J Nephrol (2014) 27:689–697
DOI 10.1007/s40620-014-0100-1

ORIGINAL ARTICLE

Management of mineral metabolism in hemodialysis patients: discrepancy between interventions and perceived causes of failure

Pasquale Esposito · Teresa Rampino · Marilena Gregorini · Carmine Tinelli · Annalisa De Silvestri · Fabio Malberti · Rosanna Coppo · Antonio Dal Canton · IAMM Group

Received: 18 January 2014 / Accepted: 4 April 2014 / Published online: 8 May 2014

Abstract
Background Mineral and bone disorders (MBD) in patients undergoing hemodialysis (HD) are a major clinical complication. Current therapeutic strategies do not attain the expected results. The Italian audit on mineral metabolism was implemented to investigate MBD management through a "patient-oriented" approach.
Methods Clinical and laboratory data pertinent to MBD from 509 prevalent adult patients on chronic HD were recorded and examined (audit), after which individual strategies were elaborated to improve MBD control. Their effectiveness was evaluated 6 months after the audit (Post-6).
Results The audit disclosed poor MBD control in a high percentage of patients (56 %). Low compliance to treatment was the major determinant of failure (in 43.5 % of cases). Logistic regression showed a direct correlation between high degree of compliance and the achievement of therapeutic targets, e.g. parathyroid hormone: odds ratio (OR) 2.48, $p = 0.015$. In contrast, a minority of the proposed interventions (14.7 %) included strategies to improve patient compliance. At Post-6, despite a significant increase in drug prescription ($p < 0.05$ vs. audit), the rate of successful MBD control was unchanged.
Conclusions Low compliance with treatment is a major, but still neglected, cause of failure in the achievement of MBD control in HD patients.

Keywords Clinical audit · Compliance · Hemodialysis · Mineral disorders · Quality improvement

Introduction

Disturbances of mineral and bone metabolism, classified as chronic kidney disease-mineral and bone disorders (CKD-MBD), are common in patients undergoing regular hemodialysis (HD) [1]. These disorders, characterized by altered calcium (Ca), phosphate (P) and parathyroid hormone (PTH) serum levels, are associated with a number of clinical symptoms and complications and have been considered an important risk factor for cardiovascular disease in HD patients [2, 3]. Because of their clinical relevance, control of CKD-MBD is a main target of dialytic strategy and is a thrust for development of new drugs, such as calcimimetics or vitamin D analogues [4]. However, neither tailoring of dialysis to attain strict calcium and phosphate balance nor the availability of novel drugs has significantly improved the overall rate of therapeutic success, so that uncontrolled MBD is increasingly perceived by care stakeholders as an unavoidable condition.

The members of the IAMM Group are listed in the "Appendix".

P. Esposito (✉) · T. Rampino · M. Gregorini · A. Dal Canton
Department of Nephrology, Dialysis and Transplantation, Fondazione IRCCS Policlinico "San Matteo" and University of Pavia, Piazzale Golgi 19, 27100 Pavia, Italy
e-mail: pasqualeesposito@hotmail.com

C. Tinelli · A. De Silvestri
Unit of Biometry and Clinical Epidemiology, Fondazione IRCCS Policlinico "San Matteo", Pavia, Italy

F. Malberti
Divisione di Nefrologia e Dialisi, Istituti Ospitalieri di Cremona, Cremona, Italy

R. Coppo
Nephrology, Dialysis and Transplantation Unit, City of Health and Science of Turin, Regina Margherita Children's Hospital, Turin, Italy

Clinical audits consist in measuring a clinical outcome or process against well-defined standards set on the principles of evidence-based medicine, in order to identify the changes needed to improve the quality of care [5]. While in HD patients clinical audit has already proven its utility in different clinical issues, in the context of MBD control the contribution of audits to improving the achievement of therapeutic targets has never been investigated [6–8]. Therefore an Italian audit on mineral metabolism (IAMM) was planned to identify the barriers to therapeutic success and to guide implementation of quality improvement strategies.

Subjects and methods

Patients and personnel involved

The IAMM project was undertaken in 36 public and private hemodialysis centers located in Italy and was supported by the Italian Society of Nephrology and National Academy of Medicine (ANM). In each center, 20 % of patients were blindly selected by an independent statistician for case examination. Patients had to have been on regular HD for at least 3 months; patients acutely ill or with vascular access dysfunction (defined as failure to attain and maintain an extracorporeal blood flow of at least 200 ml/min) were excluded.

Patient data collection

We recorded the following data for each individual patient on an anonymous patient chart: demographic information, clinical history, dialysis parameters, biochemical and instrumental evaluations and data on pharmacological therapy. The study was conducted in accordance with the Helsinki Declaration, and all patients provided written informed consent to data collection and analysis.

