

Prevention of aluminium exposure. Actions at European Community level

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RESUMEN

Papel de la Comunidad Económica Europea en la prevención de la exposición al aluminio.

La comisión de la Comunidad Económica Europea toma parte de forma activa en la prevención de la exposición al aluminio desde 1982. Esto se lleva a cabo mediante el establecimiento de normas dictadas por dicho organismo para minimizar la exposición al aluminio. En el momento actual representan sólo una guía, pero tras su aprobación definitiva por el Parlamento europeo serán leyes de obligatorio cumplimiento en los países comunitarios.

SUMMARY

Prevention of aluminium exposure: actions at European Community level.

The Commission of the European Community (CEC) has started in 1982 actions towards the protection from aluminium toxicity in patients undergoing dialysis. After consulting the experts the CEC has produced several proposals which are so far a set of guidelines, but from which, after the Council approval, compulsory rules for all the EEC countries will derive.

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Introduction

The Commission of the European Communities has started action towards the protection of persons undergoing dialysis from aluminium toxicity in 1982 when an international workshop was held in Luxembourg¹.

In the same year a survey regarding aluminium analysis in the dialysis centres within the ten Member States of the European Community was carried out together with the Registry of the European Dialysis and Transplant Association²; also an intercomparison programme with 15 laboratories on the analytical problems related with the measurements of aluminium in dialysis fluids was undertaken³.

Taking into account the results of these studies and following consultations with experts from the Member States of the Community, the Commission has submitted in June 1983 to the Council of Ministers a proposal for a Council Directive relating to the protection of dialysis patients by minimising the exposure to aluminium⁴ and a revised proposal in 1985⁵.

Proposal for a council directive

The directive indicates recommended reference levels of aluminium in plasma or serum and compulsory limits in the water used for dilution of dialysis fluids and in the dialysis fluids themselves, recommended monitoring frequency and analytical methods.

As for the persons undergoing dialysis, it is considered that there is excessive build up of

aluminium body burden if aluminium in the plasma or serum exceeds 60 µg/l; increased monitoring frequency and specific health surveillance should be undertaken if 100 µg/l of aluminium are exceeded; measures should be taken so that the level of 200 µg/l of aluminium in plasma or serum is never exceeded in individual persons undergoing dialysis.

The total amount of aluminium present in dialysis concentrates shall not contribute more than 10 µg/l to the aluminium concentration of the dialysis fluids when made up; the aluminium concentration in the prepared dialysis fluid supplied for peritoneal dialysis shall not exceed initially 15 µg/l and then shall be reduced to 10 µg/l; the aluminium concentration in the prepared haemofiltration and peritoneal dialysis solutions and concentrated saline solutions for haemodialysis shall not exceed 10 µg/l.

The diluting water has to be prepared from water which complies with all the requirements of the Directive 80/778/EEC Council directive of 15.7.80 relating to the quality of water intended for human consumption⁶; except those related with aluminium. The diluting water has to be appropriately treated for the removal of aluminium if its level exceeds initially 30 µg/l and then shall be reduced to 10 µg/l.

As far as practicable, analytical methods with a detection limit of 10 µg/l of aluminium should be used for the analysis of water, dialysis fluids and dialysis concentrates; the detection limit of 5 µg/l is suggested for peritoneal dialysis solutions and haemofiltration solutions.

With the exception of water softening, both demineralisation and reverse osmosis techniques may be used for the treatment of the water.

At present the text of the proposal is still under discussion at Council.

Table I. Centres Responses to the CEC-EDTA Questionnaire Comparison between the surveys carried out in 1982 and 1984

Member State	Number of centres known		Number of centres replied		Replies %	
	1982	1984	1982	1984	1982	1984
European Community	1049	1406	437	880	42	62.6
Belgium	53	59	20	46	38	78.0
Denmark	12	11	8	9	67	81.8
Eire	4	5	4	3	100	60.0
Federal Republic of Germany	281	325	126	222	45	68.3
France	196	212	102	154	52	72.6
Greece	52	52	16	26	31	50.0
Italy	337	387	89	196	26	50.6
Luxembourg	5	5	1	3	20	60.0
Netherlands	47	48	31	29	66	60.4
Portugal	—	39	—	26	—	66.7
Spain	—	198	—	119	—	60.1
United Kingdom	62	65	40	47	65	72.3

