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Assessment of urea removal in haemodialysis and the impact of the European Best Practice Guidelines

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Abstract

Background. Dialysis adequacy, assessed by urea kinetics, is an important determinant of patient outcome, and is therefore an important clinical performance indicator. In this perspective, renal registry data may be useful to compare practices across countries. To serve that purpose available data should be comparable and preferably collected using a standardized procedure. The aim of this study, initiated by the European Renal Association–European Dialysis and Transplantation Association (ERA–EDTA) QUality European STudies (QUEST) initiative, was to make an inventory of the different methods used to determine urea kinetic measurements in the light of the European Best Practice Guidelines.

Methods. Via their national and regional registries, European haemodialysis centres were invited to complete a questionnaire regarding their practice of measuring dialysis adequacy.

Results. Fourteen regional or national registries among 51 sent back 255 questionnaires. Great variability in the methodology to assess Kt/V was observed. The urea reduction ratio (URR) was used alone by 37% (in association 46%) of dialysis centres, spKt/V by 25% (35%) and online clearance by 4% (12%), whereas only 10% (13%) used eKt/V, as recommended by EBPG. Forty percent of centres measured urea removal less than once a month, 6% of which never measured urea removal and 9% only every 6 months or less frequently.

Conclusion. Despite the fact that the use of URR is not recommended by EBPG, it was the most commonly used indicator to measure urea removal, whereas eKt/V was only used by a small minority of centres. This study allowed us to point out the need to standardize definitions and procedures and to develop an effective plan for implementation of the guidelines.

Keywords: best practice guidelines; dialysis adequacy; ESRD registry; Kt/V; urea removal

Introduction

The aim of the QUality European STudies (QUEST) initiative is to produce solid databases allowing direct comparisons of European Best Practice Guidelines (EBPG) goals with actual clinical achievements, which is the basis for quality improvement programmes [1,2]. In this perspective, these databases should allow comparison of clinical performance indicators between European renal registries. The aim of dialysis guidelines, such as the EBPG, is to harmonize treatment policies from a European perspective. Until now, data related to haemodialysis (HD) dose measurement and its delivery in Europe outside the DOPPS centres and Fresenius Medical Care clinic network are scarce and little is known concerning the implementation of the EBPG for HD part 1 (published in 2002) with regard to dialysis adequacy [3].

Traditionally, HD dose has been quantified referring to the kinetics of urea. For this purpose, different methods are available. Frequently used is the index Kt/V_{urea}, the

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product of urea clearance (K) times the length of the treatment time (t), in relation to the urea distribution volume (V) of the patient. In 2002, the EBPG recommended that Kt/V should be reported in terms of equilibrated Kt/V_{urea} (eKt/V) with the equation based on the regional blood flow two-pool urea kinetic model [4]. In contrast, in 2006, updated K-DOQI guidelines advocated the use of the single-pool Kt/V_{urea} (spKt/V), derived from the single-pool variable volume urea kinetic model, considering the absence of more evidence that would favour the additional effort and target-range adjustment required to substitute eKt/V for spKt/V [5].

Although the difference of one method from another is to some extent systematic (eKt/V is usually 0.15–0.20 lower than spKt/V) [6], it is also related to treatment characteristics such as the treatment time. In addition, in daily practice, dialysis adequacy is also frequently expressed by means of simplified formulas such as the urea reduction rate (URR), or by measurements based on on-line clearance. The use of different methodologies to express dialysis dose may hamper collaborative research into this subject, and also the use of urea removal as a clinical performance indicator [7].

The purpose of this project, initiated by the QUEST working group on dialysis adequacy, was to make an inventory of the different methods used to determine Kt/V and other markers of urea removal in European dialysis centres in the light of the EBPG (EBPG for HD part 1) published in 2002.