Standard and compliance assessment

Concerning which standard to follow as a target, we decided to leave each dialysis center free to choose between the 2003 Kidney Disease Outcomes Quality Initiative (KDOQI) and the 2009 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [9, 10]. Each center had to declare the chosen target before the audit. Compliance with prescribed drug treatment was evaluated by administration to each patient of the Simplified Medication Adherence Questionnaire, a tool that has been previously validated in HD patients [11].

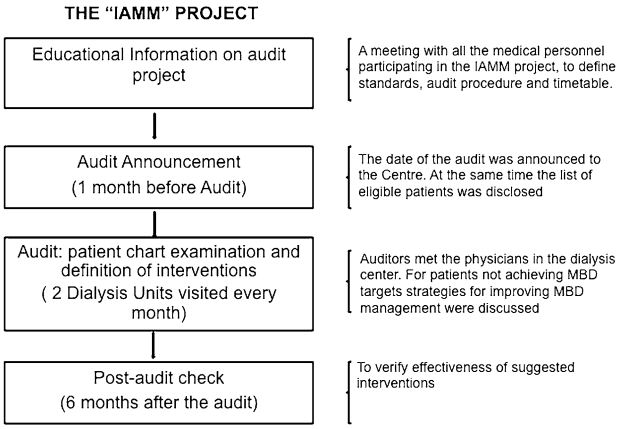

Fig. 1 Study design and timetable of the IAMM project

Study design and intervention strategies

The audit started on July 2010 and consisted of four distinct steps (Fig. 1). As a preliminary, we distributed to all personnel participating in the audit a proposal for intervention strategy based on the KDOQI, Canadian Society of Nephrology, and Renal Association guidelines, asking for feedback comments and suggestions. A general consent was obtained on the following general intervention strategy [9, 12, 13]:

1. Assessment of individualized diet. Organization of individual meeting to deliver information and advice on dietary phosphate management. Involvement of family and whenever possible support by specialist renal dieticians.
2. Modification of dialysis prescription (e.g. calcium dialysate and dialysis dose).
3. Optimization of drug therapy, including tactics to improve compliance.

The recommended interventions were formalized in a memorandum and made available for consultation within a week after the audit on a password-protected website (http://sinaudit.accmed.org). Attending physicians were responsible for their applications.

Clinical and laboratory data were collected at the time of the audit meeting (Audit), from July to December 2010, and after 6 months (Post-6).

Statistical analysis

Quantitative variables were represented by mean ± standard deviation or median and interquartile range (IQR) if they were not normally distributed; qualitative ones by number and percentage. Collected data were compared by means of Chi-square test or Fisher's exact test, as

appropriate, for categorical variables or by Student's *t* test or nonparametric Mann–Whitney test in the case of quantitative variables. Comparisons between Audit and Post-6 were done by means of Friedman's or McNemar's test, Wilcoxon test or *t* test for paired samples. All tests were two-sided. Associations among biochemistry MBD parameters, clinical factors and dialysis parameters were assessed fitting logistic regression models. A p value <0.05 was considered statistically significant. Data analysis was performed with STATA statistical package (vers:11; Stata Corporation, College Station, 2010, Texas, USA).

Results

Center and patient data

Of the 36 centers involved in the IAMM project, 19 (53 %) adopted the 2009 KDIGO guidelines, and 17 adopted the 2003 KDOQI guidelines. A total of 509 patient cases were audited, but 72 (14 %) did not complete the 6-month observation (27 were transplanted, 29 died and 16 were transferred to other dialysis units). Patient characteristics are summarized in Table 1.

Status of MBD control

As shown in Table 2, the mean P and Ca levels at time of Audit were 4.6 ± 1.4 and 8.8 ± 1.5 mg/dl, achieving therapeutic targets in 52.8 and 74 % of cases, respectively.

Table 1 Basal characteristics of the HD patients involved in the IAMM project

n	509
Male/female	337/172
Age, years	66.1 ± 14.3
Dialytic age, months, median (IQR)	44 (21–77.5)
Diabetic patients, n (%)	99 (19.4)
Dialysis modality	
HD, n (%)	351 (69)
HDF, n (%)	96 (19)
AFB, n (%)	40 (8)
Other, n (%)	22 (4)
Dialysis length (h/week)	11.1 ± 2.3
Dialysate calcium content (mmol/l)	
1.25, n (%)	67 (13.2)
1.5, n (%)	425 (83.5)
1.75, n (%)	10 (2.0)
2, n (%)	7 (1.3)
spKT/V	1.35 ± 0.27

HD hemodialysis, *HDF* hemodiafiltration, *AFB* acetate-free biofiltration, *spKT/V* single-pool KT/V

The mean intact PTH (iPTH) levels were 299 ± 286 pg/ml. In centers adopting the KDOQI guidelines, 38.4 % of patients achieved the iPTH target, while 15.5 % achieved simultaneously Ca, P and iPTH targets. These percentages were higher in centers adopting the KDIGO guidelines, respectively 67.2 and 19.8 %.

