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## RESEARCH ARTICLE

### EFFECTIVENESS OF TEST OF TROMBOELASTOGRAFIA AGAINST GLOBAL COAGULATION TESTS AS A GUIDE IN TREATMENT OF PATIENTS WITH CHRONIC HEPATIC OR RENAL INSUFICIENCIA SHOWING AN EPISODE OF "HEMORRHAGE"

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Transfusion Associated Circulatory Overload; TRALI;  
Transfusion-Related Acute Lung Injury  
IHC: Chronic Hepatic Insuficiencia;  
ERC: Chronic Renal Disease;  
TEG®: Tromboelastograma.  
Global Coagulation Tests:  
(TP, TTP, INR, Bleeding Time, Fibrinogen and Platelet Count).

#### ABSTRACT

**Background:** Mortality from hemorrhage in renal failure and liver, chronic units critical is 40% and the deleterious effects related to transfusion are high, the decision to transfuse should be selected, methods of interpretation of coagulation go global test methods like tromboelastograma, however what is most effective for guiding a better decision making?

**Method:** A study was conducted in patients with bleeding in the Naval General Hospital of high specialty of the city of Mexico with diagnostic Insuficiencia hepatic or Renal chronic who were randomized into two arms, one global test of coagulation and the other the tromboelastograma, for both hemoglobin goal was more than 7 grams/dl and venous saturation greater than 65%, during resuscitation was assessed the occurrence of lung injury and circulatory overload transfusion as well as presence of thrombosis-associated.

**Results:** 31 patients who met the screening criteria were included where TEG® when compared with global testing showed reduction of transfusion in the treatment of hemorrhage (1. 71± 1.2 vs 3.41 ± 3.04, P: 0.04) without complications (p < 0.05)

**Conclusion:** TEG® is effective to reduce the use of procedures and thereby reduce complications and mortality.

#### INTRODUCTION

Coagulation courses three processes, one of platelets and endothelium-dependent primary and secondary which depends on coagulation factors and finally the system of fibrinolysis, which removes excess clots and the proper relationship of them promotes correction of a bleeding episode, this makes being a complex system to understand, but in 1964 of Davie and Ratnoff (RG, 1964) they postulated coagulation cascade from a via intrinsic and extrinsic mutually exclusive that initiated a phase of contact, and this demonstrated it in the laboratory, however over time found that there were still some nooks and crannies for clarifying that live out of lab diseases behave differently, such as hemophilia that lack of Factor VIII or IX generates dysfunction of a single via, the "intrinsic" (Marshall, 2014) (Kitchens, 2013), then what the extrinsic pathway not supplements this deficiency if there is two-way?, also applies to something more common like the chronic renal insuficiencia generated platelet dysfunction by impairment of exposure

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factor of von willebrand of Weibel - Palade by uremia (Fishbane, 2016) bodies (Andrássy, 2015) (M, 2012) where it is also noted that the increase of sialic acid by its low clearance rate generates its adherence to Fibrinogen and subsequent disfrinogenemia (school G, 2005), another similar situation is observed in the liver insuficiencia that currently it is known that a liver disease have higher risk of thrombosis than bleeding (D'Amico G, 2006) (L.Kujovich, 2015), since the hemostasis system not only have descent of procoagulant factors but also natural anticoagulants as Antithrombin III, protein C and S, this generates a strategic rebalancing of coagulation (Tripodi, 2011) and although in the static tests such as prothrombin time indicate otherwise there is increased tendency to thrombosis (Valerie L. Ng, 2009), is why the 2001 Dr. Monroe and Dr. Hoffman (DM, 2001) showed that in vivo coagulation starts on the cell surface after the exposure of the tissue factor This was the development of methods of interpretation of hemostasis, and so we go from static tests such as PT, APTT, time of bleeding, platelet count and Fibrinogen, which are useful in the theory of Davie and Ratnoff but insufficient for the cell theory where testing dynamics as the tromboelastograma TEG® they object in real time to the three stages of hemostasis and this has been validated in multiple settings as in the obstetrician (Collis