Methods

In December 2006, the QUEST working group contacted 51 ESRD registries covering 29 European countries to ask if they were willing to participate in this study. The study was also presented at the registries meeting at the ERA–EDTA congress in Barcelona (June 2007) to enlarge participation. All registries who responded positively were individually contacted at least twice to remind them on the protocol and deadlines. Via their national and regional registries, all HD centres within a specific geographic area were invited to complete a questionnaire including items on frequency, method and timing of the measurement of urea removal, method to assess urea distribution volume, timing and method of urea sampling, the inclusion of residual renal function in the assessment of urea removal, the use of on-line clearance methodology and on potential recent changes in methodology (see questionnaire in Appendix 1). The questionnaires were sent back to the national and regional registries and then to the French ESRD registry in charge of the study. The data were kept in an access database and a file was sent back to the registries for control. Each registry was contacted when some missing or inconsistent data were found. The results are presented by the number of centres for each variable in each registry. The percentages are presented for the group as a whole. The registries with the low response rate (50% or less of the centres) were compared to registries with the higher response rate by chi-square tests. Statistical analyses were performed with SAS software, version 9.0 (SAS Institute, Inc., Cary, NC, USA).

Results

Fourteen (27%) regional or national registries responded positively and sent back a total of 255 questionnaires. Romania and French-speaking Belgium sent their questionnaires in an aggregated way; for the other countries and regions (Bosnia Herzegovina, Bourgogne, Cantabria, Estonia, Finland, FYR of Macedonia, Italy, Lorraine, the Netherlands, Nord-Pas de Calais, Norway and the United Kingdom), individual questionnaires were available. The response rate was >90% in French-speaking Belgium, Finland, FYR of Macedonia, Cantabria and Romania; it was about two-third in the three French regions, Estonia, Norway and Bosnia Herzegovina, one-third in the United Kingdom and the Netherlands and only 1% in Italy (Table 1). The percentages of missing data were <5% for treatment modality, type of centre, frequency of measurement of urea removal, session of the week and formula used; 5–10% for the number of urea samples, timing and method of urea sampling and the inclusion of residual renal function into the measurement of urea removal.

The majority of the centres were public and provided full care HD (Table 1). Sixty percent of them declared to perform a measurement of urea removal at least once a month to see if the patient received sufficient dialysis. In contrast, 16 centres (6%) declared never to perform such a measurement and 22 (9%) only every 6 months or less frequently (Table 2). The frequency varied between countries; from 22% in FYR of Macedonia to 100% of the centres in French-speaking Belgium did a measurement at least once a month. There were huge differences in practice consensus concerning the way to measure the HD urea removal (Table 3). More than half of the centres performed a mid-week measurement, but 40% did it after the long break. More than 80% of the centres used only two urea samples. The post urea sample was taken immediately after the end of the HD session in one-third of the cases and during the first 5 min in a quarter of the cases. Half of the centres used the slow-flow method and one-third the stop-flow for the post-HD sampling. Almost 60% of the centres declared not to include the residual renal function in the Kt/V measurement. The urea reduction ratio (URR) was used as a single indicator by 35% of the centres (Figure 1). Single-pool Kt/V (spKt/v) and on-line measurement were used alone or together with another method in 35% and 12% of the cases, respectively. Equilibrated Kt/V (eKt/V) was used alone or together with another method by 32 centres (13%). The percentage of use of eKtV was similar between university centres and the others ($P = 0.8$). Only 42 centres declared that they had recently changed their method to assess urea removal and among them 28 (67%) declared that this change was related to the publication of EBP guidelines in 2002. Among those 28 centres, however, only five used eKt/V.

The three regions or countries with a 50% or lower response rate were similar in terms of type of centres and frequency of HD dose measurement but provided full care more often ($P = 0.03$). The eKt/V was used alone or in association with other indicators in 14% of the low response registries versus 13% in the highest response ($P = 0.8$), URR in 38% versus 53% ($P < 0.0.5$), spKt/V in

Table 1. Number of centres by type of centre or modality of care and by participating registry

