Prolonged activated partial thromboplastin time without coagulopathy in peritoneal dialysis☆

Tiempo parcial de tromboplastina activado prolongado sin coagulopatía subyacente en diálisis peritoneal

Dear Editor,

The activated partial thromboplastin time (aPTT) is the time required for fibrin to appear after mixing plasma with substitutes for platelet phospholipids. It is used as screening for alteration in the intrinsic and common coagulation pathways, to monitor treatment with heparin sodium and to determine the presence of lupus anticoagulant.[1,2]

Coagulation abnormalities are often due to pre-analysis anomalies[3] or incorrect sample collection. Moreover, aPTT is prolonged with deficiency of the coagulation factors involved, with lupus anticoagulant or in heparin therapy.

We present the cases of two patients on peritoneal dialysis (PD) (cases 1 and 2) who, on the day they were called to receive a kidney transplant, were found to have prolongation of aPTT. In both patients, four repeat coagulation tests were similar (Table 1). Possible interference was ruled out, as well as poor sample extraction. After assessment by haematology, two vials of prothrombin complex and one bag of fresh frozen plasma were administered, with no change in the intrinsic pathway values, so they were rejected for kidney transplantation. Reviewing the patients from our unit, we found that cases 3 and 4 had the same problem. All the cases were male, aged from 53 to 69, on continuous ambulatory PD with a nocturnal exchange of Extraneal. Patient 2 was being treated with acenocoumarol and received vitamin K to reverse its effect; the rest of the patients had no previous history or medication that interfered with coagulation.

After exhaustive study, coagulation abnormalities inherent to each patient were ruled out (Table 1). The coagulation study was performed with a Sysmex CS-5100 automated coagulation analyser, with Pathromtin® SL as reagent. When the reagent was changed to Actin® FS (Siemens, Marburg, Germany), the aPTT returned to normal. Samples from the affected patients had been saved, verifying the normality of the intrinsic pathway with the new reagent.

In the cases presented, there was interference from the laboratory reagent causing the false lengthening of the aPTT. It is interesting the fact that we have found several cases, all of them in PD patients. After studying 70 haemodialysis patients and 80 patients with chronic kidney disease (CKD) stages G3b, 4 and 5, we found no patients on haemodialysis or with CKD with the same interference.

Patients on PD with icodextrin are known to be subject to laboratory interferences: there may be falsely elevated blood glucose readings[4] and measured plasma amylase levels decrease.[5] However, to date, no interference with coagulation tests has been reported.

The only common factor found in our series is continuous ambulatory PD and treatment with icodextrin, although it is true that not all patients with icodextrin have had the same interference.

Reagents for measuring aPTT are composed of an activator and phospholipids (of synthetic or animal origin). The sensitivity and specificity for aPTT reagents to heparin and coagulation factors vary depending on their origin, their properties and the total concentration of phospholipids, even if the same activator is used.[6,7] The reagents used by our laboratory are differentiated according to the surface activator they use: silicon dioxide (Pathromtin® SL) or ellagic acid (Dade Actin® FS). They have a strong correlation coefficient, but comparability is low.[8] Our hypothesis is that the metabolites of icodextrin can competitively interfere in the binding of silicon dioxide surface activator, preventing the correct reading of the aPTT.

We would like to inform all nephrologists of this situation, as the laboratory interference had significant repercussions: cases 1 and 2 could not have a kidney transplant until the complete coagulation study was performed.

Nephrologists therefore need to be aware that a prolonged aPTT may indicate the existence of a bleeding disorder, be associated with an increased risk of thrombosis (due to lupus anticoagulant) or lack any thrombotic or haemorrhagic implications (in patients with PD it may be the result of interference with the laboratory reagent).

DOI of original article:
https://doi.org/10.1016/j.nefro.2018.07.006.

☆ Please cite this article as: Santos García A, Millán del Valle I, Cruzado Vega L, Ruiz Ferrús R, Tordera Fuentes D, Sabater Belmar A, et al. Tiempo parcial de tromboplastina activado prolongado sin coagulopatía subyacente en diálisis peritoneal. Nefrologia. 2019;39:210–211.

Table 1 – Coagulation study performed with Sysmex CS-5100 automated analyser, with Pathromtin® reagent.

