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ACID-BASE STATUS OF PREVALENT PERITONEAL DIALYSIS PATIENTS : RDPLF DATA

Statut acido-basique des patients prévalents en dialyse peritoneale

Données du RDPLF

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Résumé

Le statut acido-basique des patients en dialyse péritonéale est influencé par de multiples facteurs. L'acidose métabolique est une anomalie fréquente dans l'insuffisance rénale chronique et le traitement dialytique permet d'apporter des substances alcalines permettant le maintien d'une balance acide-base normale. Le présent travail rapporte la prévalence des troubles acido-basiques chez les patients en dialyse péritonéale et leurs associations avec les paramètres cliniques et biologiques. Il s'agit d'une étude rétrospective transversale ayant inclus l'ensemble des patients en DP enregistrés dans la base de données du RDPLF. Une acidose métabolique est retrouvée chez 20,4% des patients alors que 27,8% des patients présentaient une alcalose métabolique. Il existe une relation significative entre l'âge, l'apport protidique estimé par le nPNA et le taux de la réserve alcaline plaidant en faveur de l'influence des apports alimentaires dans le maintien d'une acidose métabolique. Une fonction rénale résiduelle faible est associée à une plus faible probabilité d'être en alcalose métabolique. Les résultats de cette étude pourraient permettre un choix individualisé du tampon du dialysat dans le but d'obtenir en permanence un statut acido-basique stable chez les patients en dialyse péritonéale.

Mots clés : acidose, dialyse péritonéale, statut acido-basique, RDPLF

Abstract

Acid-base status of patients on peritoneal dialysis is influenced by multiple factors. Metabolic acidosis is a common feature of chronic renal failure and dialysis treatment provides alkali in the dialysate in order to maintain a normal acid-base balance. This paper reports the prevalence of acid-base disorders in peritoneal dialysis patients and their associations with clinical and laboratory parameters. This is a cross-sectional retrospective study that included all PD patients registered in the RDPLF database. Metabolic acidosis was found in 20.4% of patients while 27.8% of patients had metabolic alkalosis. There is a significant relationship between age, protein intake estimated by nPNA and the level of alkaline reserve pleading in favor of the influence of dietary intakes in the maintenance of metabolic acidosis. Low residual renal function is associated with a lower probability of being in metabolic alkalosis. These results could allow an individual choice of the dialysate buffer in order to permanently obtain stable acid-base status in patients on peritoneal dialysis.

Keywords : acidosis, peritoneal dialysis, acid-base status, RDPLF

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INTRODUCTION

Maintaining a normal serum bicarbonate and blood pH level requires daily intake of alkalis that have been consumed in the process of neutralizing the acidic ions produced by the body's metabolic processes. In patients with normal renal function, the alkaline stock is regenerated from the removal of acidic ions by the kidney in the form of ammonia and titratable acidity. In patients with renal impairment, the alkaline stock is made by dialysis solutions containing bicarbonates or metabolic precursors of this anion such as lactate or acetate.

A decrease in serum bicarbonate concentration considered as a metabolic acidosis is quite common in chronic renal failure and is associated with deleterious metabolic effects such as hypercatabolism responsible for undernutrition, chronic inflammation, bone involvement, and endocrine functions (1). Also, acidosis is one of the cardinal manifestations of chronic renal failure : its correction is an obvious goal in dialysis treatment.

The purpose of this study is to investigate the determinants of acid-fast status in patients with chronic renal failure treated with peritoneal dialysis (PD) and whose clinical and laboratory parameters are recorded in the French Language Peritoneal Dialysis Registry (RDPLF) database.

MATERIALS AND METHODS

The RDPLF data base is includes a general exhaustive module, and several optional modules : a nutrition module is one of these optional. In order to meet the objective, we conducted a cross-sectional study based on RDPLF data (general module and nutrition module). We included in this study all the patients treated with PD who had at least one biological check-up recorded in the RDPLF nutrition module between January 2000 and February 2015. For each patient included, only the last record of the period was kept. . We included socio-demographic data (age at the time of the assessment, sex), clinical data (lean body mass, BMI, nephropathy, residual diuresis), and data on peritoneal dialysis (PD fluid protein loss, PD treatment duration, phosphorus chelator used) as well as biological data (venous alkaline reserve, albuminemia, aPNA).

The definition of acid-base status was based on the alkaline reserve, thus considering: a metabolic acidosis is defined as an alkaline reserve less than 22 mmol / L, the acid-base balance was considered normal with a alkaline reserve between 22 and 27 mmol / L and metabolic alkalosis was defined for an alkaline reserve greater than 27 mmol / L. The primary endpoint of the study was the value of aPNA measured in g / kg / 24h.

