

Calcium levels in acid concentrate are critical - A case series of post-hemodialysis hypercalcemia due to high calcium in acid concentrate

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ABSTRACT

Introduction: There are very few studies on the discrepancies between prescribed and measured hemodialysis (HD) electrolyte levels, and most of the related studies address discrepancies in dialysate sodium concentrations. To the best of our knowledge, there are no studies on the discrepancy between prescribed and measured dialysate calcium concentrations due to higher-than-expected calcium concentrations in acid concentrates.

Objectives: The current study investigated the causes of post-HD hypercalcemia and associated clinical features.

Patients and Methods: Due to one episode of post-HD encephalopathy associated with post-HD hypercalcemia, pre- and post-dialysis calcium concentrations were checked with dialysate electrolyte concentrations for all eleven HD patients in the case series. All biochemical and clinical details were collected from hospital records. Paired T-tests and McNamar tests were conducted for statistical analysis of biochemical and clinical variables.

Results: A pattern of post-dialysis hypercalcemia was noted in all eleven patients due to a higher measured dialysate calcium concentration (mean \pm SD) of 8.591 ± 0.5224 mg/dL as opposed to the prescribed dialysate calcium concentration of 6 mg/dL (1.5 mmol/L). A higher calcium content in the acid concentrate was found to be the reason behind post-dialysis hypercalcemia. The calcium content of the product water of the water treatment plant was found to be within the recommended limits. Future dialysis sessions were performed with HD containing measured calcium, which was within the recommended limits of prescribed dialysate calcium. A significantly greater number of patients who received dialysis with higher calcium dialysate developed intradialytic hypertension than did those who received dialysis with normal calcium dialysate ($p=0.031$).

Conclusion: The discrepancy between the measured and prescribed calcium concentrations may be due to the higher-than-expected calcium concentration in acid concentrate, which can cause post-HD hypercalcemia.

Implication for health policy/practice/research/medical education:

Elevated calcium content in acid concentrate can be a cause of post-hemodialysis hypercalcemia. Therefore, measuring dialysate electrolytes whenever a new batch of acid concentrate is used can help reduce discrepancies between prescribed and measured dialysate electrolyte concentrations and related adverse effects.

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Introduction

In India, end-stage renal disease is quite prevalent and is observed in approximately 130 000 patients, 120 000 of whom are receiving hemodialysis (HD) (1). A large amount of freshly prepared dialysate is needed, which is prepared with AAMI standard product water, acid concentrate, and base concentrate mixed in a fixed proportioning ratio (2). The recommended dialysate

calcium concentration (DCa^{++}) for HD is between 1.25 mmol/L and 1.5 mmol/L (3). The final hemodialysate should have a calcium (Ca^{++}) concentration within $\pm 5\%$ of the prescribed value (4). There are very few studies on the discrepancy between prescribed and measured dialysate electrolyte levels, and most of those studies involve discrepancies in dialysate sodium concentrations (4). To the best of our knowledge, there are no studies on the

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discrepancy between prescribed and measured DCa^{++} in HD due to the higher-than-expected Ca^{++} concentration in acid concentrate.

Objectives

The current study investigated the reasons behind post-HD hypercalcemia in a tertiary care center. The clinical presentation of patients with post-HD hypercalcemia was also assessed.

Patients and Methods

In this study, we present a case series of 11 patients who developed post-hemodialysis hypercalcemia. In our center, in the 2nd week of July 2020, one patient developed encephalopathy post-HD. After an electrolyte imbalance was suspected, the patient's serum electrolytes were sent for analysis. Moreover, all the patients who planned for dialysis soon after were requested a pre-dialysis serum sample. It was observed that the patient with encephalopathy was hypercalcemic. Hence, pre- and post-dialysis Ca^{++} concentrations were checked for all patients who underwent dialysis thereafter. Along with this, the dialysate sample was also sent to check electrolyte concentrations. By the time the first few patients had arrived, eleven patients had already been dialyzed. Future dialysis appointments were postponed until the new dialysate solution was ensured to confirm the recommended calcium concentration by biochemical measurements.

All 11 patients were included in the study. Demographic data, medical history (including comorbidities), clinical presentation (including interdialytic weight gain), biochemical data (dialysate electrolytes [DNa^+ , DK^+ , DCa^{++} , and DMg^{++}]), and serum calcium and serum albumin concentrations were collected from hospital records.

The clinical parameters and biochemical parameters (dialysate and serum electrolytes) were compared between

the two groups: a) eleven patients who underwent dialysis with high-than-recommended calcium dialysate and b) the same eleven patients who underwent dialysis with dialysate containing normal dialysate calcium and magnesium. The reason behind the high dialysate calcium concentration was studied.

