Artigo / Article

Platelet count and mean volume (MPV) in association with plasma HCO_3^- in regular hemodialysis patients

Parâmetros hematológicos associados ao HC0 $_3$ - plasmático de pacientes em hemodiálise

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*End-stage renal failure often is associated with abnormal bleeding that may represent an important complication of this disorder. The hemorrhagic tendency currently is attributed to altered primary hemostasis, mainly platelet dysfunction. The aim of the present study was to elucidate whether and how in patients, with uremia on hemodialysis, the level of plasma HCO_3^- affects the mean PLT volume (MPV) and count. The total patients were 36 (f=15, m=21). The mean patients' age was 46 (±16) years. The mean length of the time patients had received hemodialysis was 32 (±36) months. The mean PLT count was 165 (±70) [x10³µ/L]. The mean MPV was 9 (±1) fl. The mean plasma HCO_3^- was 20 (±2.6) mEq/L. In this study a significant inverse correlation of PLT count with MPV and a significant positive association of PLT count with plasma HCO_3 and also a significant inverse correlation of MPV with plasma HCO_3^- were found. Positive association of mild relative acidemia with PLT count and its negative correlation with MPV may further support the reverse epidemiology of serum bicarbonate in end-stage renal disease patients on hemodialysis which needs more attention as a protective role in mild relative acidosis of regular hemodialysis patients. Rev. bras. hematol. hemoter. 2006;**28**(2):127-130.*

Key words: *Platelet count; hemodialysis; end-stage renal failure; mean platelet volume (MPV); plasma HCO_3^-.*

Introduction

The renal elimination of nonvolatile acids, mainly formed by oxidation of sulfuric amino acids, is about 70 mmol/day. In hemodialysis (HD) patients cannot eliminate the excess of H^+ via the kidneys.[1] Metabolic acidosis is associated with chronic renal failure (CRF). Often, maintenance dialysis therapies are not able to reverse this condition. The major systemic consequences of chronic metabolic acidosis are increased protein catabolism, decreased protein synthesis, and a negative protein balance that improves after bicarbonate supplementation.[2] Patients with end-stage renal disease suffer from complex hemostatic disorders. Uremic patients show a bleeding diathesis that is mainly due to abnormalities of primary hemostasis.[3,4] The increased bleeding tendency of chronic renal failure patients has been attributed to platelet dysfunction.[3-5] The most common abnormalities are defective platelet aggregation, decreased platelet adhesiveness, decreased availability of platelet factor-3, and prolongation of the bleeding time.[6] Some of the pathophysiologic mechanisms which have been implicated include platelet inhibition by plasma metabolites,

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e.g., urea, guanidinosuccinic acid, phenolic acid; increased vessel wall prostacyclin; abnormal platelet arachidonic acid metabolism and increased levels of parathyroid hormone.[6] Recently, an index related to platelet count has been provided by hematologic analyzers. Concerning the platelet parameter, the mean platelet volume (MPV) has been described.[7] Platelet volume is a marker and possibly a determinant of platelet function in that large platelets are more active than normal sized platelets. Mean platelet volume (MPV), a measure of platelet size, reflects changes in either the level of platelet stimulation or the rate of platelet production.[8] Increased mean platelet volume may reflect increased platelet activation or increased numbers of large, hyperaggregable platelets, and is accepted as an independent coronary risk factor.[9] Mean platelet volume could also be an independent risk factor for myocardial infarction in the general population and also CHD in hemodialysis (HD) patients.[10,11] Regarding the present data, studies concerning the association of relative acidosis of maintenance hemodialysis and plasma HCO_3^- level with MPV and platelet count in HD patients are quiet scarce. Therefore, the aim of the present study was to elucidate whether and how, in patients with uremia on hemodialysis, the level of plasma HCO_3^- affects the mean PLT volume and count.

