics Calculator (Statpac, Inc., Minneapolis, MN) and SAS version 9.2 (SAS Institute Inc., Cary, NC). Comparisons were performed using unpaired Student *t*-test for continuous variables and χ^2 or Fisher exact test for categorical variables. For the time survival analysis, logistic regression was used to estimate, for each group, the hazard probabilities of achieving therapeutic anticoagulation during each time interval along with corresponding hazard odds ratios that compared the anti-Xa HA group to the aPTT group. Cumulative probabilities of achieving therapeutic anticoagulation by the end of each 24-hour interval were estimated from the hazard probabilities by applying the product-limit method.[35] A p value <0.05 was considered statistically significant.

Results

A total of 172 patients were screened to obtain 50 patients in the analysis for each group. The most prevalent reasons for

exclusion included heparin infusion for less than 24 hours and inadequate protocol compliance. Inadequate protocol compliance was the reason for exclusion in 13 of 40 patients excluded from the anti-Xa HA group and 9 of 32 patients excluded from the aPTT group. The sample included a high proportion of critically ill patients, as 20 (40%) of the 50 patients in both groups received UFH in the ICU. Patient demographics and baseline characteristics are summarized in Table 3. The 2 groups had similar demographic characteristics, but differences were observed in history of cardiomyopathy and concurrent clopidogrel use.

The primary and secondary outcomes of this study are summarized in Table 4. The mean time to achieve therapeutic anticoagulation was significantly less in the anti-Xa HA group compared with the aPTT group ($p < 0.0001$). Furthermore, a significantly greater percentage of patients achieved therapeutic anticoagulation at 24 hours (OR 3.5; 95% CI 1.5 to 8.7; $p < 0.01$) and 48 hours (OR 10.9; 95% CI 3.3 to 44.2; $p < 0.001$) in the anti-Xa HA group compared to the aPTT group (Figure 1). At the 72-hour interval, most patients had achieved therapeutic anticoagulation and the advantage of the anti-Xa HA protocol was no longer observed (OR 1.3; 95% CI 0.1 to 12; $p = 0.82$). Patients in the anti-Xa HA group also had more test values within the therapeutic range (66% vs 42%, $p < 0.0001$) and fewer subtherapeutic or supratherapeutic test values than the aPTT group (Figure 2). A significant difference was seen in the number of aPTT or anti-Xa HA tests performed per 24 hours ($p < 0.01$) and number of infusion rate

Table 3. Baseline Patient Characteristics

Variable	aPTT (n = 50)	Anti-Xa (n = 50)	p Value
Age, y, mean (SD)	58 (15)	56 (14)	0.47
Men, n (%)	27 (54)	31 (62)	0.54
Actual weight, kg, mean (SD)	84 (31)	88 (22)	0.47
Ideal weight, kg, mean (SD)	65 (11)	65 (11)	0.93
Height, inches, mean (SD)	68 (4.3)	67 (4.7)	0.85
Creatinine clearance, mL/min, mean (SD)	81 (53)	76 (50)	0.65
Concurrent drugs, n (%)			
aspirin	13 (26)	12 (24)	1
clopidogrel	0 (0)	8 (16)	<0.01
warfarin	37 (74)	33 (66)	0.51
Comorbidity, n (%)			
previous VTE[a]	16 (32)	22 (44)	0.30
antiphospholipid syndrome	1 (2)	3 (6)	0.61
atrial fibrillation	7 (14)	9 (18)	0.79
cardiomyopathy	3 (6)	13 (26)	0.01
chronic kidney disease	11 (22)	18 (36)	0.19
coronary artery disease	16 (32)	17 (34)	1
diabetes	11 (22)	13 (26)	0.81
dyslipidemia	12 (24)	11 (22)	1
heart failure	10 (20)	14 (28)	0.48
hypertension	26 (52)	31 (62)	0.42
prosthetic heart valve	6 (12)	5 (10)	1
Indication for UFH, n (%)			
LE DVT and/or PE (acute)	23 (46)	21 (42)	0.84
upper extremity DVT (acute)	8 (16)	6 (12)	0.77
bridging of chronic outpatient anticoagulation therapy	14 (28)	16 (32)	0.83
other or unknown	5 (10)	7 (14)	0.76