Statistical analysis

Continuous variable data are presented as the mean \pm standard deviation or median \pm interquartile range depending on the data distribution tested with the Kolmogorov-Smirnov test. A paired t-test was used to compare biochemical data (dialysate and blood electrolytes) between the two groups. The incidence of intradialytic hypertension was compared between the two groups by the McNemar test. A P value <0.05 was considered to indicate statistical significance.

Results

A common batch of acid concentrates was used for the patient who developed hypercalcemic encephalopathy post-HD and the eleven patients in the case series (Table 1).

All 11 patients developed hypercalcemia. Post-dialysis hypercalcemia was noted in the above patients due to a higher-than-expected measured calcium concentration, DCa^{++} (mean \pm SD) 8.59 ± 0.52 , as opposed to the prescribed DCa^{++} of 6 mg/dL (1.5 mmol/L), i.e., 43% higher than prescribed (Figure 1). None of the patients received calcium during the HD session. Subsequent HD was performed with a new batch of acid concentrate. The measured DCa^{++} (mean \pm SD) of the HD prepared from the new acid concentrate was 6.07 ± 0.27 mg/dL, which was within the recommended limits (only 1.1% higher than expected).

DCa^{++} , the blood-dialysate Ca^{++} gradient and post-HD S. Ca^{++} levels were significantly greater in patients who received HD with dialysate made from 1st acid concentrate (higher Ca^{++} dialysate) than in those who subsequently

Table 1. Clinical characteristics of the eleven patients in the study

Clinical parameter	Value
Age (y), Mean \pm SD	59.45 \pm 7.75
Gender, %	
Male	90.9
Female	9.10
Vascular access, %	
AV fistula	81.80
Tunneled hemodialysis catheter	18.2
Duration on Hemodialysis (months), Mean \pm SD	60.5 \pm 68.55
Percentage of patients with diabetes, %	45.45%
Percentage of patients with hypertension, %	81.82%
Interdialytic weight gain in kg (During HD with acid concentrate with higher calcium), Mean \pm SD	3.355 \pm 1.105
Interdialytic weight gain in kg (During dialysis with corrected acid concentrate), Mean \pm SD	3.336 \pm 0.9902

SD, Standard deviation.

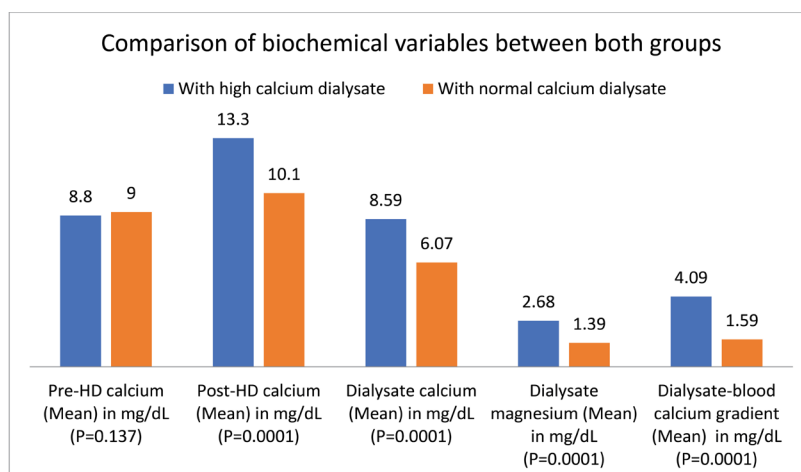


Figure 1. Comparison of biochemical variables between two groups: Group dialyzed with high-calcium dialysate, and Group dialyzed with normal dialysate. A paired t-test was used to compare the data within groups ($P < 0.05$ was considered to indicate statistical significance).

used normal DCa^{++} (Figure 1).

After evaluating the cause of the high Ca^{++} concentration in the dialysate, a higher-than-expected Ca^{++} concentration was found in the acid concentrate, whereas the Ca^{++} concentration in the product water was within the recommended limits (Figure 2).

The amount of dialysate magnesium was also greater in the higher Ca^{++} dialysate than in the normal dialysate due to the higher magnesium content in the acid concentrate (Figures 1 and 2). The measured dialysate concentrations of Na^+ , K^+ , chloride, and bicarbonate were within the prescribed levels.

Among the patients who received dialysis with higher-than-normal Ca^{++} dialysate, intradialytic hypertension was observed in 72.12% of patients, whereas only 18.18% of the patients who received dialysis with normal Ca^{++} dialysate was diagnosed (Figure 3).

The concentrations of dialysate sodium, potassium, and bicarbonate were similar in both groups. None of the 11 patients who received dialysis with higher-than-normal Ca^{++} dialysate developed encephalopathy, arrhythmia, abdominal pain, etc.