Sixty-four patients (12.5 %) presented a history of fractures, while vascular calcifications were recognized by instrumental evaluations [Doppler ultrasonography or computed tomography (CT)-angiography] in 268 (52 %). Table 3 shows the results of logistic regression analysis that highlighted the crucial role of compliance with treatment in the achievement of the therapeutic targets. In particular, compliance with drug treatment was directly associated to the achievement of P and iPTH targets [odds ratio (OR) 2.58, $p = 0.005$, confidence interval (CI) 1.32–5.04; OR 2.48, $p = 0.015$, CI 1.19–5.14, respectively]. No significant correlations were found among biochemical parameters and dialysis-related factors, except for Ca serum levels that were higher in patients treated with dialysate containing a lower concentration of calcium—1.25 mmol/l—with respect to those treated with 1.5 mmol/l (9.4 ± 0.9 vs. 8.7 ± 1.5 mg/dl, $p < 0.05$). Patients treated

Table 2 Laboratory and treatment parameters collected at basal evaluation (Audit) and after 6 months (Post-6) in the course of the IAMM project

	Audit	Post-6
Number	509	437
Calcium serum levels (mg/dl)	8.8 ± 1.5	8.6 ± 1.5
Patients on calcium target, n (%)	377 (74)	325 (74.3)
Phosphorus serum levels (mg/dl)	4.6 ± 1.4	4.7 ± 1.3
Patients on phosphorus target, n (%)	269 (52.8)	251 (57.4)
iPTH serum levels (pg/ml)	299.7 ± 286.9	305.6 ± 232.5
Patients on iPTH target, n (%)	243 (47.7)	216 (49.4)
Alkaline phosphatase (IU/l)	151.3 ± 121.8	145.3 ± 112.4
Patients undergoing MBD-related pharmacological therapies, n (%)	481 (94.4)	405 (92.8)
Phosphate binders, n (%)	336 (66.0)	374 (85.5)*
Calcitriol (per os), n (%)	164 (32.2)	126 (28.8)
Paricalcitol, n (%)	165 (32.4)	233 (53.3)*
Cinacalcet, n (%)	81 (15.9)	145 (33.2)*
Compliance with medications, n (%)		
Nonadherent	221 (43.3)	193 (44.2)
Adherent	288 (56.7)	244 (55.8)
Specific diet prescribed, n (%)	63 (12.3)	65 (14.8)

Percentages of patients achieving P, Ca and iPTH targets were defined on the basis of the guidelines chosen by each dialysis unit before beginning the audit process

iPTH intact parathyroid hormone

* $p < 0.05$ vs. Audit

Table 3 Logistic regression analysis of the variables involved in the achievement of therapeutic targets at the basal evaluation

	Variables		OR	95 % CI	p
Calcium on target	Compliance with drugs	No	1.0		
		Yes	0.92	0.47–1.8	0.8
	Use of calcimimetics	No	1.0		
		Yes	0.55	0.34–0.89	0.015
	Dialysate calcium concentration	1.25	1.00		
		more	1.71	1.17–2.51	0.005
Phosphorus on target	Compliance with drugs	No	1.0		
		Yes	2.58	1.32–5.04	0.005
	Use of phosphate binders	No	1.0		
		Yes	1.05	0.72–1.53	0.8
	Hours/week of dialysis	1 h increase	0.94	0.85–1.03	0.2
	Specific diet prescriptions	No	1.0		
		Yes	0.93	0.54–1.59	0.8
PTH on target	Compliance with drugs	No	1.0		
		Yes	2.48	1.19–5.14	0.0015
	Use of calcimimetics	No	1.0		
		Yes	1.07	0.64–1.79	0.78
	Use of paricalcitol	No	1.0		
		Yes	1.47	0.98–2.2	0.058

OR odds ratio, *CI* confidence interval, *PTH* parathyroid hormone

with a dialysate calcium concentration of 1.5 mmol/l or higher also had a significantly higher probability of reaching an adequate calcium control compared to those treated with a dialysate calcium concentration of 1.25 mmol/l (OR 1.71, $p = 0.005$, CI 1.17–2.5).

Notably, among the drugs used to control hyperparathyroidism only paricalcitol was associated to an increased probability of achieving PTH target, even if this correlation was not statistically significant (OR 1.47, $p = 0.058$, CI 0.98–2.2).

Intervention strategies

Based on blood levels of indicators, clinical presentation and the presence of calcifications, MBD was considered uncontrolled in 285 (56 %) out of the 509 audited patients. The main causes of poor MBD control were: (1) low compliance with drug treatment (43.5 % of cases), (2) insufficient or excessive drug therapy (30.8 %), (3) inadequate dialysis prescription (15.7 %), and (4) severe comorbidity (10 %).