RE 2015) (Cerneca F, 1997), surgical (Spiess BD, 1987), Sepsis (Fritz & Kresler Ulf, 2009) (S, 2013), cardiac surgery (Thai J, 2011) and liver (Cerutti, 2004) (Ferguson JW, 2008), prevention of thrombosis in hospitalized patients with use of heparin (JD 2008), patient polytraumatized (Carroll, 2009) and more recently in critically ill patients in intensive care (Halset, 2015) in a study carried out in Norway in June, 2012 to September 2013 in patients without hemorrhage or factors known trombofilicos was observed approximately 73% had a TEG® profile of hypercoagulability reflected by a high value of AM while the global tests showed normal or even need for transfusion, this is probably because a the severe inflammatory state that they were doing, and if this happen to them, also happens in patients with chronic organ dysfunction as the renal or liver basal way show complex alterations , and under stress as an episode of bleeding event alterations would be even more drastic, so were interested in this issue and we have a cohort of patients with these diseases aleatorizandolos into two arms, one global test-driven and the other by the tromboelastograma.

## MATERIALS AND METHODS

A study of comparative efficacy of the use of diagnostic tests of coagulation in patients IMSS users high Naval General Hospital and military specialty, 1 you inclusion criteria were people older 18 years of age with a diagnosis of chronic liver failure, or chronic renal failure showed that have presented an acute event of haemorrhage and have been its inclusion and management with the signing of a consent under information, agreement and were excluded those with any Hemostatic dyscrasia known or active by any disease anticoagulant treatment , and were eliminated during the course of the study those who have not decided to continue as part of this study either submitted death prior to obtaining results of tromboelastografia or global coagulation tests.

The primary objective of it was reducing transfusions, complications and mortality at 90 days in patients with CKD or IHC, and as secondary objectives was to determine the incidence of hospital readmission in the use of one or another therapy, the incidence of adverse reactions associated with the transfusion as a TACO or TRALI and thrombosis at 48 hours after resuscitation strategy and as well as number of procedures blood products or agents Hemostatic agent used in either strategy. The hypothesis was that the use of the tromboelastografia would reduce the appearance of complications and mortality using smaller transfusions compared to the global tests. In this way all patients with a bleeding episode, is randomized at random into two groups, group one (n: 17) revived based on global coagulation tests (TP, TTP, bleeding time, Fibrinogen, platelet count), and group two (N: 14) with the tromboelastograma decision making to maintain a hemoglobin above 7 grams/dl and a venous saturation above 65% according to the (Mark E. Brecher AABB guidelines 2013) made each arm test to demarcate the need for use of procedures such as platelets, plasma fresh frozen, crioprecipitados, blood derivatives as factor VII activated prothrombin complex or concentrated Fibrinogen, as well as the use of Hemostatic agents as ethamsylate, Aminocaproic acid, was assessed during resuscitation the occurrence of TRALI (injury pulmonary acute associated with Transfusion for its acronym in English) and TACO (associated circulatory overload transfusion) as well as the occurrence of

venous thrombosis deep vein and pelvic members porta via ultrasound doppler 48 hours, as well as the need for readmission and mortality at 90 days.

## RESULTS

We studied 31 patients, 51.6% (16) carrier of IHC and rest with IRC, with an average age of 65. 23±13. 79 years (range of 37 to 89 years), no difference ( $p = 0.33$ ) in relation to pathology, the 54.8% (17) of the entire universe of study were women, without associated with any type of pathology ( $p = 0.10$ ), 60% (9/15) men had IRC while the 68.8% (11/16) of the women presented IHC. From a global point of view, the 54.8% (17) of the patients was treated with clotting and the rest with tromboelastografia tests.