Discussion

The measured Ca^{++} concentration in HD should be within $\pm 5\%$ of the prescribed value (3). In our study, during initial sessions of dialysis, the difference between the measured Ca^{++} (mean) and the expected D Ca^{++} (6 mg/dL or 1.5 mmol/L) was 2.59 mg/dL (43.18% greater than the prescribed value), which was much greater than the allowed margin ($\pm 5\%$). Due to the significantly greater blood-to-dialysate Ca^{++} gradient, all patients who received dialysis with higher Ca^{++} dialysate concentrations had significantly greater post-HD Ca^{++} levels (Figure 1).

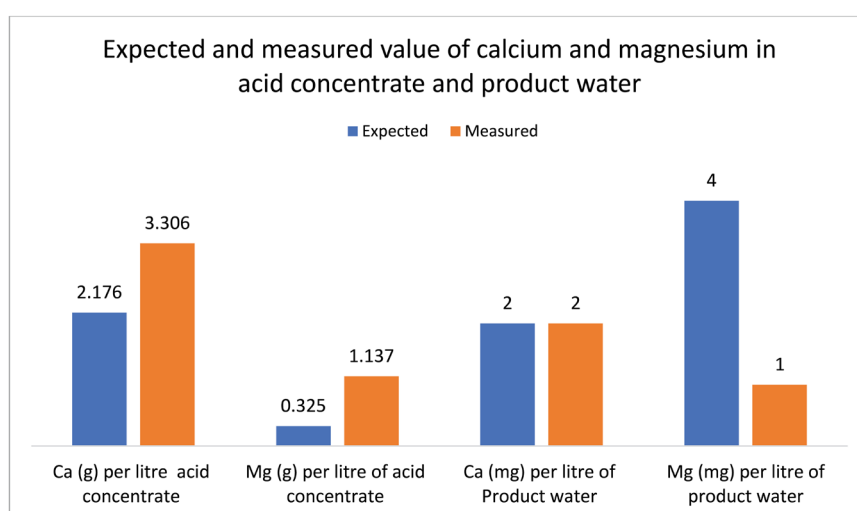


Figure 2. Expected and measured values of calcium (Ca^{++}) and magnesium (Mg^{++}) in acid concentrate (initially used) and product water in g/L and mg/L, respectively.

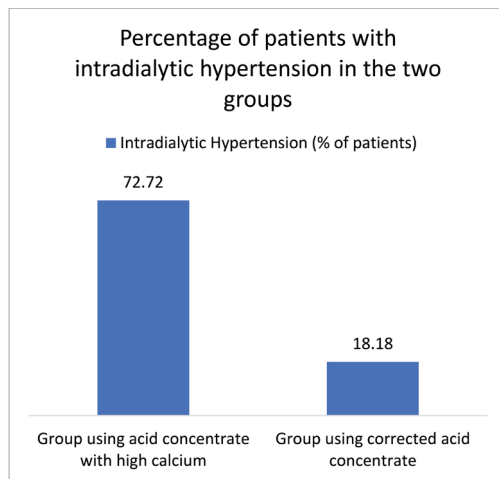


Figure 3. Percentage of patients in each above-mentioned group with interdialytic hypertension. The percentages of patients with interdialytic hypertension in the above two groups were different ($P=0.031$). Comparisons were performed between the two groups using the McNemar test ($P<0.05$ indicated statistical significance).

The source of high Ca^{++} in HD could be either from product water or from acid concentrate. On evaluation, we found that the Ca^{++} content in the acid concentrate was 51.9% (1130 mg/L), greater than expected, whereas the Ca^{++} concentration in the product water of the reverse osmosis treatment plant in our HD unit was normal (Figure 2). The proportioning ratio used in the HD machines was 1:1.83:34, i.e., 1 L of acid concentrate mixed with 1.83 liters of bicarbonate solution and 34 L of water produced 36.83 L of HD.

One liter of high Ca^{++} acid concentrate contained 3306 mg of calcium. Thus, the expected DCa^{++} (in the high-calcium acid concentrate group) should be $3306/36.83 = 89.7$ mg/L or 8.97 mg/dL.

The mean measured DCa^{++} (high calcium-acid concentrate group) was 8.59 mg/dL, which is close to the above-calculated value. The difference between the measured and expected values could be due to variations in the ion content of the acid concentrate container.

In our study, higher dialysate magnesium concentrations were also observed due to the higher magnesium content in the acid concentrate (Figures 1 and 2).

Post-HD hypercalcemia called hard water syndrome, has been previously observed with technical failure when softener is used in water treatment plants, causing high calcium levels in the product water (5,6). To the best of our knowledge, there are no studies on higher-than-expected Ca^{++} in HD due to the high Ca^{++} content in acid concentrate.