	BEL	BOS	BOU	CAN	EST	FIN	MAC	ITA	LOR	NET	NPC	NOR	ROM	UK	Total	
Number of centres (*N*)	24	24	8	2	3	28	18	658	13	63	18	21	71	72	1023	
Response rate (%)	100	58	63	100	67	96	100	1	69	38	83	76	93	32	25	
Number of questionnaires (*N*)	24	14	5	2	2	27	18	9	9	25	15	16	66	23	255	100
	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	%
Type of centre																
Public, non university	11	8	1	0	1	19	17	7	4	18	8	10	45	12	161	63.1
Public, university	3	3	0	2	1	8	1	2	1	2	1	4	9	9	46	18.0
Private, not for profit	10	1	2	0	0	0	0	0	2	4	1	0	0	0	20	7.8
Private, for profit	0	0	0	0	0	0	0	0	1	0	5	0	12	0	18	7.1
Combinations	0	2	2	0	0	0	0	0	1	1	0	0	0	1	7	2.7
Unknown	0	0	0	0	0	0	0	0	0	0	0	2	0	1	3	1.2
Modality																
Centre full care	0	6	0	2	2	17	18	5	7	18	0	14	55	17	161	63.1
Centre limited and home care	24	0	2	0	0	5	0	0	1	3	4	0	0	2	41	16.1
Centre limited care	0	8	0	0	0	1	0	2	0	1	0	0	11	0	23	9.0
Centre full and limited care	0	0	3	0	0	2	0	2	1	2	10	0	0	1	21	8.2
Centre full and home care	0	0	0	0	0	2	0	0	0	1	0	0	0	2	5	2.0
Home care	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
Unknown	0	0	0	0	0	0	0	0	0	0	1	2	0	1	4	1.6

BEL, French-speaking Belgium; BOS, Bosnia Herzegovina; BOU, Bourgogne–France; CAN, Cantabria–Spain; EST, Estonia; FIN, Finland; MAC, FYR of Macedonia; ITA, Italy; LOR, Lorraine–France; NET, the Netherlands; NPC, Nord-Pas de Calais-France; NOR, Norway; ROM, Romania; UK, the United Kingdom.

Table 2. Number of centres by frequency of measurement of urea removal and by participating registry

	BEL	BOS	BOU	CAN	EST	FIN	MAC	ITA	LOR	NET	NPC	NOR	ROM	UK	Total	%
	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	%
Number of questionnaires	24	14	5	2	2	27	18	9	9	25	15	16	66	23	255	100
Frequency of HD dose measurement																
At least 1/month	24	5	5	2	1	14	4	3	7	13	9	13	33	20	153	60.0
1/3–4 months	0	5	0	0	1	11	0	4	2	11	5	2	14	3	58	22.7
1/6 months or less	0	4	0	0	0	2	0	1	0	1	1	0	13	0	22	8.6
Never	0	0	0	0	0	0	14	1	0	0	0	0	1	0	16	6.3
Unknown	0	0	0	0	0	0	0	0	0	0	0	1	5	0	6	2.4

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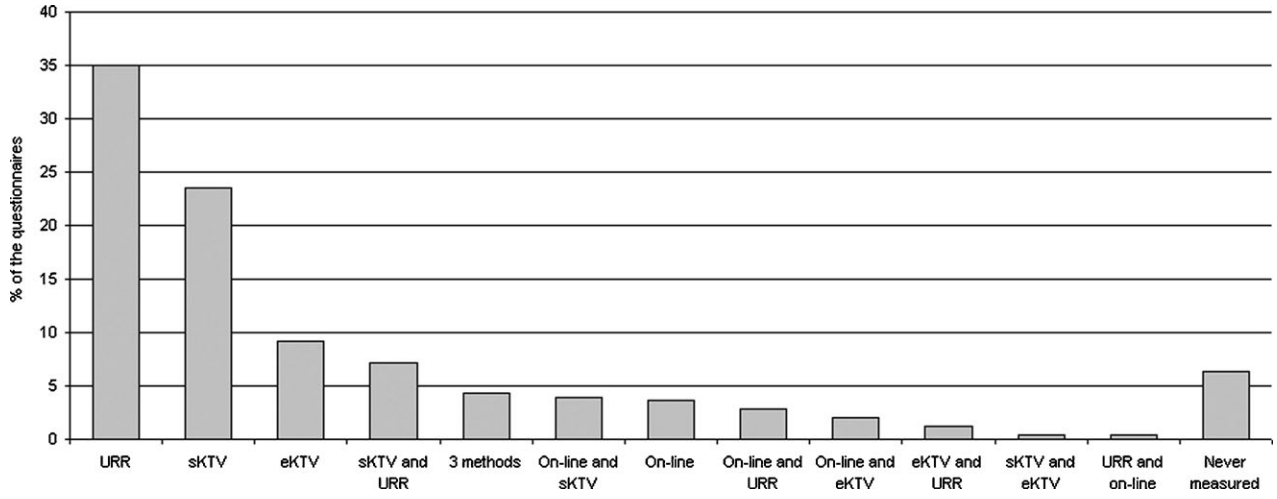