The clinicopathological factors of patients in relation to the type of treatment used (tromboelastografia versus coagulation tests) are shown in table 1. We found that the tromboelastografia in relation to the main objective proved to be more effective in comparison with tests of coagulation in patients with CKD and IHC in the treatment of hemorrhage, because based on his information was possible employment of fewer packages of transfusions and therefore significant absence of complications ( $p < 0.05$ ), in addition to these results, can also be mentioned that patients treated with tromboelastografia had a lower mortality compared with patients treated with clotting tests, however, this difference was not significant ( $p > 0.05$ ). These results are shown in the table 2. Table 3 shows the relationship between the frequency of mortality of the patients and their underlying pathology. Mortality was more frequent in the IHC, however, this relationship was not significant ( $p > 0.05$ ). Table 4 shows the relationship between the different types of complications and their underlying pathology, thrombosis was common in both diagnoses, however, this relationship was not significant ( $p > 0.05$ ). Table 5 shows the comparison of the number of packages of employees in relation to the type of Pathology procedures; You can see that patients with IHC required twice, being this significant difference ( $p < 0.05$ ). Within the secondary objectives, relationship between the re-entry of the patients and their underlying pathology, re-entry into the 90 days was similar in both diagnoses, with a non-significant relationship ( $p > 0.05$ ), this is shown in table 6.

## DISCUSSION

The present study shows similarity to that found by (Linda Shore-Lesserson, 1999) to show that the use of tromboelastograma involves fewer transfusion of blood components when compared with a traditional therapy based on routine laboratory tests, another study (Cerutti, 2004) study the hepatic coagulopathy in 10 patients undergoing right hepatectomy for (THDV) living donor liver transplantation, all performed screening of complete coagulation before operation, coagulation profile was evaluated by the count of platelets, PT, APTT, INR, and TEG at the beginning and at the end of the surgery, and in the 1st 3, 5, and 10 after operation, donors will give them prophylactic anticoagulation post surgery with heparin low molecular weight (LMWH), without showing preoperative evidence of a prothrombotic State in all cases, the TEG was normal in the beginning of surgery and in the postoperative period despite the decrease in platelet level,

**Table 1. Clinicopathological factors of patients in relation to the type of treatment used (tromboelastografia versus coagulation tests)**

	TREATMENT		
	Tromboelastografia (n = 14)	Coagulation tests (n = 17)	P
Male sex	59% (7)	41.2% (7)	0.62
Age (years)	63.5 ± 11	66.65 ± 15.92	0.52
Pathology IRC	50% (7)	47.1% (8)	0.87
IHC	50% (7)	52.9% (9)	
Hypothermia	14.3% (2)	0	0.19
Replacement therapy	28.6% (2)	62.5% (5)	0.21
Time of diagnosis (years)	7.36 ± 3.77	8.65 ± 3.39	0.32

IRC = Chronic Renal insufficiency, IHC = chronic liver failure

**Table 2. Comparison of the efficacy of the Tromboelastografia versus global coagulation in patients with IRC and IHC tests**

	Treatment		
	Tromboelastografia (n = 14)	Coagulation tests (n = 17)	P
Mortality Yes	7.1% (1)	11.8% (2)	0.57
No. HC packages	1.71 ± 1.2	3.41 ± 3.04	0.04 *
Reentry	35.71% (5)	35.3% (6)	0.51
<b>COMPLICATIONS</b>			
TRALI	0	5.9% (1)	0.003 *
TACO	0	5.9% (1)	
Other types of thrombosis	0	52.9% (9)	
No	100% (14)	35.3% (6)	

IRC = Renal Failure chronic, IHC = chronic liver failure, = HC = procedures, TRALI, TACO =, \* statistical significance.

**Table 3. Frequency of mortality in relation to the type of pathology**

P = 0.52		Underlying pathology			Total
		Chronic Renal Failure	Chronic liver failure		
Mortality	Yes	1 6.7%	2 12.5%	3 9.7%	
	No	14 93.3%	14 87.5%	28 90.3%	
Total		15 100.0%	16 100.0%	31 100.0%	

**Table 4. Frequency of different types of complications in relation to the type of pathology**

Complications		Underlying pathology		Total
		Chronic Renal Failure	Chronic liver failure	
TRALI	0 .0%	1 6.3%	1 3.2%	
	0 .0%	1 6.3%	1 3.2%	
	4 26.7%	5 31.3%	9 29.0%	
	11 73.3%	9 56.3%	20 64.5%	
Total		15 100.0%	16 100.0%	31 100.0%

**Table 5. Averages of packages of different procedures used as treatment to the patients, taking into account the type of pathology**