Eight of the 11 patients (72.72%) developed intradialytic hypertension while receiving HD with dialysate containing high calcium and magnesium concentrations, whereas only 2 of the 11 patients (18.18%) who received HD with dialysate containing normal calcium and magnesium concentrations had intradialytic hypertension ($P=0.031$;

Figure 3). The mean intradialytic weight gain was not significantly different between the two groups ($P=0.924$). Clinical variables and dialysate variables (in addition to DCa^{++} and DMg^{++}) were similar in both situations. Higher dialysate calcium and magnesium concentrations might have contributed to intradialytic hypertension (Figures 1 and 2). Acute hypercalcemia can cause an increase in blood pressure (5-7). Acute hypercalcemia causing endothelial dysfunction could explain interdialytic hypertension due to high dialysate calcium levels (8).

The findings of our study highlight the possibility of discrepancies between prescribed and measured dialysate electrolyte concentrations. To prevent such discrepancies, dialysate electrolytes should be measured whenever a new batch of acid concentrate arrives at an HD unit. Our study also highlights that significantly higher-than-expected hemodialysate calcium and magnesium concentrations can occur due to the higher-than-expected calcium and magnesium concentrations in acid concentrate. A DCa^{++} and DMg^{++} higher than expected can cause intradialytic hypertension.

Conclusion

A cause for the discrepancy between the measured and prescribed calcium levels could be due to the higher than expected calcium concentration in acid concentrate, which can cause post-HD hypercalcemia.

Limitations of the study

The data on serum magnesium concentrations were unavailable, which might have helped us determine the incidence of post-HD hypermagnesemia in our study. A study with a larger sample size is needed to confirm the role of high dialysate calcium concentrations in intradialytic hypertension.

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Authors' contribution

Conceptualization: Nabadwip Pathak.

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Investigation: Sunil Kumar Nanda.

Methodology: Nabadwip Pathak, Sunil Kumar Nanda.

Resources: Nabadwip Pathak.

Validation: Nabadwip Pathak.

Supervision: Sunil Kumar Nanda.

Visualization: Nabadwip Pathak.

Writing-original draft: Nabadwip Pathak.

Writing-review and editing: Sunil Kumar Nanda.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This case series was conducted in accordance with the World Medical Declaration of Helsinki. The study was approved by PIMS Institute ethics committee with IEC No.RC/2020/78. PIMS institute ethics committee is registered with CDSCO-Reg.No.ECR/400/Inst/Py/2013. Informed consent was obtained from all the patients. Furthermore, the authors have addressed all ethical issues, including plagiarism, data fabrication, and double publication.

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References

1. Varughese S, Abraham G. Chronic Kidney Disease in India: A Clarion Call for Change. *Clin J Am Soc Nephrol*. 2018;13:802-804. doi: 10.2215/CJN.09180817.
2. Kohn OF, Kjellstrand CM, Ing TS. Dual-concentrate bicarbonate-based hemodialysis: know your buffers. *Artif Organs*. 2012;36:765-8. doi: 10.1111/j.1525-1594.2012.01524.x.
3. Pérez-García R, García Maset R, Gonzalez Parra E, Solozábal Campos C, Ramírez Chamond R, Martín-Rabadán P, et al. Comisión de Expertos de la Sociedad Española de Nefrología para la creación de la Segunda Edición de la Guía de Gestión de Calidad del Líquido de Diálisis. Guideline for dialysate quality of Spanish Society of Nephrology (second edition, 2015). *Nefrologia*. 2016;36:e1-e52. doi: 10.1016/j.nefro.2016.01.003.
4. Gul A, Miskulin DC, Paine SS, Narsipur SS, Arbeit LA, Harford AM, et al. Comparison of Prescribed and Measured Dialysate Sodium: A Quality Improvement Project. *Am J Kidney Dis*. 2016;67:439-45. doi: 10.1053/j.ajkd.2015.11.004.
5. Leonard H, Pile T. Hard water syndrome: a case series of 30 patients from a London hemodialysis unit. *Clin Kidney J*. 2019;13:111-112. doi: 10.1093/ckj/sfz050.
6. Murlidharan P, Chan CT, Bargman JM. Catastrophic hypercalcemia as a technical complication in home hemodialysis. *NDT Plus*. 2011;4:251-2. doi: 10.1093/ndtplus/sfr051.
7. Weidmann P, Massry SG, Coburn JW, Maxwell MH, Atleson J, Kleeman CR. Blood pressure effects of acute hypercalcemia. Studies in patients with chronic renal failure. *Ann Intern Med*. 1972;76:741-5. doi: 10.7326/0003-4819-76-5-741.
8. Nilsson IL, Rastad J, Johansson K, Lind L. Endothelial vasodilatory function and blood pressure response to local and systemic hypercalcemia. *Surgery*. 2001;13:986-90. doi: 10.1067/msy.2001.118368.

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