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RESEARCH ARTICLE

PLATELET MAPPING IN PATIENTS WITH HIP FRACTURE AND CHRONIC INGESTION OF ANTIAGGREGANTS THAT REQUIRE SURGICAL TREATMENT

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ABSTRACT

Background: There are currently a large number of elderly patients with hip fracture who require surgical treatment; However, it can be delayed by the intake of antiaggregants, which justifies the present study to avoid delaying the definitive treatment and thus reduce the associated morbidity and mortality.
Objective: To establish the behavior of platelet mapping in patients with chronic intake of antiaggregants that have required surgical treatment for hip fracture.
Methods: 51 patients were included in the HOSGEAES from 2015 to 2016. They were divided into three groups: A. Acetylsalicylic acid (n = 22), B. Clopidogrel (n = 22) and C. Dual therapy (n = 7). The universal variables were recorded, coagulation tests result of platelet mapping and percentage of inhibition. The analysis of variance was applied to compare three or more means, Chi square or Fisher's exact test. The data were processed with the SPSS 17 package, $p < 0.05$ was taken as statistical significance.
Results The abnormal platelet mapping rate was 62.7% vs 37.3% normal. The most unfavorable antiaggregant was dual therapy, 54.5% in those taking acetylsalicylic acid ($p = 0.02$). The presence of Arterial Hypertension was significantly associated with normal platelet mapping ($p = 0.01$); In the stratified analysis, it was observed that 100% of the patients in group C had SAH and abnormal platelet mapping compared to 55% in group B and 44.4% in those in group A ($p = 0.03$).
Conclusions 19 patients (37.3%) resulted with normal platelet mapping, 10 patients belong to group A (19.7%), 9 patients (17.7%) to group B; therefore, they can be operated on for the hip fracture without further delaying the procedure. The combination of acetylsalicylic acid with clopidogrel (group C) should be carefully evaluated since it alters platelet mapping in 100% of cases. The presence of Arterial Hypertension is an important covariate associated to both the mapping alteration and the combined use of both drugs.

INTRODUCTION

It is increasingly common that patients and especially elderly patients receive treatment with antiaggregant, drugs that increase the risk of bleeding complications related to surgery (Dos Santos, 2015 and Hoogendijk, 2016). On the other hand, the temporary suppression of antithrombotic therapy can cause episodes of thromboembolism. Both circumstances must be taken into account when performing any pre-anesthetic assessment (Gerber, 2013; Lovato, 2015 and Gretchen, 2004). In any case, the need to suspend or not to suspend these treatments and the way to do it should be individualized in each case, depending on the risk factors of thromboembolism and bleeding of the patient, as well as its general clinical condition. The most widely used antiaggregant is acetylsalicylic acid (AA).

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It irreversibly inhibits cyclooxygenase in platelets, so its effect lasts as long as platelets, usually 7-10 days (Van Rensburg, 2006; Manning, 2004; Dickinson, 1998 and Horlocker, 2011). It has been documented an increase in the risk of perioperative bleeding and in transfusion needs in patients undergoing major surgery who have taken AA in the 7 days prior to surgery. However, this is not clear nor the actual clinical repercussion of this effect in terms of morbidity and mortality, it is advisable to suspend the AA 7 days before major surgery. However, it is estimated that less than one in ten patients who undergo a major surgery intervention while receiving ASA treatment have some complication in the form of bleeding (Carrillo, 2012 and Yende, 2001). Clopidogrel acts by inhibiting platelet adenosine diphosphate (ADP) receptors irreversible form, so that its effect lasts 7-10 days. This is associated with an increase in postoperative bleeding in patients undergoing major surgery, although there is less experience in this regard with regard to AA. Although it is possible that its antiaggregant effect is superior to that of AA,

there are currently recommendations based on controlled clinical trials regarding its management in the perioperative period (Urwin, 2000 and Manning, 2004). Platelet mapping is a modification of standard thromboelastography, which measures the percentage of platelet aggregation in the presence of ADP or AA, which helps us to evaluate the therapeutic inhibitory effect of clopidogrel or acetylsalicylic acid respectively. It is formed for typical traces. Two traces are performed simultaneously: one is heparinized blood treated with activator F and measures the contribution of fibrin to the maximum amplitude (internal trace); the second traces are heparinized whole blood with the activator F and the agonist (middle trace). These are compared to the traces of kaolin heparinase (external trace). For the interpretation of the results, a response to the drug was defined as an inhibition greater than 50% MA, a partial response as an inhibition of 30-50% and a lack of response as inhibition of less than 30% (Tantry, 2005; Weitzel, 2012; Lenk, 2012; Craft, 2004 and Alstrom, 2006).