Given the presence of a large number of missing data, we carried out multiple imputation (10 iterations) with an assignment of a plausible value to each missing data and the results are collected to obtain a robust estimate of each parameter of the nutrition module. After a descriptive analysis of the data, bivariate analyzes were conducted to select candidate variables for the multivariate model. A multivariate logistic regression conducted on each of the imputed datasets was constructed to estimate the association between clinical and laboratory parameters and patients' acid-base status.

Table I: Patient Description

	N = 2043					
Characteristic	**MV[1]**	**%[1]**	**M[2]**	**S.D.[2]**	**n[2]**	**%[2]**
Age (years)	0	0,0%	66,6	17,4		
Sex	0	0,0%				
woman					842	41,2%
Lean body mass (kg)	9	0,4%	38,9	13,0		
Body Mass index (kg/m²)	5	0,2%				
< 18,5					101	4,9%
[18,5 ; 25 [					917	44,9%
[25 ; 30[					692	33,9%
≥ 30					328	16,1%
Nephropathy	0	0,0%				
Interstitial					337	16,5%
Diabetic					377	18,5%
Glomerular					378	18,5%
Vascular					653	32,0%
Other					70	3,4%
Unknown					228	11,2%
Residual Diuresis (L)	0	0,0%				
≤ 0,5					773	37,8%
]0,5 ; 1]					526	25,7%
> 1					744	36,4%

[1] VM = Number of patients with one missing value ; % = percentage of total patients.
[2] M = mean ; S.D. = Standard deviation ; n = number of patients ; % = percentage of total patients.

RESULTS

Two thousand and forty-three patients were studied. The average age was 66.6 years with a majority of men (58.8%). Thirty-two percent of patients had vascular nephropathy that caused renal failure, 10.5% glomerular

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nephropathy, 18.5% diabetic nephropathy, 16.5% interstitial nephropathy, 3.4% other nephropathies and in 11.2% of patients the etiology of chronic renal failure was unknown. Fifty percent of patients had normal BMI, 34% of patients with a BMI between 25 and 30 Kg / m² and 16% of patients had a BMI greater than 30 Kg / m². Residual diuresis was less than 0.5 L for 37% of patients, between 0.5 and 1 L / day for 26% of patients and greater than 1 L / 24h for 36.4% of patients (Table 1).

The average protein loss in the effluent peritoneal dialysate was 8.24 g / 24h, but with a wide standard deviation of 15.79. The average value of the nPNA was 0.9 ± 0.38 g / Kg / 24h. Forty percent of patients had no phosphorus chelator. The mean albumin level was 33 ± 5.5 g / L. The seniority on dialysis was 23.3 ± 22.6 months. An alkaline reserve less than or equal to 22 mmol / L was found in 20.4% of patients, 47.7% had an alkaline reserve of between 22 and 27 mmol / L, and 27.8% of patients had a higher alkaline reserve. at 27 mmol / L (Table 2).

Table II: Results

	N = 2043					
Characteristic	**MV[1]**	**%[1]**	**M[2]**	**S.D.[2]**	**n[2]**	**%[2]**
Protein loss (g/24 h)	100	4,9%	8,24	15,79		
Alkaline reserve (mEq/L)	85	4,2%				
≤ 22					416	20,4%
]22 ; 27]					975	47,7%
> 27					567	27,8%
Albumin (g/L)	23	1,1%	33,0	5,5		
aPNA (g/kg/24 h)	10	0,5%	0,90	0,38		
Dialysis vintage (months)	20	1,0%	23,3	22,6		
Phosphate binders	0	0,0%				
Calcium					550	26,9%
Lanthane carbonate					123	6,0%
Sevelamer carbonate					102	5,0%
Sevelamer chlorhydrate					368	18,0%
Other					57	2,8%
Without binders					843	41,3%

[1] VM = Number of patients with one missing value ; % = percentage of total patients.

[2] M = mean ; S.D. = Standard deviation ; n = number of patients ; % = percentage of total patients.

The distribution of alkaline reserve values is reported in Figure 1. The distribution of patients according to the level of alkaline reserve is identical whether they are treated by automated peritoneal dialysis or continuous ambulatory peritoneal dialysis (Figure 2).