Fig. 1. Percentage of centres by detailed methods used to measure Kt/V.

Table 3. Number of centres by detailed methods used to measure urea removal and by participating registry

	BEL	BOS	BOU	CAN	EST	FIN	MAC	ITA	LOR	NET	NPC	NOR	ROM	UK	Total	
	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	%
Number of questionnaires	24	14	5	2	2	27	18	9	9	25	15	16	66	23	255	100
Dose never measured	0	0	0	0	0	0	14	1	0	0	0	0	1	0	16	6.3
Session in the week																
After the long break	24	7	1	0	1	4	1	3	2	20	5	4	18	6	96	40.2
Middle session	0	7	3	2	1	22	3	3	6	3	10	11	40	17	128	53.6
Before the long break	0	0	0	0	0	1	0	2	1	1	0	0	3	0	8	3.3
Unknown	0	0	1	0	0	0	0	0	0	1	0	1	4	0	7	2.9
Number of urea sampling																
Two	24	14	5	2	2	23	4	5	8	11	13	13	57	19	200	83.7
Three	0	0	0	0	0	4	0	3	1	14	0	1	2	1	26	10.9
Unknown	0	0	0	0	0	0	0	0	0	0	2	2	6	3	13	5.4
Timing of urea sampling																
30 min before	0	0	0	0	0	7	0	0	0	0	1	0	0	0	8	3.3
1 min before	0	0	2	0	0	0	0	0	0	0	0	0	0	0	2	0.8
Immediately post	0	4	2	0	1	10	0	4	7	8	7	8	29	6	86	36.0
1–4 min post	0	6	0	0	1	6	3	2	0	12	4	6	11	8	59	24.7
5–9 min post	24	3	0	2	0	1	1	0	2	4	0	0	7	6	50	20.9
10–29 min post	0	1	0	0	0	3	0	2	0	1	1	0	4	2	14	5.9
30–60 min post	0	0	0	0	0	0	0	0	0	0	0	0	6	0	6	2.5
Unknown	0	0	1	0	0	0	0	0	0	0	2	2	8	1	14	5.9
Method of sampling																
Slow-flow	24	7	2	2	2	15	4	3	3	9	10	9	20	9	119	49.8
Stop-flow	0	6	0	0	0	6	0	4	4	13	2	4	32	11	82	34.3
Unchanged	0	0	1	0	0	6	0	0	1	3	2	2	8	0	23	9.6
Unknown	0	1	2	0	0	0	0	1	1	0	1	1	5	3	15	6.3
Residual renal function																
No	0	11	4	2	1	15	4	6	7	2	15	13	45	16	141	59.0
Yes	24	2	0	0	1	12	0	2	2	23	0	2	7	3	78	32.6
Unknown	0	1	1	0	0	0	0	0	0	0	0	1	13	4	20	8.4
Formula used																
URR	24	3	3	0	0	1	2	0	1	3	0	0	40	11	88	36.8
sKTV	0	4	0	2	0	8	0	2	1	12	1	7	17	5	59	24.7
eKTV	0	0	1	0	0	3	0	3	1	2	4	2	6	1	23	9.6
On-line	0	6	0	0	0	0	0	0	0	0	1	1	0	1	9	3.8
eKTV and URR	0	0	0	0	0	0	0	0	0	0	2	0	0	1	3	1.3
sKTV and URR	0	0	0	0	2	3	2	2	1	2	2	2	0	2	18	7.5
sKTV and eKTV	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0.4
On-line and URR	0	0	0	0	0	1	0	0	1	2	1	1	0	1	7	2.9
On-line and eKTV	0	0	1	0	0	2	0	0	0	1	1	0	0	0	5	2.1
On-line and sKTV	0	0	0	0	0	3	0	0	2	1	2	1	0	1	10	4.2
URR and on-line	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0.4
Three methods	0	1	0	0	0	5	0	0	1	2	1	1	0	0	11	4.6
Unknown	0	0	0	0	0	0	0	0	1	0	0	1	2	0	4	1.7