RESULTS

Fifty-one patients with hip fracture who consumed some type of platelet antiaggregant were recruited; of which 27 (52.9%) corresponded to the female gender and 24 (47.1%) to the masculine gender. The average age was 72.3 years with a standard deviation of 7.0 (range 65-93 years). Of the 51 patients 22 (43.1%) ingested acetylsalicylic acid, another 22 (43.1%) clopidogrel and 7 (13.7%) had dual therapy with both drugs. Platelet mapping was normal in 19 patients (37.3%) with an average inhibition percentage of 30.0 +/- 7.9% while the abnormality rate was 62.7% with an average inhibition percentage of 84.5 +/- 6.0% (p = 0.0001) Figure 1. The descriptive results of conventional coagulation tests plus percentage inhibition results are shown in Table 1. Almost half of the patients (49.0%) had prescribed a drug and only 15.7% had received previous transfusions. 60.8% of the patients were ASA II and 39.2% ASA III.

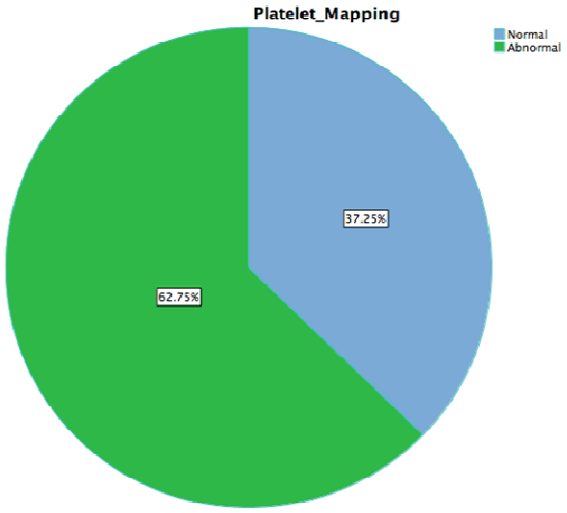

Figure 1. Outcome of platelet mapping in patients with hip fracture and chronic platelet antiaggregant intake

Table 1.

	Minimum	Maximum	Half	Typical deviation
Platelet count	127000	418000	243470.59	71768.894
Partial thromboplastin time´s	10.4	19.0	13.578	1.6231
Thrombin time's	23.90	41.30	29.3839	3.25795
International normalized ratio	.92	1.72	1.0905	.14133
Inhibition percentage	16.00	96.00	64.2510	27.47684

Figure 2. Prevalence of comorbidities in patients with hip fracture and chronic intake of platelet antiaggregants

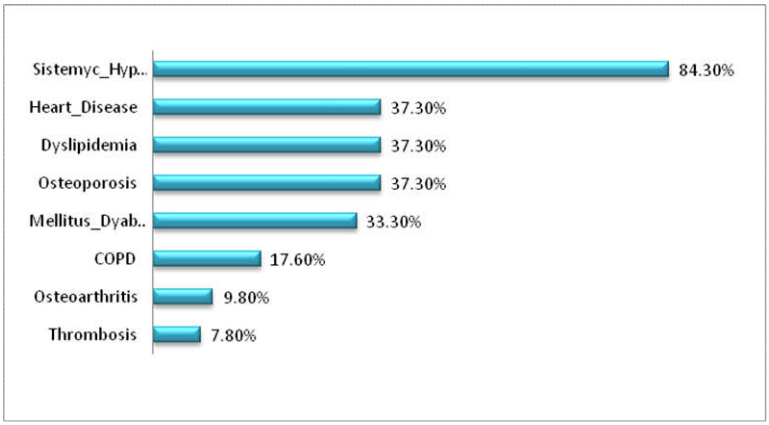

Figure 2. Prevalence of comorbidities in patients with hip fracture and chronic intake of platelet antiaggregants

As observed (Figure 3), 84.3% had Arterial Hypertension followed by 54.9% with heart disease; the lowest rate of comorbidity corresponded to thrombosis in only 7.8% of the cases.