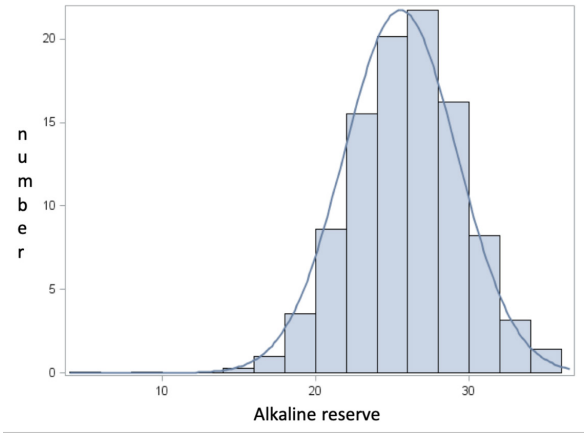

Fig. 1 : distribution of alkaline reserve

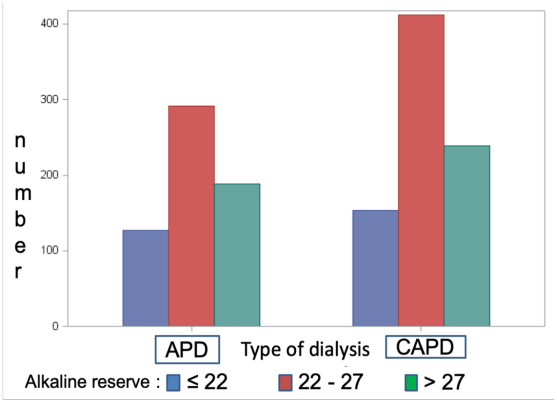

Fig. 2 : Alkaline reserve in APD and CAPD

The average age of patients with alkalosis is higher than that of patients with normal acid-base balance, which itself is higher than that of patients with acidosis (70 years versus 66 years, versus 63 years). There is no significant relationship between acid-base status and PD seniority. There is a significant relationship between the level of alkaline reserve which is lower when the value of aPNA increases ($p = 0.01$). The increase in age is significantly related to an increase in the probability of being in alkalosis rather than in equilibrium (OR = 1.01, $p = 0.03$). Overweight or obese patients have a higher probability of being in acidosis rather than in equilibrium compared with normal weight patients. Patients with residual diuresis less than or equal to 500 mL / 24h are less likely to be in alkalosis than those with normal acid base equilibrium compared to patients with a residual diuresis greater than 1L / 24h.

The increase in aPNA of 1g / kg / 24H is accompanied by a halving of the probability of being alkalosis rather than equilibrium, in other words, when the aPNA increases by 0.1 g / kg / 24h, there is a 10% decrease in the probability of being in metabolic alkalosis.

Patients treated with calcium carbonate are more likely to be in alkalosis than in equilibrium compared to

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patients without a chelator. Patients receiving sevelamer carbonate have a lower probability of being acidosis than equilibrium compared to non-chelator patients. Patients taking sevelamer hydrochloride are more likely to be acidosis than equilibrium compared to patients without chelators. The distribution of acid-base equilibrium as a function of age on the balance sheet shows that age is not related to the probability of being in acidosis rather than equilibrium. On the other hand, as age increases, the probability of being in alkalosis rather than equilibrium also increases. Patients with interstitial nephropathy have a significantly increased risk of being in metabolic acidosis than other patients. There is no significant relationship between acid-base status and other types of nephropathy.

DISCUSSION

The results of our study are consistent with the usual clinical data of patients treated with PD. Thus, the increased risk of being in alkalosis with increasing age is probably related to the decrease in food intake of protein, a source of acidic ions. Elderly people consume less protein compared to younger subjects with a greater tendency beyond 70 years. The lack of association between acid-base status and lean mass tends to reinforce this hypothesis of the exogenous origin of the acid charge. Similarly, no association with sex or dialysis seniority was found. The daily generation of hydrogen ions is closely correlated with protein intake (2). The main source of acid production is that derived from organic acids while sulfuric acid accounts for about 1/3 of total daily acid production. The reduced risk of being in alkalosis with the increase in protein intake estimated by aPNA supports this hypothesis : the increase in protein intake is accompanied in a linear way by the decrease of nearly 50% of the protein intake probability of being in alkalosis rather than equilibrium.

The existence of a relationship between the increase in BMI and the risk of acidosis goes in the same direction. We do not have a body composition study that could have supported this relationship if it showed that patients with a high BMI were in better nutritional status than leaner subjects. Patients with interstitial nephropathy are at risk for acidosis. This association can be explained by the fact that these patients at the dialysis stage more often have a residual diuresis preserved which can be responsible for a urinary loss of bicarbonate thus increasing the risk of acidosis. Concomitantly, patients with chronic interstitial nephropathy often have hyperchloremic acidosis associated with tubular dysfunction induced by interstitial disease independently of its etiology. This mechanism may be predominant in the genesis of the risk of acidosis in patients with chronic interstitial nephropathy, taking into account the fact that a low residual renal function with diuresis of less than 0.5 L / 24h is associated with a reduction in the risk of alkalosis without a significant association between the risk of being in acidosis and a reduced residual diuresis.