Anti-Xa = antifactor Xa; aPTT = activated partial thromboplastin time; DVT = deep vein thrombosis; LE = lower extremity; PE = pulmonary embolism; UFH = unfractionated heparin; VTE = venous thromboembolism.
[a]VTE is defined as any PE or upper/lower extremity DVT.

Table 4. Outcomes

Outcome	aPTT	Anti-Xa	p Value
Time to therapeutic anticoagulation (h), mean (SD)	48 (26)	28 (16)	<0.0001
Percent of tests within therapeutic range, mean (SD)	42 (20)	66 (18)	<0.0001
Monitoring tests performed/24 h, mean (SD)	2.8 (0.6)	2.5 (0.6)	<0.01
Infusion rate changes/24 h, mean (SD)	1.6 (0.7)	0.8 (0.5)	<0.0001
Major hemorrhage, n (%)	6 (12)	5 (10)	1
Length of stay (days)			
mean (SD)	25 (34)	17 (15)	0.13
median (IQR)	10 (7-23)	10 (6-23)	
VTE or bleeding-related mortality, n (%)	3 (6)	1 (2)	0.62

Anti-Xa = antifactor Xa; aPPT = activated partial thromboplastin time; IQR = interquartile range; VTE = venous thromboembolism.

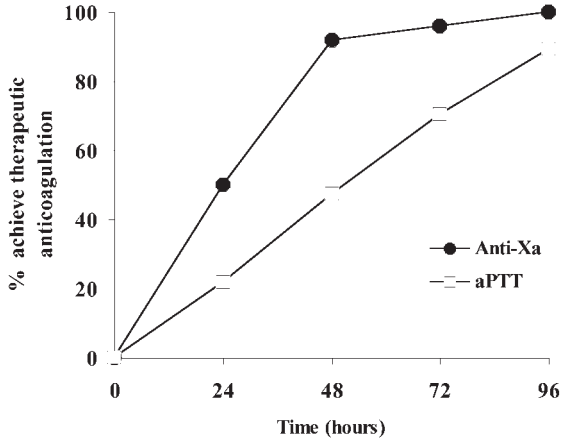

Figure 1. The cumulative percentage of patients who achieved therapeutic anticoagulation (2 consecutive therapeutic test values) for Anti-Xa and aPTT was 50% vs 22% at 24 hours (OR 3.5; 95% CI 1.5 to 8.7; $p < 0.01$), 92% vs 47% at 48 hours (OR 10.9; 95% CI 3.3 to 44.2; $p < 0.001$), 96% vs 71% at 72 hours (OR 1.3; 95% CI 0.1 to 12; $p = 0.82$), and 100% vs 89% at 96 hours. Anti-Xa = antifactor Xa; aPTT = activated partial thromboplastin time.

changes per 24 hours ($p < 0.0001$) between the 2 groups. Despite the increased exposure to clopidogrel in the anti-Xa HA group, there was no significant difference in the incidence of major hemorrhage. There were also no significant differences in death associated with bleeding or VTE, duration of therapy, or length of stay.