BEL, French-speaking Belgium; BOS, Bosnia Herzegovina; BOU, Bourgogne–France; CAN, Cantabria–Spain; EST, Estonia; FIN, Finland; MAC, FYR of Macedonia; ITA, Italy; LOR, Lorraine–France; NET, the Netherlands; NPC, Nord-Pas de Calais–France; NOR, Norway; ROM, Romania; UK, the United Kingdom.

44% versus 34% ($P = 0.1$) and on-line 11% versus 14% ($P = 0.5$).

Discussion

Renal registries are interesting tools to follow clinical performances indicators, and also may allow large-scale collaborative research in the field of dialysis. However, this study shows a wide variation in the assessment of dialysis dose as assessed by urea kinetics between registries and individual centres.

Expression of urea removal in the light of the EBPG (EBP guidelines, part 1, II.1.2) [4]

The EBP guidelines, part 1, recommended that 'HD dose should be expressed in terms of equilibrated Kt/V with the rate equation based on the regional blood flow two-pool urea kinetic model' (evidence level: B). However, a surprising finding of this study is the very limited use of eKt/V in daily practice. In five of the registries, centres declared that they never used eKt/V. In the remaining nine registries, eKt/V was used by 17% of the centres. Thus, overall, only 13% of centres used eKt/V alone or in association with monitor dialysis adequacy. Twenty-five percent of the centres used spKt/V, the single-pool variable volume urea kinetic model, and was as such the second most commonly used parameter to express urea removal. As holds true for eKt/V, spKt/V is well validated in terms of the relation with outcome [8]. But a potential disadvantage of spKt/V, circumvented by the use of eKt/V, is the fact that compartmentalization of urea during dialysis, resulting in significant post-dialytic urea rebound, is not taken into account. This problem would be most pronounced in short-term dialysis treatments but may

also exist in long slow haemodialysis [9,10]. The reason why eKt/V is used in such a limited way by the participating centres is not clear. Although there is a paucity of research into the implementation of EBPG in clinical practice, recent data suggest clear changes in clinical practice in practice patterns after publication of EBPG [3]. Our data do not support this with regard to the methods used to assess urea removal. We hypothesize that a possible explanation for the limited use of eKt/V might reside in the assumption that for the calculation of eKt/V, blood sampling 30 min after dialysis is needed. Indeed, eKt/V may be calculated by using the spKt/V formula with a blood sample taken 30 min after dialysis, which might be difficult to achieve from a practical point of view in a busy dialysis clinic with limited time between subsequent (morning/afternoon or evening) dialysis sessions. However, the EBPG also allow the calculation of eKt/V as a mathematical conversion of spKt/V. As such, no additional parameters beyond those used in the calculation of spKt/V are needed. Another explanation for the limited use of eKt/V is the fact that spKt/V measurements are advocated by the influential NKF/K-DOQI guidelines published in 2006 (guideline 4.2) [5].