Patients and Methods

Patients

This cross-sectional study was conducted on patients with end-stage renal disease (ESRD), who were undergoing maintenance hemodialysis treatment with acetate based dialysate and polysulfone membranes. The study was carried out in the hemodialysis section of Hajar Medical educational & Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord, Iran. According to the severity of secondary hyperparathyroidism, each patient being treated for secondary hyperparathyroidism was given oral active vitamin D3 (Calcitriol; Rocaltrol) (Roche Hexagon; Roche Laboratories Inc, New Jersey, USA), calcium carbonate capsules, and Rena-Gel (sevelamer; Genzyme Europe B.V.; United Kingdom/Ireland) tablets at various doses. According to the severity of anemia, patients were prescribed intravenous iron therapy with iron Sucrose (Venofer - International Inc. St. Gallen Switzerland) at various doses after each dialysis session. All patients received treatments of 6 mg folic acid daily, 500 mg Acetyl- L-Carnitine (Jarrow Formulas, Inc™ Los Angeles, CA) daily, oral vitamin B-complex tablets daily, and 2,000 U intravenous Eprex (recombinant human erythropoietin [Rhuepo] [Janssen-Cilag; Cilag - AG International 6300 Zug, Switzerland) after each dialysis session. Exclusion criteria were active or chronic infection and use of NSAID or ACE inhibitor drugs and also the use of other drugs that have adverse effects on platelet production or function.

Laboratory methods

Blood samples were collected after overnight fasting from patients, complete blood count containing WBC count, hemoglobin (Hgb), hematocrit (Hct), platelet (PLT) count and also Mean Platelet Volume (MPV) (Ref. Range 7.5 - 11.5 fl) were measured using a Sysmex-KX-21N cell counter (Sysmex Corporation; Mundelein, Illinois, Sysmex America, Inc.). Levels of serum iron, ferritin, C-reactive protein (CRP), calcium (Ca), and also serum albumin (Alb) were measured using standard kits. serum ferritin was measured by radioimmunoassay (RIA). Plasma HCO_3^- was measured by arterial blood gas. Duration and dosages of hemodialysis treatment were calculated from the patients' records. The duration of each hemodialysis session was 4 hours. For the efficacy of hemodialysis the urea reduction rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data.

Statistical analysis

Results are expressed as means ± SD. Statistical correlations were assessed using the partial correlation test. All statistical analyses were performed using SPSS (SPSS Inc, Chicago, IL; version 11.5.00). Statistical significance was determined at a *p*-value lower than 0.05.

Results

The total patients were 36 (f=15, m=21). Table 1 summarized patients' data. The mean patients' age was 46 (±16) years. The mean length of time patients had received hemodialysis was 32 (±36) months. The mean PLT count was 165 (±70) [$x10^3\mu/l$]. The mean MPV was 9 (±1) fl. The mean plasma HCO_3^- was 20 (±2.6) mEq/l. In this study a significant inverse correlation of PLT count with MPV (r= -0.54, p = 0.001) (adjusted for age) was seen. A significant positive association of PLT count with plasma HCO3$^-$ (r= -0.40, p = 0.048) (adjusted for age, duration and doses of dialysis, WBC count, Hgb, serum Ca, CRP, Alb, iron and ferritin) and a significant inverse correlation of MPV with plasma HCO_3^- (r= -0.37, p = 0.050; Figure 1) (adjusted for age, duration and doses of dialysis, WBC count, serum Ca, Alb, iron and ferritin) were seen too.

Discussion

In this study we found a significant inverse correlation of PLT count with MPV. A significant positive association of PLT count with plasma HCO_3 and a significant inverse correlation of MPV with plasma HCO_3^- were also found. The greatest role in the development of haemostatic disturbances in patients with chronic renal failure (CRF) is ascribed to the platelets. Although the platelet parameter, the mean platelet volume has been routinely available to clinicians for some time, its role in the diagnosis and

Table 1
Mean ±SD, minimum and maximum of age, duration and doses of hemodialysis and also laboratory results of patients

Total patients = 36	Minimum	Maximum	Mean
Age years	16	80	46±16
DH* months	2	156	32±36
Dialysis dose sessions	36	1584	294±393
URR%	39	76	59±9
Creat mg/dl	3	18	9±3
BUN mg/dl	30	180	82±33
Ca mg/dl	5	10	7.6±0.9
Iron micg/dl	10	1515	350±454
Alb g/dl	2.4	4.8	3.8±0.5
PLT count [x10³u/l]	264	396	165±70
MPV fl	7	11	9±1
Ferritin ng/dl	35	1250	518±299
CRP mg/l	3	40	8.7±6.6
Hgb g/dl	5	13	9±2
HCT%	14	40	28±6
WBC count cells/mm³	1000	11200	5600±2000
HCO_3^- mEq/l	14	25	20±2.5