Discussion

To our knowledge, this is the first study to document that patients with anti-Xa HA–based protocols for UFH monitoring achieve therapeutic anticoagulation more rapidly compared to patients with aPTT-based protocols. The importance of achieving rapid therapeutic anticoagulation after a thrombotic event is well established in clinical trials.[28,36-41] For example, Hull et al. reported that failure to exceed an aPTT value of more than 1.5 times the control in the first 24 hours of UFH treatment was associated with a markedly increased risk of subsequent recurrent VTE (25% vs 2%, $p = 0.02$).[41] The current study found that the odds of reaching therapeutic anticoagulation at 24 hours are 3.5 times higher for anti-Xa HA patients than for aPTT patients, and at 48 hours the likelihood of achieving therapeutic anticoagulation increased to 10 times greater for anti-Xa HA patients. Therefore, it would be prudent to adopt a UFH protocol that achieves therapeutic anticoagulation more rapidly, especially in patients admitted to an ICU with acute pulmonary embolism.

Conflicting data exist about excessively prolonged aPTT and its effect on hemorrhagic risk; while some studies have shown an increased risk, others have not.[11,42-47] Given the ambiguity of aPTTs in this regard, sustained periods of surpassing the therapeutic range should be avoided.[27,48-50] This presents another advantage of anti-Xa HA–based monitoring of UFH. In this study, the anti-Xa HA demonstrated better sustainability of laboratory values within the therapeutic range, with the anti-Xa HA group experiencing fewer supratherapeutic test values than the aPTT group. Although the duration over which laboratory values were collected pre- and posttherapeutic anticoagulation varied among patients, the results provide evidence that aPTT-based protocols lead to greater fluctuation compared to anti-Xa HA–based protocols.

These concepts along with several other factors have resulted in an increasing number of hospitals transitioning to anti-Xa HA–based monitoring, despite the lack of clinical outcomes data.[6,9,15,51] One contributing factor to the shift toward the anti-Xa HA is the notion that patients with anti-Xa HA monitoring needed fewer infusion rate changes and monitoring tests than patients with aPTT monitoring, resulting in a decrease in resource use (laboratory monitoring, repeat bolus doses, and infusion changes).[16] This finding has been confirmed in the current study. Importantly, besides potential cost savings, the decreased need to adjust infusion rates might also improve patient safety by decreasing the chance for titration errors. Another contributing factor to the increased popularity of the anti-Xa HA is that the aPTT is merely a surrogate marker for UFH activity that must be defined based on heparin concentrations by anti-Xa analysis, but it displays a poor and imprecise correlation.[6,9,14,42]

Although low-molecular-weight heparins are often used as first-line treatment for acute VTE, and direct factor Xa and thrombin inhibitors have recently been developed, UFH is still used in many clinical circumstances. The introduction of the novel agents generated excitement and anticipation, but they are not without drawbacks. For example, data regarding their use in the prevention and treatment of VTE and cost-effectiveness analyses are limited, and their long-term effects remain largely unknown.[52,53] Given the uncertainty about the role of the new molecular agents, UFH remains a first-line treatment option for many indications, and development of monitoring methods more precise than the aPTT remains critical.[2] Recognizing difficulties of standardizing and establishing an appropriate therapeutic range for the aPTT, it may be logical to avoid the risk of inaccuracy by using the anti-Xa HA, since it measures heparin concentrations with less variability.[9,16,54]

There are a number of limitations to the current study. A power calculation was not performed prior to beginning data collection. The decision to include 50 patients in each arm was based on feasibility of data collection and analysis within the time frame that was allowed for the project. Despite this, a significant difference was found between the 2 groups for the primary endpoint. Although no significant dif-