In this survey, the URR was the most commonly used parameter to express dialysis dose. For the calculation of URR, only pre- and post-dialytic urea measurements are needed. It is therefore a simple and easily calculated index. However, a serious drawback of URR resides in the fact that urea removal by ultrafiltration is not taken into account, nor the urea generation during dialysis. Thus, its application in individual therapy quantification introduces significant errors [11]. It has been suggested that due to these limitations, the use of URR as index of dialysis dose might have a negative effect on treatment outcome, even if some studies showed a good correlation between URR and survival [12,13]. Although, to the best of our knowledge, the predictive value of URR has not been formally tested, neither EBPG nor K-DOQI advocate URR as a first line method to assess dialysis adequacy [4,5]. In the 2002 EBPG on dialysis adequacy, the URR was even deemed an unacceptable method to express dialysis dose, although in the 2007 EBPG on dialysis strategies (EBP guidelines for HD part 2), it was suggested that URR be used as an approximation for practical purposes, but not as a substitute for formal urea kinetic modelling [14].

On-line clearance measurements are used by 12% of the centres. Complete systems for on-line monitoring which are integrated into the dialysis machine have become commercially available. The advantage of those methods is that they do not need blood or dialysate sampling, and when available they are easy, non-invasive and inexpensive. But extensive validation of those methods and harmonization with formal urea kinetic modelling is still lacking. As such, dialysis adequacy expressed by on-line clearance measurements was not recommended as first line parameter neither by the EBPG in 2002 or updated NKF-K DOQI guidelines [4,5]. In the EBPG part 2 (guideline 3.2), online clearance is considered as an acceptable method for calculating HD on a treatment-by-treatment basis, as long as the difference between Kt/V calculated by the online clearance and the reference method is taken into account [14]; online clearance should not substitute for monthly measurements using the reference method (evidence level: opinion).

Blood urea samples in the light of the EBPG (EBP guidelines, part 1, II.4.1) [4]

For the assessment of dialysis adequacy by urea kinetic modelling, the methodology to take post-dialytic urea samples is crucial. Access and/or cardiopulmonary recirculation may lead to an underestimation of post-dialytic urea and an overestimation of Kt/V if appropriate methodology for post-dialytic blood sampling is not applied [15]. The 2002 EBPG proposed a procedure based on a slow blood flow. The NKF-KDOQI 2006 update recommended either the slow-blood-flow method with a urea sample at 15 s or the stop-dialysate-flow method with the urea sample at 3 min (guideline 3). In general, the great majority of centres used methods to correct for access and/or cardiopulmonary recirculation. Three percent of the centres use a urea sampling 30 min before the end as it has been proposed by Bhaskaran *et al*. [16]. With 6% of missing data concerning timing and method of sampling, one may argue that some nephrologists do not pay much attention to the details of the measurement of the dose of dialysis and that they may not even know what the nurses are actually doing.

There was also great variation in the timing of the assessment of dialysis dose, 40% performing the measurements after the long inter-dialytic interval, and 54% during the midweek session. These discrepancies might be due to the fact that neither the EBPG nor NKF/ K-DOQI guidelines mention a clear preference for the timing of the measurements [4,5].

Monitoring of treatment in the light of the EBPG (EBP guidelines, part 1, II.4.2) [4]

Although it is recommended by the 2002 EBPG that 'the delivered dose of HD should be checked at least monthly' (guideline II.4.2, evidence level: B) as well in the NKF/DOQI (guideline 2.1), 40% of the centres mentioned that they measure urea removal less frequently than once a month. This is of importance, as Lambie *et al*. showed considerable variability in delivered dialysis dose [17]. Monitoring of adequacy would then require even more frequent assessment of Kt/V than is currently recommended. As urea removal has implications for clinical outcomes—satisfying guidelines for Kt/V is associated with improved survival and decreased incidence of hospitalization and hospital days [18,19]—its regular measurement is important in therapy planning. We therefore feel that the unexpected degree of centres not, or only very infrequently, monitoring HD dose—9% of the centres did measure urea removal but only twice a year or less frequent, whereas 6% stated that they never performed any such measurements!—may be a reason for considerable concern. The limited availability of randomized-controlled trials exploring the relation between HD dose and survival may also contribute to any limited interest of a dialysis centre to measuring urea removal for assessing their prescriptions.