P = 0.009		Underlying pathology	N	Media	Deflection tip.	Error tip. of the average
No. procedures packages	Chronic Renal Failure		15	1.47	1.302	.336
	Chronic liver failure		16	3.75	2.887	.722

**Table 6. Frequency of reentry in relation to the type of pathology**

P = 0.45		Underlying pathology			Total
		Chronic Renal Failure	Chronic liver failure		
Reentry	28 days	0 0.0%	1 6.3%	1 3.2%	
	90 days	4 26.7%	6 37.5%	10 32.3%	
	No re-entry	11 73.3%	9 56.3%	20 64.5%	
Total		15 100.0%	16 100.0%	31 100.0%	

increase in the PT-INR, and the normal values of the APTT, however TEG showed the progressive development of hypercoagulability in 4 subjects at days 5 and 6 to day 10, as well as a donor with doubt of hypercoagulability in TEG on day 5, who underwent deep vein thrombosis (DVT) in the 8th, which was resolved with the therapeutic dose of LMWH, so even though routine tests that suggest hypercoagulability and LMWH prophylaxis, TEG follow-up showed the unexpected emergence of hypercoagulability in most subjects after hepatectomy for THDV monitoring TEG could be useful in the perioperative management of donors to guide treatment antitrombosis and increase security, as in our study TEG showed trends of hypercoagulability and thus braking job of Hemostatic agents or procedures that could reinvigorate hypercoagulability, as we saw it more pronounced in the group where only used global coagulation tests where there was a higher incidence of thrombosis.

On the other hand in patients in ICU where the variability of critical patients show variabilities in TEG® in 73% and not in comparison with tests of coagulation (Halset, 2015), which was a study in Norway, in the period of June 2012 to September 2013, showing a MA and high G suggesting hypercoagulability in patients in the ICU without bleeding or known factors. By what finds like these must be taken into account when interpreting the observations obtained in TEG® in patients of critics because of thrombosis complications raise the morbidity of patients, as we saw in our study population.

## Conclusion

Found that TEG in relation to the main objective to compare to the global coagulation tests showed reduction in the need for transfusion in patients with IRC and IHC, in the treatment of hemorrhage, since required fewer procedures packages ( $1.71 \pm 1.2$  vs  $3.41 \pm 3.04$ , with a 0.04 P) with statistical significance, being understood that procedures to the Globular packages Center, concentrated platelet, plasma, fresh frozen and crioprecipitados and not showed no complications ( $p < 0.05$ ) and compared with the strategy of global coagulation tests with the presence of 1 case of TRALI was) (5.9%), TACO in 1 case (5.9%) and the presence of thrombosis was in 9 cases (52.9%), 4 in patients with IRC (26.7%) and 5 in IHC (31.3%), in the IRC group which was a case of pulmonary thromboembolism gender an ominous outcome and I evidencio through the analysis of necropsy, other cases of thrombosis were minimal and is associated with patients with ERC hemodialysis catheter thrombosis which only there was need for removal and repositioning of the catheter, for IHC thrombosis cases were associated to the greatest extent in cases of deep venous thrombosis in lower pelvic limbs which only attended with phlebitis and sign of Homans, Olow of physical examination and to carry out survey with USG doppler evidence of subocclusively venous thrombosis which required only observation and follow-up. In addition to these findings, also is worth mentioning that, tromboelastografia-treated patients had a lower mortality 7.1% (1) vs. 11.8% (2) with a 0.57 q: compared with patients treated with clotting tests, however, this difference was not significant ( $p > 0.05$ ). In relation to the incidence of hospital readmission in the use of one or another therapy to 90 days was prevalent in both diagnoses, however, this relationship was not significant ( $p > 0.05$ ).

The incidence of TRALI was 5.9% only 1 case like the TACO, being these two cases in the Group of global coagulation tests where the number in the number of employees in relation to the type of Pathology procedures; It was found that patients with IHC required twice, being this significant difference ( $p < 0.05$ ) and from a global point of view, the 54.8% (17) of the patients was treated with clotting and the rest with tromboelastografia tests.

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