	Case 1	Case 2	Case 3	Case 4	Normal range
aPTT; s	90.3	64.3	86.6	71.3	25–38
aPTT; ratio	2.91	2.07	2.89	2.38	0.5–1.2
Prothrombin time; s	13.7	15.7	12.5	11.8	
Quick ratio; %	79	61	83	100	70–100
INR	1.1	1.3	1.1	1	1–1.3
Clotting factors; %					
Factor II	84.6	NA	99	110	70–120
Factor V	155.9		184	118	70–120
Factor VII	197.1		185	166	55–170
Factor VIII	285.0		315	314	60–150
Factor IX	241.9		182	219	60–150
Factor X	121.5		115	118	70–120
Factor XI	186.3		118	210	60–150
Factor XII	127.3		171	171	60–150
Von Willebrand factor; %					
Activity	249.7	NA	349	192	40–150
Antigen	271.2		482	178	45–150
Platelet function; s					
Collagen/adrenaline	101	NA	170	150	85–165
Collagen/ADP	71		104	129	71–118

ADP: adenosine diphosphate; aPTT: activated partial thromboplastin time; INR: international normalised ratio; NA: not available.

REFERENCES

1. Schmaier AH. Contact activation: a revision. Thromb Haemost. 1997;78:101–7.
2. Langdell RD, Wagner RH, Brinkhous KM. Effect of antihemophilic factor on one-stage clotting tests; a presumptive test for hemophilia and a simple one-stage antihemophilic factor assay procedure. J Lab Clin Med. 1953;41:637–47.
3. Adcock DM, Kressing DC, Marlar RA. Minimum specimen volume requirements for routine coagulation testing: dependence on citrate concentration. Am J Clin Pathol. 1998;109:595–9.
4. Plum J, Gentile S, Verger C, Brunkhorst R, Bahner U, Faller B, et al. Efficacy and safety of a 7.5% icodextrin peritoneal dialysis solution in patients treated with automated peritoneal dialysis. Am J Kidney Dis. 2002;39:862–71.
5. Wang R, Skoufos L, Martis L. Glucose monitoring for diabetic patients using icodextrin. Perit Dial Int. 2004;24:296–7.
6. Kitchen S, Cartwright I, Woods TA, Jennings I, Preston FE. Lipid compostion of seven APTT reagents in relation to heparin sensitivity. Br J Haematol. 1999;106:801–8.
7. Denis-Magdelaine A, Flahaultb A, Verdya E. Sensivity of sixteen APTT reagents for the presence of lupus anticoagulants. Haemostasis. 1995;25:98–105.
8. Derek L, Zivkovic M, Hasperger D, Juricek J, Romic Z. Comparability of Pathromtin SL, Dade Actin FS i STA Cephascreen reagents for activated partial thromboplastin time measurement. Biochem Med. 2009;18:81–7.

Alba Santos García[a,*], Isabel Millán del Valle[a], Leonidas Cruzado Vega[a], Rosalía Ruiz Ferrús[a], Diana Tordera Fuentes[a], Alejandra Sabater Belmar[a], Romina Valenciano Moreno[a], Angela Mompel Sanjuan[b]

[a] *Servicio de Nefrología, Hospital General Universitario de Elche, Elche, Alicante, Spain*
[b] *Servicio de Hematología, Hospital General Universitario de Elche, Elche, Alicante, Spain*

[*] *Corresponding author.*
E-mail address: albasantosgarcia@gmail.com (A. Santos García).

https://doi.org/10.1016/j.nefroe.2019.03.004

Skin reactions with the use of icodextrin in peritoneal dialysis patients☆

Reacciones cutáneas debido al uso de icodextrina en pacientes en diálisis peritoneal

Dear Editor,

Icodextrin is a starch-derived glucose polymer which is metabolised into maltose. Its use in peritoneal dialysis (PD) has been an alternative to glucose as an osmotic agent, obtaining greater ultrafiltration (UF) for long dwells.

DOI of original article: https://doi.org/10.1016/j.nefro.2018.07.002.
☆ Please cite this article as: Vizcaino Castillo B, Beltrán Catalán S, Molina Vila P, Gonzalez Moya M, Noguera-Morel L, Pallardó Mateu LM. Reacciones cutáneas debido al uso de icodextrina en pacientes en diálisis peritoneal. Nefrologia. 2019;39:211–213.