Policy of the ESRD registries in Europa

The multiplicity of urea sampling techniques and formula used as seen in this study was also found in a national survey in the UK in 2002 [7]. Because of those variations and because of the predictive value for patient outcomes still being under debate, the UK Renal Registry made the choice to routinely collect pre- and post-dialysis blood urea concentration on a quarterly basis, and it reports on each centre's performance against the Renal Association audit standard for URR (>65%) [20] in its annual report [21]. Also the French-speaking Belgium registry collects annual raw data for pre- and post-dialysis blood urea concentration and calculates URR and Basile Kt/V [23]. In the French REIN registry [24] and the Catalonian registry (personal communication), the nephrologists are asked for both Kt/V and for the formula used. The Finnish Registry just asks for Kt/V but not for the method used (personal communication). Except for the UK and French-speaking Belgium registries, none of those registries had given specific recommendations to the nephrologists how to collect this information. To the best of our knowledge, the Andalusian registry asks for the complete raw data (dialysis membrane type and surface, weight loss and urea before and after dialysis) [25].

Standardizing measurement methods

The recent European renal best practice (ERBP) project, a body installed by the European Renal Association–European Dialysis and Transplantation Association (ERA–EDTA) to continue the initiatives previously taken by the EBPG, aims at improving EBP guidelines by clearly and explicitly separating statements based on high-level evidence (guidelines) and those based on judgement (recommendations) [26]. This was also the reason why EBPG was renamed into ERBP. While standardizing treatment is a difficult and sometimes controversial exercise, to our point of view, standardizing measurement methods is highly desirable and should not be controversial. Clinical performance indicators and outcomes should be reported in a standard way so that they are suitable for comparison. Also, to avoid confusion the harmonization of the guidelines will be an important step that should be derived from the collaboration between ERBP and the global Kidney Disease: Improving Global Outcomes (KDIGO) initiative, a non-profit foundation that aims to develop and implement worldwide nephrologic clinical practice guidelines since 2003 [27].

To be able to make some comparisons from one registry to another concerning HD dose, we suggest to implement a clear urea sampling procedure, to collect raw data and then apply a common formula to all the patients. In addition, to be able to calculate eKt/V, further data are needed with pre- and post-dialysis blood urea concentration as dialyzer clearance, urea distribution volume, treatment time and intradialytic weight loss, which unfortunately increases the data collection for the registries. Alternatively, an internet-based calculation programme might be of help.

Limitations of the study

The results presented here comprise a description of the current practice in the participating registries (14 among 51, i.e. 27%) and responding centres (255 among 1023, i.e. 25%). In view of the sample size and the response rate, we cannot consider them to be representative of the non-participating registries and non-participating centres.

We feel that it is likely that this study suffers from a positive selection bias. The participating registries and the medical teams who responded to the questionnaire may represent the ones more interested and more compliant with the guidelines. Although there were no significant differences in terms of frequency of measurement of urea removal or the use of eKt/V between low response registries and higher response registries who did participate in this survey, we think the situation in non participating centres or registries is most likely worse than emerged in this survey.

Because of those limits, this study should not substitute for national or regional reporting at centre level and cannot be used to evaluate the efforts of National Societies to diffuse the EBPG and quality improvement programmes.

In conclusion, the results of our study show that 5 years after the publication of EBPG, there still appears to be a great variability in the procedures to measure urea removal in European HD patients. In general, with regard to this aspect, the EBPG are not well implemented. This study in the framework of the QUEST initiative allows us to point out (1) the need for guideline setting authorities, especially ERBP, to standardize definitions and procedures concerning the way to measure and report outcomes, (2) the need for an effective plan to implement those guidelines in each country, to allow comparisons [28]. Periodic audits, like this one, may be a way for helping convergence towards guidelines standard and goals [29].

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Conflict of interest statement. None declared.

Appendix 1: Questionnaire 'methods used to assess dialysis dose in Europe'

Centre ID:

How often do you assess dialysis dose to see if the patient receives sufficient dialysis?