The most frequent intervention operated by attending physicians was a change in prescribed drug therapy (193 patients, i.e. 67.7 % of the 285 patients that were poorly controlled at the basal evaluation), followed by initiatives aimed to improve dialysis efficacy, e.g. by increasing dialytic dose or modulating dialysate calcium content (50 patients, 17.6 %). Forty-two patients (14.7 %) were referred to nutritional and/or psychological counselling for an individualized dietary prescription or to improve compliance with drug treatment.

Effects of audit on MBD control

As shown in Table 2, no significant changes occurred after the audit in the achievement of any laboratory target. In contrast, 6 months after the audit there was a significant increase in the phosphate binders, paricalcitol and calcimimetics prescription ($p < 0.05$ vs. Audit) (Fig. 2). Of note, the number of patients receiving specific nutritional and psychological counselling, as well as the degree of compliance with drug therapy was unchanged throughout the audit process. Similarly, in spite of auditor recommendation, also dialysis prescriptions were not appreciably modified.

In order to determine the factors related to the achievement of therapeutic targets, we repeated the logistic regression analysis with the data collected at Post-6 (Table 4). Interestingly, the results of the regressions were similar to those found when analyzing the basal values. In particular, compliance with treatment confirmed to be the most important factor related to the achievement of therapeutic targets, being directly associated with the achievement of P and iPTH targets (OR 10.5, $p < 0.001$, CI 4.7−23.4; OR 5.41, $p < 0.001$, CI 2.5–11.6, respectively), while drug administration continued to have no significant effect.