*Duration of hemodialysis treatment

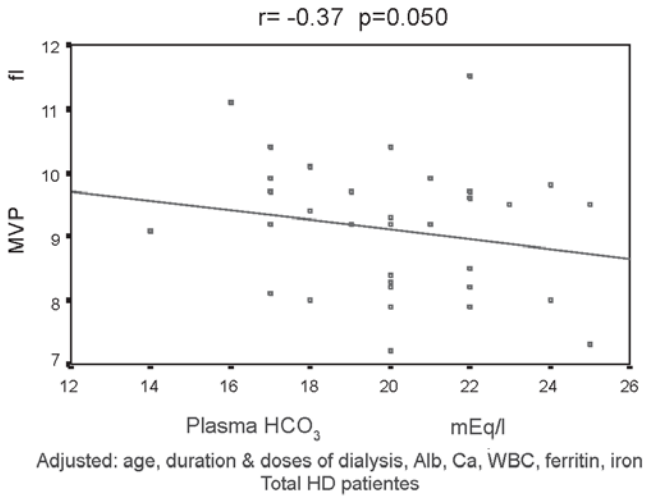

Figure 1. Significant inverse correlation of MPV with plasma HCO_3^-

management of patients remains unclear. While factors affect PLT count and volume during hemodialysis is under investigation, it is believed that platelet activation and aggregation, and coagulative activation are the earliest and most important phenomena that occur after contact between blood and artificial membranes.[12] Mean platelet volume is a physiological variable of hemostatic importance.[13] Large platelets are more reactive, produce more prothrombotic factors[13-15] and aggregate more easily. They also contain more dense granules and release more serotonin and ß-thromboglobulin than small platelets do.[15-17] Platelets have no nuclei and their characteristics are determined by their progenitor cell, the bone marrow megakaryocyte. It is generally accepted that platelet volume and density are determined at thrombopoiesis and that, once in the circulation, platelets do not change in size.[17-19] The mechanisms controlling platelet production are obscure, although it has been suggested that both MPV and platelet counts are under independent hormonal control,[19-22] however larger platelets are more reactive.[22,23] The inverse association of PLT counts and MPV which was shown in our study was also shown in the studies conducted by Bancroft and Lamparelli *et al*.[22-24] Lamparelli showed an inverse correlation between platelet volume and platelet number in 564 normal subjects and 297 pregnant women.[24] Available data suggest that metabolic acidosis is both catabolic and anti-anabolic.[2] In contrast to the metabolic studies, many epidemiologic studies in maintenance dialysis patients have indicated a paradoxically inverse association between mildly decreased serum bicarbonate and improved markers of protein-energy nutritional state. Hence metabolic acidosis may be considered as yet another element of the reverse epidemiology in ESRD patients. Interventional studies have yielded inconsistent results in CKD and ESRD patients, although in peritoneal dialysis patients, mitigating acidemia appears to more consistently improve nutritional status and reduce hospitalizations.[25] In this study, the positive association of mild relative academia with PLT count and its negative correlation with MPV may further support the reverse epidemiology of serum bicarbonate in ESRD patients on hemodialysis. To our knowledge this is the first study, concerning the association on plasma HCO_3^- with PLT count and MPV. Our conclusion is that more attention is required for hemodialysis patients.

Resumo

O estágio terminal de suficiência renal freqüentemente está associado a sangramentos anormais e que representam complicações importantes na evolução desta moléstia. A tendência hemorrágica é atribuída a alterações primárias de hemostasia, decorrentes principalmente da disfunção plaquetária. O objetivo deste estudo foi o de elucidar quando como pacientes urêmicos, em hemodiálise o nível de HCO_3 afeta a contagem plaquetária e o seu volume médio. O número de pacientes estudados foi 36 (fem.15, masc. = 21). A idade foi de 46 ± 16 anos. A contagem média das plaquetas foi de 165(± 70) x $10^3\mu$/l, o volume médio foi de 9 (± 1) fl. O HCO_3 plasmático médio foi de 20 (± 2,6) mEq/l. No estudo foi observada uma correlação inversa entre a contagem plaquetária e o volume médio associado com associação positiva significante das plaquetas com o HCO_3 do plasma e também correlação sig-

*nificativa inversa do volume médio plaquetário e HCO_3 plasma. A associação positiva e sua correlação negativa com o volume médio plaquetário podem sugerir reversão da epidemiologia do estágio terminal de insuficiência renal de pacientes em hemodiálise que necessitam de maior proteção quando da acidose leve em vigência de hemodiálise. Rev. bras. hematol. hemoter. 2006;**28**(2):127-130.*

Palavras-chave: *Plaquetas; hemodiálise; insuficiência renal; volume médio plaquetário; HCO_3^- plasmático.*

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