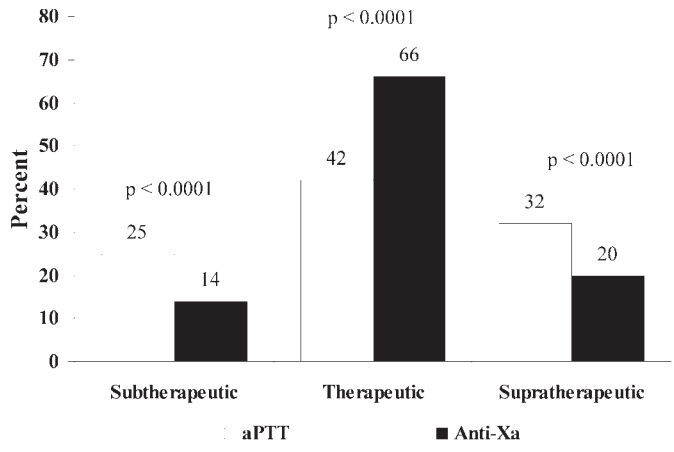

Figure 2. The percent of total laboratory values in the subtherapeutic, therapeutic, or supratherapeutic ranges during the study period. The percentage of aPTT and Anti-Xa values in each range was determined by dividing the number of values in the respective range by the total number of tests across all 3 categories. Anti-Xa = antifactor Xa; aPTT = activated partial thromboplastin time.

ferences in major bleeding, length of stay, or mortality secondary to VTE or major bleeding between the 2 groups were proven, we acknowledge that this study was insufficiently powered to detect any significant differences with respect to these parameters. Because the study was performed at a single center, this may limit the application of its results to other institutions. Also, as a retrospective observational study that was conducted over a 4-year period, other unknown factors could have influenced the results, and important data could have been missing from patient records. Additionally, bias could have been introduced if there were differences in illness severity between the 2 groups that were not captured through data collection. However, because of similar baseline characteristics between the groups, we expect limited risk for bias. Increased exposure to clopidogrel in the anti-Xa HA group could have resulted in an increased bleeding risk, which was not substantiated in the descriptive analysis.

It is noteworthy that 31% of excluded patients from both arms were not included because of noncompliance with 25% or more of the protocol elements. These patients were excluded because evaluation of the protocol effectiveness using either type of laboratory test is not possible if the protocol is not followed the majority of the time. Compliance with 75% of the protocol elements was chosen as a practical measure, since in our experience, 100% protocol compliance does not routinely occur in clinical practice.

In conclusion, monitoring intravenous UFH infusions with the anti-Xa HA compared to aPTT results in a more expeditious achievement of therapeutic anticoagulation, longer maintenance of therapeutic levels, and fewer laboratory tests and heparin dosage changes. Our results provide additional support for the growing sentiment that the anti-Xa HA is a superior test for monitoring UFH. On the basis of these data, it seems that the anti-Xa HA should be considered in place of the aPTT for monitoring intravenous UFH. However, a large, multicenter randomized trial is needed to further answer this question and before recommending anti-Xa HA–based monitoring globally.

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Tiempo de Activación Parcial de Tromboplastina Contra el Ensayo de Antifactor Xa de Heparina en el Monitoreo de Heparina no Fraccionada Administrada por Infusión Intravenosa Continua

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EXTRACTO

TRASFONDO: Heparina no fraccionada (UFH, por sus siglas en inglés) ha sido usada clínicamente por las pasadas cinco décadas. A pesar de ser una piedra angular en anticoagulación, UFH está limitada por su perfil farmacocinético impredecible, lo que hace necesario monitoreo de cerca. Los 2 métodos más comunes de monitoreo de UFH son tiempo de activación parcial de tromboplastina (aPTT) y el ensayo del antifactor Xa de heparina (anti-Xa HA), pero ambos ensayos presentan desafíos y el método óptimo para monitorear UFH no está claro.

OBJETIVO: Comparar el funcionamiento de aPTT con anti-Xa HA para eficiencia y seguridad en el monitoreo de infusiones intravenosas de UFH.

MÉTODOS: Estudio retrospectivo, cohorte por observación llevado a cabo en un centro médico académico de 852 camas.