Bivariate analysis

As can be seen (Table 2) with the exception of ischemic heart disease (p = 0.08), in the other variables noted the differences between the antiaggregant treatment groups were statistically significant; Note especially the differential result of platelet mapping since 54.5% of patients who consumed aspirin had an abnormal result versus 59.1% of those who consumed clopidogrel and 100% of those who had dual therapy (both drugs) (p = 0.02). This last group had means of thromboplastin time, thrombin time and percentage of inhibition significantly higher than those of the other two treatment groups.

Hypertension in contrast to the total patients with abnormal mapping 75% had Arterial Hypertension (Table 3).

Multivariate analysis

Through multivariate analysis of variance, it was observed that, independently of the platelet antiaggregant that they were consuming, patients with Arterial Hypertension invariably have a lower average number of platelets (p = 0.01), as can be clearly seen in Figure 3. However, through the stratified analysis it can be observed (Table 4) that, in the first place, regardless of the type of antiaggregant, the few cases (n = 8) without Arterial Hypertension had an abnormal mapping; however, in the stratum that suffers from Arterial Hypertension, the percentages of abnormal mapping were 44.4% for those who consumed acetylsalicylic acid, 55.0% for clopidogrel and 100% for dual therapy (p = 0.03).

Table 2. Laboratory tests, associated comorbidities and platelet mapping results according to the type of platelet antiaggregant treatment in patients with hip fracture

Associated variables	Antiaggregant			P
	Acetylsalicylic acid (n = 22)	Clopidogrel (n = 22)	Dual therapy (n = 7)	
Age	72.1 +/- 6.9	72.7 +/- 7.2	71.5 +/- 7.9	0.94 Anova
Abnormal platelet mapping	12 (54.5%)	13 (59.1%)	7 (100.0%)	0.02 Chi^2
Partial thromboplastin time´s	14.0 +/- 1.1	12.7 +/- 1.4	14.6 +/- 2.4	0.006 Anova
International normalized ratio	1.06 +/- 0.07	1.06 +/- 0.10	1.24 +/- 0.26	0.004 Anova
Inhibition percentage	60.4 +/- 27.0	59.9 +/- 28.4	89.7 +/- 4.8	0.02 Anova
Previous transfusions	4 (18.2%)	2 (9.1%)	2 (28.6%)	0.43 Chi^2
Medication prescription	12 (54.5%)	9 (40.9%)	4 (57.1%)	0.59 Chi^2
ASA II	13 (59.1%)	16 (72.7%)	2 (28.6%)	0.11 Chi^2
Mellitus Diabetes	5 (22.7%)	8 (36.4%)	4 (57.1%)	0.23 Chi^2
Arterial Hypertension	18 (81.8%)	20 (90.9%)	5 (71.4%)	0.43 Chi^2
Dyslipidemia	7 (31.8%)	7 (31.8%)	5 (71.4%)	0.14 Chi^2
Ischemic Cardiopathy	9 (32.1%)	13 (46.4%)	6 (21.4%)	0.08 Chi^2
COPD	3 (13.6%)	6 (27.3%)	0 (0.0%)	0.12 Chi^2
Osteoarthritis	1 (4.5%)	3 (13.6%)	1 (14.5%)	0.51 Chi^2
Thrombosis	3 (13.6%)	1 (4.5%)	0 (0.0%)	0.30 Chi^2
Osteoporosis	11 (50.0%)	6 (27.3%)	2 (28.6%)	0.26 Chi^2