>1×/month	1×/month	1×/3 month	1×/6 months	Less often	Never
☐	☐	☐	☐	☐	☐

At which session do you measure dialysis dose?

Session after the long break	Session before the long break	Middle session (midweek)
☐	☐	☐

How do you measure dialysis dose?

Urea reduction ratio (URR)	Single-pool Kt/V (e.g. Gotch, Daugirdas II, log ratio)	Equilibrated Kt/V (e.g. Daugirdas III, Smye)	On-line measurement (e.g. Diascan)	Other, please specify
☐	☐	☐	☐	☐. . .. .

Do you include residual renal function in the Kt/V measurement?

Yes	No
☐	☐

How many urea samples are taken?

Two	Three
☐	☐

When is the post-dialysis urea sample taken?

Immediately post	1–4 min post	5–9 min post	10–29 min post	30–60 min post	Other, please specify
☐	☐	☐	☐	☐	☐. . .. .

Which method is used for the post-HD sampling?

Stop-flow	Slow-flow	Unchanged blood flow
☐	☐	☐

Do you include dialyser clearance values in the Kt/V calculation

Yes	No
☐	☐

If yes, which method to assess urea distribution volume do you use?

Anthropometric	Urea kinetic modelling	Other, please specify
☐	☐	☐. . . . .

Did you recently (from 2001) change your methodology to assess dialysis dose?

Yes	No
☐	☐

If so, was this change related to the publication of EBPG?

Yes	No
☐	☐

In which kind of dialysis centre do you work?

Private, for profit	Private, not for profit	Public, university	Public, non-university	Other, please specify
☐	☐	☐	☐	☐. . .. .

What type of care does your centre provide?

Centre, full care	Centre, limited care	Home care
☐	☐	☐

Place for free comments:

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Acute phase reaction to gadolinium-DTPA in dialysis patients

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Abstract

Background. Several late sequelae of the administration of gadolinium (Gd)-containing MRI contrast agents have been described in patients with advanced renal failure. In an observational series, we found a remarkable frequency of peracute reactions after administration of Gd-DTPA used for cardiovascular evaluation before renal transplantation.

Methods. In a 26-month observational period, 13 of 136 haemodialyzed or CAPD patients exhibited onset of fever, chills and nausea within hours after administration of Gd-DTPA peracute. A minority showed persistent cessation of residual diuresis. We performed blood cultures in most patients and evaluated white blood cell (WBC) counts, eosinophils, CRP, heart rate and blood pressure.

Results. Within an average of 12 h (range 12–36 h) after Gd administration, the 13 patients (9 males, 4 females; median age 61 years, range 47–79) developed consistent symptomatology with fever (median 39.0°C, range 37.5–39.5), chills, malaise, hypotension, vomiting, dyspnoea—initially raising suspicion of septicaemia. Subsequent blood cultures on bacterial contamination of the injected product remained negative throughout; bacterial or endotoxin contamination of the reagent was excluded. Steroids were tried in the first two patients without a noticeable effect. In all subsequent patients, symptoms were attenuated during the first 5 h dialysis (F60HPS with 280 ml/min blood flow) and disappeared within 72 h. CRP levels remained markedly elevated up to 14 days. Lymphopenia was seen in all patients, and polymorphic neutrophils (PMN) remained normal. Two polyuric patients developed persistent anuria. After a median of 16 months, none of these patients developed nephrogenic systemic fibrosis.

Conclusion. This series with unusually severe acute phase reactions was caused by one specific preparation. Such peracute reactions may be relevant for the so-far largely unresolved pathogenesis of the skin reaction to some Gd products in end-stage renal disease (ESRD) patients. It remains unresolved whether the reaction observed with Gd-DTPA do in principle also occur with other Gd reagents.

Keywords: acute phase reaction; acute renal failure; dialysis; gadolinium; lymphopenia

Introduction

Since the first observation [1], there have been numerous reports on gadolinium (Gd)-induced nephrogenic systemic

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