The type of phosphate chelator used is significantly associated with the risk of acidosis when this phosphate binder is sevelamer hydrochloride possibly by the addition of hydrochloric acid contained in the product. However, an indication bias can not be eliminated in that sevelamer is more prescribed in subjects who are less anorexic and with higher lean mass than in the elderly. Our results confirm the alkalizing power of calcium carbonate since patients receiving this chelator are more likely to be in metabolic alkalosis than equilibrium compared to non-chelator patients. It was not possible to find a relationship between acid-base status and albuminemia because biases may be assumed due to different plasma albumin assay methods (colorimetric or nephelemetry).

We did not calculate in our study the difference between automated or continuous ambulatory dialysis methods. However, in incident patients treated with PD we found an almost 50% increase in the probability of being metabolic acidosis in patients treated with APD (unpublished data). This is consistent with the fact that the final acid-base status in PD patients is the result of acidic metabolic production as a function of protein intake and perdialytic alkali transfer. In dialytically and metabolically stable patients, the mutual influences of these two factors determine the plasma concentration of bicarbonate and provide a neutral basic balance. It should be remembered that the intake of alkali comes from the peritoneal transport of bicarbonate or its precursors (lactate or acetate). There is feedback between the plasma level of bicarbonates and the peritoneal transport of this substance. Thus, when the plasma concentration of bicarbonates decreases in plasma due to an increase in acid production of metabolic origin, the loss of plasma bicarbonate to the dialysate decreases and the peritoneal transport of alkaline substance from dialysate to plasma increases thus making it possible to neutralize the total acid-base balance. In addition, in patients who have significant net ultrafiltration, the decrease in alkaline gain from the dialysate tends to reduce the plasma concentration of bicarbonate. This further decrease in plasma bicarbonate concentration reduces the loss of bicarbonate in the effluent dialysate and thereby restores the previous dialytic gain. In this way, the body alkaline balance

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remains neutral but the plasma concentration of bicarbonate decreases (3,4).

It has been shown in many studies that a low plasma bicarbonate concentration is a risk factor for mortality in patients treated with PD (5). This association may be related to a persistent inflammatory syndrome and a faster loss of residual renal function associated with metabolic acidosis (6). In the general population, low plasma bicarbonate has also been shown to be associated with increased mortality independent of systemic pH and other confounding factors. This association seems independent of the cause of the decrease in plasma bicarbonates (metabolic acidosis or respiratory alkalosis). Metabolic alkalosis is also associated with higher mortality in the general elderly population (7).

The effect of metabolic acidosis on nutritional status is well demonstrated by numerous studies (8,9). It has also been shown that the correction of metabolic acidosis in CAPD patients reduces proteolysis via the ubiquitin-proteasome system in muscle and through an increase in the plasma concentration of branched amino acids along with a decrease in their degradation (10). The role of residual renal function in maintaining a good nutritional status is currently well established. A recent study has found a significant association between low bicarbonate levels and decreased residual renal function in PD patients (11,12). Thus, maintaining a normal acid-base status seems essential to reduce the risk of morbidity and mortality in patients treated with PD.

Finally, the role of peritoneal permeability in obtaining an acid-base balance cannot be neglected, given that this permeability governs the gain or loss of alkali. A decision tree combining nutrition and peritoneal permeability has been proposed (13, Figure 3).

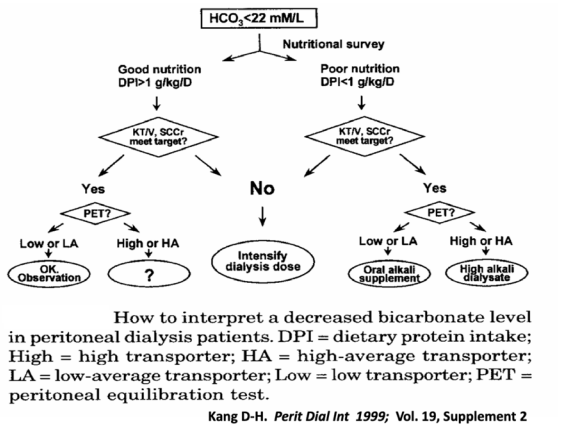

Fig.3 : Decision tree, fromKang (13)

CONCLUSION

Despite its retrospective nature, our study confirms the relationships of acid-base status with the clinical parameters of patients treated with PD. On a prospective basis, adaptation of the dialysate buffer could thus be adjusted to the individual characteristics of the patients. It could thus be proposed to use a buffer containing a high concentration of bicarbonate in patients with a high BMI and a relatively high protein intake thus making it possible to correct metabolic acidosis whereas solutions containing low concentrations of bicarbonate can be used in patients with a lower weight and lower protein intake, thus avoiding the installation of metabolic alkalosis (14). Thus, an individualized approach to the prescribing parameters of PD could be carried out with the aim of avoiding the installation of malnutrition, preserving the residual renal function and ultimately improving the prognosis.

CONFLITS D'INTERET

Les auteurs déclarent ne pas avoir de conflit d'intérêt

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