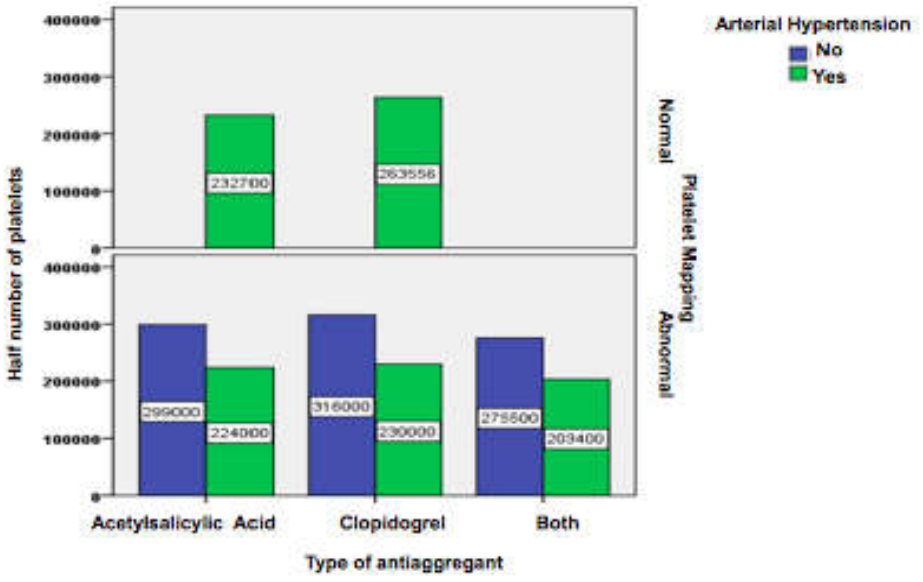

Figure 3. Average number of platelets according to type of platelet antiaggregant and presence or absence of Arterial Hypertension in patients with hip fracture

Platelet mapping was only significantly associated with the presence or absence of Arterial Hypertension (p = 0.017 Fisher's exact test) in the sense that the total number of patients that resulted with normal platelet mapping had Arterial

Finally, through the same procedure above, it is now observed that in the case of the presence or absence of heart disease, the abnormal mapping rates according to the type of antiaggregant were almost significantly different in the stratum of positive to heart disease with 66.7% for acetylsalicylic acid, 61.5% for

clopidogrel and 100% again for dual therapy users (p = 0.09) as noted in Table 5.

According to frequency of Platelet Mapping Result we can realize that 37.3% of patients may be within normal, therefore,

Table 3. Association between platelet mapping results and Arterial Hypertension in patients with hip fracture and chronic platelet antiaggregant ingestion

		Platelet mapping		Total
Arterial Hypertension		Normal	Abnormal	
	No	0	8	8
		0%	25.0%	15.7%
	Yes	19	24	43
		100.0%	75.0%	84.3%
Total		19	32	51
		100.0%	100.0%	100.0%

Table 4. Percentages of abnormal platelet mapping according to antiaggregant consumed and Arterial Hypertension stratum in patients with hip fracture

Arterial Hypertension	Platelet mapping	Platelet Antiaggregant			P
		Acetylsalicylic Acid	Clopidogrel	Dual Therapy	
Yes	Abnormal	8 (44.4%)	11 (55.0%)	5 (100.0%)	0.03*
	Normal	10 (55.6%)	9 (45.0%)	0 (0.0%)	
No	Abnormal	4 (100.0%)	2 (100.0%)	2 (100.0%)	----
	Normal	0	0	0	

Table 5. Percentages of abnormal platelet mapping according to antiaggregant consumed and stratum of Ischemic Cardiopathy in patients with hip fracture

Ischemic Cardiopathy	Platelet mapping	Antiaggregant Platelet			P
		Acetylsalicylic acid	Clopidogrel	Dual therapy	
Yes	Abnormal	6 (66.7%)	8 (61.5%)	6 (100.0%)	0.09*
	Normal	3 (33.3%)	3 (38.5%)	0 (0.0%)	
No	Abnormal	6 (46.2%)	5 (55.6%)	1 (100.0%)	0.46
	Normal	7 (53.8%)	4 (44.4%)	0 (0.0%)	