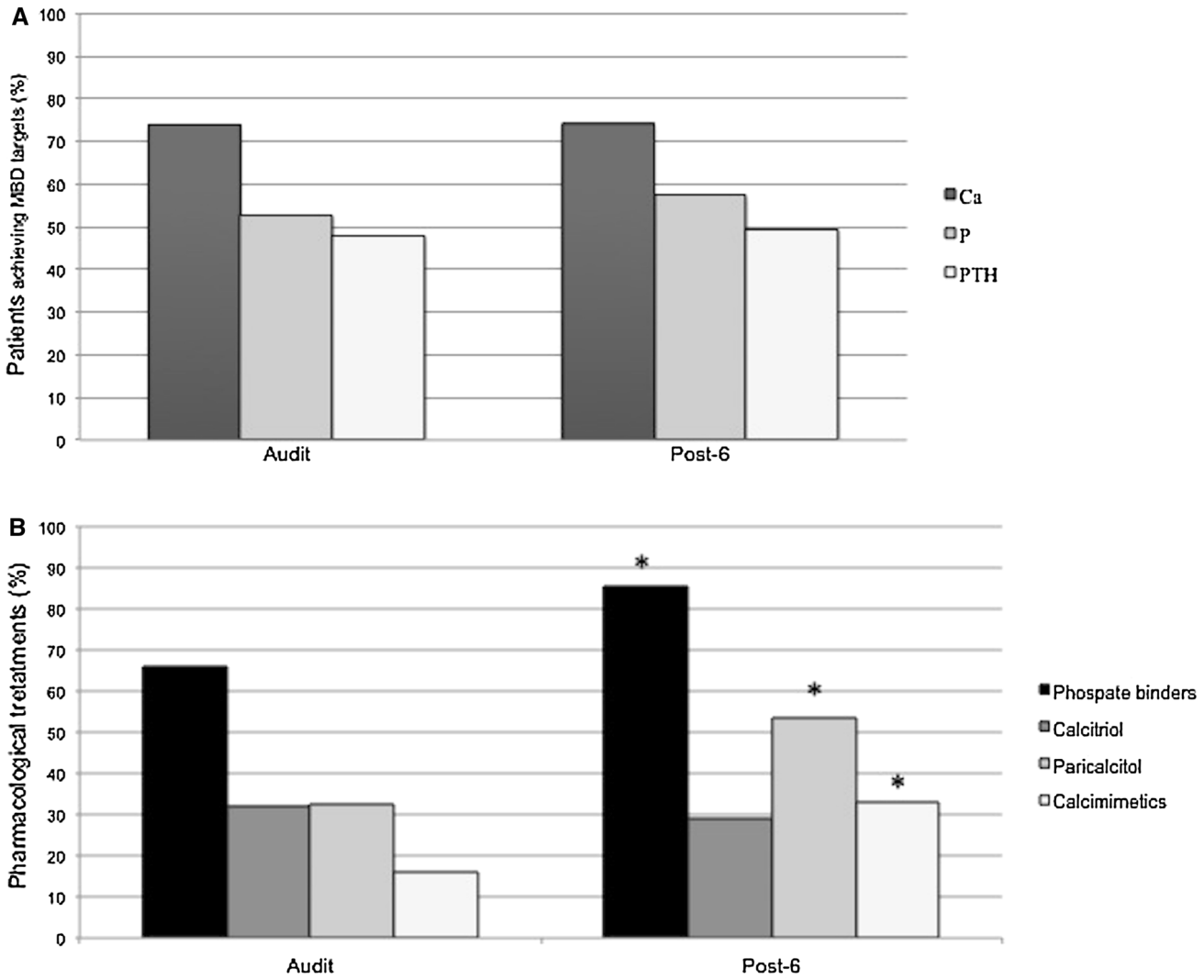

Fig. 2 Number of HD patients achieving therapeutic targets (**a**) and pharmacological therapy administrated (**b**) during the IAMM project, expressed as percentages. Six months (Post-6) after the basal evaluation (Audit) there was a significant increase in the prescription of all drug categories (except calcitriol), which did not correspond to an improved control of mineral bone disorders (MBD). *$p < 0.05$ vs. Audit

Discussion

Although MBD in HD patients is the object of intense research activity that has increased our understanding of the disease, its prevention and treatment still remain unsatisfactory [14, 15]. The present report highlights the obstacles that hamper a successful control of MBD as detected by a straightforward "patient-oriented" approach, i.e. by collecting information from a number of audit procedures structured and designed for the purpose.

First of all, we confirmed the data regarding the difficulty to achieve therapeutic targets, showing that only 15–20 % of the evaluated patients presented Ca, P and PTH values simultaneously controlled [16, 17].

Different reasons might explain the high rate of treatment failure, including the heterogeneity of diagnostic evaluations and therapeutic options adopted in clinical practice. In order to standardize the quality of care, several international guidelines have been released, including the widely credited KDOQI 2003 and KDIGO 2009 guidelines [9, 10].

However, in spite of their popularity, these guidelines give recommendations that are based on weak evidence and their implementation in clinical practice has been shown to be limited [18, 19]. Our audit carried out in 2010–2011 confirms the dominant position of the KDIGO guidelines, but at the same time underlines that in daily clinical practice there is not a generalized consensus on the therapeutic targets (in particular for PTH), as demonstrated

Table 4 Logistic regression analysis of the variables involved in the achievement of therapeutic targets at the Post-6 evaluation

	Variables		OR	95 % CI	p
Calcium on target	Compliance with drugs	No	1.0		
		Yes	1.24	0.66–2.33	0.5
	Use of calcimimetics	No	1.0		
		Yes	0.85	0.51–1.42	0.5
	Dialysate calcium concentration	1.25	1.00		
		more	6.4	0.37–11	0.2
Phosphorus on target	Compliance with drugs	No	1.0		
		Yes	10.5	4.7–23.4	<0.001
	Use of phosphate binders	No	1.0		
		Yes	1.07	0.70–1.63	0.8
	Hours/week of dialysis	1 h increase	0.98	0.91–1.05	0.6
	Specific diet prescriptions	No	1.0		
		Yes	0.69	0.40–1.20	0.2
PTH on target	Compliance with drugs	No	1.0		
		Yes	5.41	2.51–11.6	<0.001
	Use of calcimimetics	No	1.0		
		Yes	0.82	0.50–1.35	0.4
	Use of paricalcitol	No	1.0		
		Yes	1.12	0.75–1.66	0.6

OR odds ratio, *CI* confidence interval, *PTH* parathyroid hormone

by the high percentage of centers still adopting the KDOQI 2003 guidelines. Since the choice of different targets is an important factor in the determination of therapeutic success and clinical management, our data clearly indicate that standardization of care still remains an unsolved problem.

However, in addition to physician- and organization-related factors, also patient behavior may influence the quality and the success of care [20]. Toussaint et al. administered to HD patients, nephrologists and dialysis nurses questionnaires evaluating knowledge and awareness of CKD-MBD. Interestingly, both physicians and dialysis nurses considered the low grade of compliance with drug therapy and dietary restrictions as the main determinants of treatment failure [21]. Similarly, our evaluations demonstrated that low adherence to treatments influenced therapeutic success, as also confirmed by logistic regression analysis performed both at basal and Post-6 evaluations, that revealed a significant relationship between the achievement of therapeutic targets and the extent of compliance.

Our audit methodology required that, after identification of the individual factors related to poor CKD-MBD control, the audit teams should elaborate personalized, feasible strategies for each patient, according to a structured intervention algorithm [22]. Such an apparently rational approach, however, was frustrated by an unexpected discrepancy between the analysis of factors accounting for therapeutic failure and the interventions planned. In fact, while low compliance was recognized as the main cause of therapeutic failure, only a minority of patients were provided with interventions specifically addressed at improving the compliance, e.g. by delivering nutritional and psychological counselling or educational initiatives. Rather, most of the interventions were focused on pharmacological therapy.

Consequently, 6 months after the audit we found that, while the degree of drug adherence was unaffected by the interventions, there was a significant increase in the amount of drugs prescribed (mainly paricalcitol and calcimimetics).