RESULTADOS: Cien pacientes recibiendo UFH intravenosa para una variedad de indicaciones fueron incluidos en el estudio. El tiempo para alcanzar anticoagulación terapéutica fue significativamente menor en el grupo anti-Xa HA comparado con el grupo aPTT (28 h ± 16 h vs 52 h ± 38 h, $p < 0.001$). Además, un porcentaje mayor de pacientes del grupo anti-Xa HA comparado a pacientes del grupo aPTT alcanzaron

anticoagulación terapéutica a las 24 horas (OR 3.5; 95% CI 1.5 y 8.7) y 48 horas (OR 10.9; 95% CI 3.3 y 44.2). Los pacientes en el grupo anti-Xa HA tuvieron más valores de las pruebas dentro del rango terapéutico (62% vs 44%, $p < 0.0001$). Una diferencia significativa fue observada entre los dos grupos en el número de pruebas aPTT o anti-Xa HA llevado a cabo por 24 horas ($p < 0.0001$) y el número de cambios en la razón de infusión en 24 horas ($p < 0.0001$), ambos favoreciendo al grupo anti-Xa HA.

CONCLUSIONES: Monitorear infusiones intravenosas de UFH con anti-Xa HA cuando se compara a aPTT permite alcanzar anticoagulación terapéutica más rápido, mantiene los valores dentro del rango deseado por más tiempo, y requiere menos ajustes en dosis y menos repetición de pruebas.

Traducido por Sonia I Lugo

Mesure de l'Activité Anticoagulante par le Temps de Thromboplastine Partielle Activée ou par la Mesure de l'Activité Anti-Facteur Xa lors du Suivi de la Perfusion Intraveineuse Continue d'Héparine non Fractionnée

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RÉSUMÉ

HISTORIQUE: L'héparine non fractionnée (HNF) est utilisée en clinique depuis une cinquantaine d'années. Malgré le fait que ce médicament est la pierre angulaire de l'anticoagulothérapie, son utilisation est limitée par son profil pharmacocinétique imprévisible, ce qui exige un suivi serré par des tests de laboratoire. Les 2 méthodes les plus utilisées pour assurer le suivi de l'héparine non fractionnée sont le temps de thromboplastine partielle activée (TTPA) et la mesure de l'activité anti-facteur Xa (anti-Xa), mais ces 2 méthodes présentent des difficultés et la méthode optimale demeure à préciser.

OBJECTIF: Comparer la performance du TTPA et de l'anti-facteur Xa en termes d'efficience et d'innocuité pour le suivi de la perfusion continue d'héparine non fractionnée.

MÉTHODOLOGIE: Une étude observationnelle de suivi de cohorte rétrospective a été faite dans un seul centre hospitalier universitaire de 852 lits.

RÉSULTATS: Cent patients qui ont reçu de l'HNF intraveineuse pour diverses indications ont été inclus dans cette étude. Le temps requis pour atteindre le niveau d'anticoagulation thérapeutique était significativement moindre dans le groupe anti-Xa comparativement au groupe TTPA (28 h ± 16 h vs 52 h ± 38h, $p < 0.001$). De plus, un plus grand pourcentage de patients dans le groupe anti-Xa ont atteint un niveau d'anticoagulation thérapeutique à 24 heures comparativement au groupe TTPA (rapport de cote 3.5; IC 95% 1.5 à 8.7) et 48 heures (rapport de cote 10.9; IC 95% 3.3 à 44.2). Les patients du groupe anti-Xa ont aussi eu plus de résultats de laboratoire dans l'intervalle thérapeutique (62% vs 44%, $p < 0.0001$). Une différence significative a été observée entre les 2 groupes dans le nombre de tests à faire en 24 heures ($p < 0.0001$) et dans le nombre de changements de débit de la perfusion par 24 heures ($p < 0.0001$), en faveur du groupe anti-Xa.

CONCLUSIONS: Le suivi de la perfusion continue d'héparine non fractionnée par la mesure de l'activité anti-facteur Xa, lorsque comparée au temps de thromboplastine partielle activée, permet d'atteindre un niveau d'anticoagulation thérapeutique pour un plus grand pourcentage du temps et nécessite moins d'ajustements de la dose et moins de tests de laboratoire.

Traduit par Denyse Demers