DISCUSSION

The incidence of patients suffering from a hip fracture is increasing, with consequences for the patient, health services and socioeconomic status. The majorities of these patients are fragile and have a series of associated medical conditions such as Arterial Hypertension, ischemic heart disease, osteoporosis; this leads to a treatment with antiaggregant such as acetylsalicylic acid and / or clopidogrel. Both act as irreversible platelet inhibitors. They also have a synergistic effect when used in combination, causing an increase in bleeding time for which guidelines have been developed to regulate management according to the medication, although it has been shown that the bleeding time is poorly correlated with surgical bleeding, This can give us an indication of the hemorrhagic potential during surgery. In orthopedic surgery in particular, the majority of bleeding is often from the bone in which direct hemostasis is difficult to achieve. This can have significant consequences in the typical elderly patient with a hip fracture that has little cardiovascular reserve and is less able to compensate for acute blood loss. Platelet mapping measures platelet function and shows the level of platelet inhibition, but also its thrombotic or hemorrhagic risk, evaluating the effect of the different antiaggregant administered.

Our study of fifty-one patients showed that thromboplastin time, international normalization index, percentage of inhibition and abnormal platelet mapping result had significant differences, in turn also that all patients with normal mapping result had Arterial Hypertension but only 75 % of Abnormal mapping had it; in Ischemic Heart Disease we are in the bordeline with regard to Abnormal Platelet Mapping results. we conclude that patients taking Clopidogrel or Acetylsalicylic Acid should be Mapping Platelet and according to results can be operated as soon as circumstances allow to reduce morbidity and mortality and ensure a more favorable surgical result. In a study where 462 were analyzed with hip fractures that were being treated with inhibitors of platelet aggregation, how many of these patients suffered from platelet function disorders, measured by the PFA-100, was measured. Thaler et al. Demonstrated that patients treated with acetylsalicylic acid, surgery should not be delayed and patients with clopidogrel can be operated on 3 days after stopping the medication without increasing the risk of bleeding (Haubelt, 2005). Moran et al contemplate the consequence of pre-operative delay after a hip fracture in an integrated manner. In this prospective observational study of 2660 patients who underwent surgical fixation of hip fracture at a University Hospital, it showed total overall mortality in 30 days of 9%, with a mortality of 8.7% in those operated without delay. This figure increased significantly to 10.7%, with a relative risk of 2.25 in those patients whose surgery had been delayed for more than four days (Thaler, 2009).

Lefaivre retrospectively reviewed 27 patients who took clopidogrel at the time of hip fracture and found that mortality increased as the delay in surgery approached 8 days, although this was not statistically significant (Lefaivre, 2009). Maheshwari et al. Reviewed the intentional delay to surgery due to the concomitant treatment with Clopidogrel; using a multiple regression analysis model and based on previous work, showed that the delay to surgery of 8.4 days was associated with an increased risk of medical complications and the intentional surgical delay is the only significant predictor of mortality in a year (Maheshwari, 2011).

Conclusions

Of the 51 patients studied 19 (37.3%) were normal 10 who consumed acetylsalicylic acid, 9 clopidogrel and none with dual therapy. Consequently, these 19 patients with normal mapping could be programmed for surgical intervention for hip fracture without delaying surgical treatment, which, as has been demonstrated by other studies, the greater the delay the greater post-surgical morbidity and mortality. None of the sociodemographic variables was associated with the type of antiaggregant used or the result of platelet mapping; however, the presence of Arterial Hypertension is a factor significantly associated with the increase in Mapping abnormality rate especially when both antiaggregant are used. The combination of acetylsalicylic acid with clopidogrel should be carefully evaluated since it alters platelet mapping in 100% of the cases and also the results of conventional coagulation tests. Acetylsalicylic acid and clopidogrel were used in the same proportions (43.1% respectively) and to a lesser extent their simultaneous combination (13.7%).

Declarations

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Conflict of interest: None declared.

Ethical approval: The Ethics and Local Research Committee approved The present study.

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