This approach was unsuccessful, since the control of MBD parameters did not improve, suggesting that optimization of the pharmacological therapy was more a matter of 'wishful thinking' than a bullet that reaches the target, and structured interventions on compliance were ranked as a top priority to improve MBD. Low adherence to treatment remains an important barrier in the daily clinical practice, not only for MBD but also for many other chronic diseases, such as hypertension and diabetes [23].

Validated tools to evaluate compliance are unavailable and often the personnel involved in the patient care does not have the opportunity or educational skills to carefully evaluate the degree of adherence to the treatment. In fact, while numerous studies show the positive effects on MBD management of educational interventions involving dieticians, dialysis nurses and patients [24–27], it is also manifest that this kind of approach can be time-consuming and could be unsuitable in daily clinical practice.

On the other hand, increased use (in dosage and number) of drugs might appear as a valid way to improve the achievement of clinical target. In recent years, newer treatment options have been introduced into clinical practice (e.g. paricalcitol, calcimimetics), which may affect the management of MBD. The FARO study was a prospective survey performed in an Italian population of HD patients aimed to determine the impact of the newer drugs on achieving K/DOQI targets [28]. The authors evaluated 2,637 patients during an 18-month observational period—from April 2006 to October 2007—collecting data on pharmacological treatments and laboratory parameters. They found that during the surveillance period there was a significant increase in the use of paricalcitol and calcimimetics, which was associated to a better control of iPTH and calcium levels and an increased amount of patients reaching therapeutic targets. However, at the end of the study, two-thirds of the patients did not achieve iPTH target levels, while only 11.5 % presented Ca, P and iPTH values simultaneously controlled. Therefore, also these data confirm that increased drug administration, regardless of the awareness regarding compliance to the therapy, although it may be partially effective in some cases, is insufficient to obtain an overall satisfactory rate of therapeutic success [29, 30].

In the design of this study, we were aware of some methodological problems. First of all, adequate therapeutic targets are not so clear in the Nephrology community [31]. Further, since our aim was to investigate the effects of a clinical audit in daily practice we decided to use simplified medical interviews to assess patient compliance, which might be a limitation of our study; but, on the other hand, a sound scientific method to evaluate compliance is still not available [32]. Nevertheless, despite the limitations, we believe that our results could be of help in defining a correct clinical approach to MBD management in HD, indicating that future therapeutic strategies, beyond the development of new drugs, should include the implementation of feasible educational programs addressed to both healthcare personnel and patients.

Acknowledgments We thank Elisabetta Azzoni and Alberto Rossi, part of ANM staff, for the help provided during all the phases of the study. We also thank Società Italiana di Nefrologia (SIN) for the scientific support. This study was supported by Accademia Nazionale di Medicina (ANM, Genova, Italy) that partially covered the travelling expenses for the auditors. The authors had no financial relationships with any organizations that might have an interest in the submitted work.

Conflict of interest The authors state that this manuscript has not been published previously and is not currently being assessed for publication by any other journal. At the same time, on behalf of all authors, the corresponding author states that there is no conflict of interest.

Appendix: members of the IAMM group

Alfredo Capuano, Diana Novizio (Divisione di Nefrologia Dialisi e Trapianto, Università Federico II, Napoli), Silvia Carozzi, Monica Repetto, Claudio Schelotto (Nefrologia, ASL 2 Presidio Ospedaliero San Paolo, Savona), Salvatore Carpentieri, Stefania Rossi (S.O.C. Nefrologia e Dialisi-ASL 9, Locri), Luigi Catizone, Alda Storari (U.O. Nefrologia Azienda Ospedaliera Universitaria Arcispedale Sant'Anna, Ferrara), Paolo Conti, Claudio Gabbrielli (S.C. di Nefrologia e Dialisi AUSL n 9 di Grosseto Osp. della Misericordia, Grosseto), Maria Cossu, Gianfranco Branca (S.C. di Nefrologia e Dialisi Trapianto-ASL Sassari), Ludovica Dapice, Caterina Saviano (Unità di Nefrologia e Dialisi, Ospedale Civile di Caserta), Goffredo Del Rosso, Patrizia Santarelli (U.O.C. Nefrologia e Dialisi P.O "G.Mazzini" ASL 106, Teramo), Marina Di Luca, Silvio Di Stante (U.O. Nefrologia e Dialisi A.O San Salvatore, Pesaro), Giorgio Feliciangeli, Giuseppe Cianciolo (U.O. di Nefrologia, Dialisi e Trapianto Policlinico S. Orsola-Malpighi, Bologna), Franca Giacchino, Franco Bonello (S.C. di Nefrologia e Dialisi-Ospedale Civile, Ivrea), Alessandro Leveque, Chiara Taglioni (Nefrologia e Dialisi, ASL 1, Ospedale Civile, Città di Castello), Marina Foramitti (U.O. Nefrologia e Dialisi-Istituti Ospitalieri di Cremona), Maria Cristina Mereu, Maria Chiara Cadoni (U.O. Nefrologia e Dialisi P.O. Ns Bonaria, San Gavino Monreale), Domenico Montanaro, Roberto Mioni (S.C. di Nefrologia e Dialisi-Az. Osp. Universitaria di Udine), Massimo Morosetti, Liljana Jankovic, Loredana Fortunato (U.O. Nefrologia e Dialisi Ospedale G.B. Grassi, Ostia), Lamberto Oldrizzi, Vincenzo Lidestri (U.O.C. Nefrologia e Dialisi ULSS 20, San Bonifacio), Giacomo Panarello, Domenico Schinella (S.C. Nefrologia e Dialisi, A.O. Santa Maria degli Angeli, Pordenone), Alessandra Perna (I Divisione di Nefrologia e Dialisi, Seconda Università degli Studi, Napoli), Giovanni Pertosa, Francesco Pesce (U.O. Emodialisi-Azienda Ospedaliera di Bari), Rodolfo Puccini, Raffaele Caprioli (Nefrologia Trapianti Dialisi -SSN 1, Azienda Ospedaliera Pisana, Pisa), Francesco Quarello, Marco Pozzato (S.C. di Nefrologia e Dialisi-Ospedale G. Bosco, Torino), Mario Salomone, Emanuele Stramignoni (Nefrologia e Dialisi-ASL TO 5, Chieri), Giovanna Sau, Pierina Amalia Menneas (S.S.D. Emodialisi Azienda Brotzu, Cagliari), Silvana Savoldi, Andrea Serra (S.C. di Nefrologia e Dialisi-ASL TO 4, Ciriè), Ugo Teatini, Giorgio Romei Longhena (U.O.C. Nefrologia e Dialisi Osp. di Bollate, Rho, Garbagnate, Az Osp. G. Salvini, Garbagnate Milanese), Giorgio Triolo, Alessandro Damiani (Nefrologia e Dialisi, CTO, Torino), Giuseppe Pontoriero (U.O. Nefrologia e Dialisi Ospedale Manzoni, Lecco), Ferdinando Avella, Paolo Frattolillo (Unità di Nefrologia e Dialisi, Ospedale

Santa Maria della Pietà, Nola), Piergiorgio Bolasco, Andrea Galfrè (S.C. Territoriale di Nefrologia e Dialisi-ASL Cagliari, Quartu Sant'Elena, Cagliari), Maurizio Brigante, Giuseppe Di Cienzo (U.O.C. Nefrologia e Dialisi, Ospedale, Campobasso), Giuliano Brunori, Giuseppe Mondello (U.O. Nefrologia E Dialisi Ospedale Santa Chiara, Trento), Franco Cadinu, Patrizia Vatieri (U.O. Nefrologia e Dialisi-ASL Nuoro, Ospedale San Francesco, Nuoro), Leonardo Cagnoli, Fabio Badiali (U.O.C. Nefrologia e Dialisi AUSL Rimini), Giovanni Cancarini, Corrado Camerini (U.O. Nefrologia e Dialisi-Presidio Osp. A.O. Spedali Civili, Brescia).

References

1. Moe SM, Drueke T, Lameire N, Eknoyan G (2007) Chronic kidney disease-mineral and bone disorder: a new paradigm. Adv Chronic Kidney Dis 14:3–12
2. Ganesh SK, Stack AG, Levin NW, Hulbert-Shearon T, Port FK (2001) Association of elevated serum PO(4), Ca × PO(4) product, and parathyroid hormone with cardiac mortality risk in chronic hemodialysis patients. J Am Soc Nephrol 12:2131–2138
3. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM (2004) Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. J Am Soc Nephrol 15:2208–2218
4. Martin KJ, González EA (2012) Long-term management of CKD-mineral and bone disorder. Am J Kidney Dis 60(2):308–315
5. Benjamin A (2008) Audit: how to do it in practice. BMJ 336:1241–1245
6. Esposito P, Benedetto AD, Tinelli C et al (2013) Clinical audit improves hypertension control in hemodialysis patients. Int J Artif Organs 36(5):305–313
7. Lusignan Sd, Gallagher H, Jones S et al (2013) Audit-based education lowers systolic blood pressure in chronic kidney disease: the Quality Improvement in CKD (QICKD) trial results. Kidney Int 84(3):609–620
8. Polkinghorne KR, Seneviratne M, Kerr PG (2009) Effect of a vascular access nurse coordinator to reduce central venous catheter use in incident hemodialysis patients: a quality improvement report. Am J Kidney Dis 53(1):99–106
9. National Kidney Foundation (2003) K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 42:S1–S201
10. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group (2009) KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int 76:S1–S130
11. Arenas MD, Malek T, Gil MT, Moledous A, Alvarez-Ude F, Reig-Ferrer A (2010) Challenge of phosphorus control in hemodialysis patients: a problem of adherence? J Nephrol 23(5):525–534
12. Jindal K, Chan CT, Deziel C et al (2006) Canadian Society of Nephrology Committee for Clinical Practice Guidelines. Hemodialysis clinical practice guidelines for the Canadian Society of Nephrology. J Am Soc Nephrol 17(3 Suppl 1):S1–S27
13. Steddon S, Sharples E (2010) CKD-mineral and bone disorders (CKD-MBD). http://www.renal.org/guidelines/clinical-practice-guidelines-committee#sthash.65jKeP7l.Et6UpymQ.dpbs. Accessed 15 Jan 2014
14. Young EW, Akiba T, Albert JM, McCarthy JT, Kerr PG, Mendelssohn DC, Jadoul M (2004) Magnitude and impact of abnormal mineral metabolism in hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis 44:34–38
15. Panichi V, Bigazzi R, Paoletti S, RISCAVID Study Group et al (2010) Impact of calcium, phosphate, PTH abnormalities and management on mortality in hemodialysis: results from the RISCAVID study. J Nephrol 23(5):556–562
16. Craver L, Marco MP, Martínez I et al (2007) Mineral metabolism parameters throughout chronic kidney disease stages 1–5—achievement of K/DOQI target ranges. Nephrol Dial Transplant 22(4):1171–1176
17. Gallieni M, Cucciniello E, D'Amaro E et al (2002) Collaborating nephrologists of the CARDIALISI Study Group. Calcium, phosphate, and PTH levels in the hemodialysis population: a multicenter study. J Nephrol 15(2):165–170
18. Uhlig K, Berns JS, Kestenbaum B et al (2010) KDOQI US commentary on the 2009 KDIGO clinical practice guideline for the diagnosis, evaluation, and treatment of CKD-mineral and bone disorder (CKD-MBD). Am J Kidney Dis 55(5):773–799
19. Arenas MD, Alvarez-Ude F, Gil MT et al (2006) Application of NKF-K/DOQI clinical practice guidelines for bone metabolism and disease: changes of clinical practices and their effects on outcomes and quality standards in three haemodialysis units. Nephrol Dial Transplant 21(6):1663–1668
20. Kugler C, Maeding I, Russell CL (2011) Non-adherence in patients on chronic hemodialysis: an international comparison study. J Nephrol 24(3):366–375
21. Toussaint ND, Pedagogos E, Beavis J, Becker GJ, Polkinghorne KR, Kerr PG (2011) Improving CKD-MBD management in haemodialysis patients: barrier analysis for implementing better practice. Nephrol Dial Transplant 26(4):1319–1326
22. Jamtvedt G, Young JM, Kristoffersen DT, O'Brien MA, Oxman AD (2006) Does telling people what they have been doing change what they do? A systematic review of the effects of audit and feedback. Qual Saf Health Care 15:433–436
23. Iuga AO, McGuire MJ (2014) Adherence and health care costs. Risk Manag Healthc Policy 7:35–44
24. Hecking E, Bragg-Gresham JL et al (2004) Haemodialysis prescription, adherence and nutritional indicators in five European countries: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant 19(1):100–107
25. Kuhlmann MK, Hoechst S, Landthaler I (2007) Patient empowerment in the management of hyperphosphatemia. Int J Artif Organs 30:1008–1013
26. Russell CL, Cronk NJ, Herron M et al (2011) Motivational Interviewing in Dialysis Adherence Study (MIDAS). Nephrol Nurs J 38(3):229–236
27. Kalanthar-Zadeh K (2013) Patient education for phosphorus management in chronic kidney disease. Patient Prefer Adherence 7:379–390
28. Mazzaferro S, Brancaccio D, Messa P, FARO Study Group et al (2011) Management of secondary hyperparathyroidism in Italy: results of the Italian FARO survey. J Nephrol 24(2):225–235
29. Collinson A, McMullan M, Tse WY, Sadler H (2014) Managing serum phosphate in haemodialysis patients: time for an innovative approach? Eur J Clin Nutr 68(3):392–396
30. Esposito P, Di Benedetto A, Rampino T, Stuard S, Marcelli D, Canaud B, Dal Canton A (2014) Management of mineral metabolism in haemodialysis patients: need for new strategies. Eur J Clin Nutr. doi:10.1038/ejcn.2014.72
31. Fouque D, Roth H, Pelletier S et al (2013) Control of mineral metabolism and bone disease in haemodialysis

patients: which optimal targets? Nephrol Dial Transplant 28(2):360–367
32. Meddings J, Kerr EA, Heisler M, Hofer TP (2012) Physician assessments of medication adherence and decisions to intensify medications for patients with uncontrolled blood pressure: still no better than a coin toss. BMC Health Serv Res 12:270