Table II. Centres Performing Aluminium Analysis.
Comparison between the surveys carried out in 1982 and 1984

Member State	Number of centre known		Number of centres analysing for aluminium		% Centres analysing for aluminium	
	1982	1984	1982	1984	1982	1984
European Community	1049	1406	280	569	27	40.4
Belgium	53	59	12	45	23	76.3
Denmark	12	11	7	9	58	81.8
Eire	4	5	4	3	100	60.0
Federal Republic of Germany	281	325	57	174	20	53.5
France	196	212	96	149	49	70.3
Greece	52	52	4	1	8	0.2
Italy	337	387	38	45	11	11.6
Luxembourg	5	5	1	3	20	60.0
Netherlands	47	48	24	24	51	50.0
Portugal	—	39	—	8	—	20.5
Spain	—	198	—	64	—	32.3
United Kingdom	62	65	37	44	60	67.7

Table III. Centres, having replied, performing aluminium analysis.
Comparison between the surveys carried out in 1982 and 1984

Member State	Number of centres replied		Number of centres analysing for aluminium		% Centres analysing for aluminium	
	1982	1984	1982	1984	1982	1984
European Community	437	880	280	569	64.0	64.6
Belgium	20	46	12	45	60.0	97.8
Denmark	8	9	7	9	87.5	100.0
Eire	4	3	4	3	100.0	100.0
Federal Republic of Germany	126	222	57	174	45.2	78.3
France	102	154	96	149	94.0	96.7
Greece	16	26	4	1	25.0	3.8
Italy	89	196	38	45	42.6	22.9
Luxembourg	1	3	1	3	100.0	100.0
Netherlands	31	29	24	24	77.4	82.7
Portugal	—	26	—	8	—	30.7
Spain	—	119	—	64	—	53.7
United Kingdom	40	47	37	44	92.5	93.6

Table IV. Centres Performing aluminium analysis and proportion of them analysing on their own premises. Comparison between the surveys carried out in 1982 and 1984

Member State	Number of analysing for aluminium	% Centres performing their own analyses	Number of analysing for aluminium	% Centres performing their own analyses
	1982	1982	1984	1984
European Community	280	250	569	16.7
Belgium	12	17.8	45	15.6
Denmark	7	0	9	0
Eire	4	50	3	33.3
Federal Republic of Germany	57	3.5	174	11.5
France	96	5.2	149	19.5
Greece	4	25	1	0
Italy	38	23.6	45	20.0
Luxembourg	1	0	3	0
Netherlands	24	20.8	24	29.2
Portugal	—	—	8	0
Spain	—	—	64	12.5
United Kingdom	37	13.5	44	31.8

Follow up actions

As follow up action, in 1984 the Commission has asked the European Dialysis and Transplant Association to carry out a study similar to that undertaken in 1982 in order to:

- i) evaluate the evolution regarding the concern for aluminium analysis in the dialysis centres; and
- ii) to identify the laboratories which perform aluminium analysis and would be interested in participating in a Community quality Assurance Programme.

A questionnaire was mailed at the end of 1985 to the 1406 known dialysis and centres (a small proportion being only transplant centres) within the, now twelve, Member States of the EC.

The questionnaire was formulated as to gather information on practice for aluminium analysis (internal or external) in the dialysis centres and data on the results of analyses carried out during one year (1984); the overall aim being the setting up of an European Quality Assurance Programme in 1986.

Results of the questionnaire enquiry

A comparison has been made between the rates of response of the surveys carried out in 1982 and 1984.

The results presented in table I show that the overall response rate for the European Community has increased considerably to 62.6 % in 1984 as compared with 42 % in 1982.

In 1984, the response rate varied from 50 % to 82 % depending on Member States.

Table II shows the proportion of dialysis centres which have access to aluminium analysis facilities with reference to the total number of centres contacted in both surveys, while table III gives the same information as referred to the centres which returned the questionnaire.

Only a small proportion of centres carried out their own analysis, with the vast majority contacting external laboratories to perform them (table IV). Most of these are analytical laboratories of public organisations (universities, hospitals, water authorities).

Table V shows the number of persons undergoing dialysis in whom aluminium was measured in body fluids during 1984. The total number of persons undergoing dialysis on haemodialysis in that year was calculated from returns made to the EDTA Registry on its individual patients questionnaire. The country which reported measurements of body fluid aluminium in the highest proportion was the United Kingdom, with test carried out in 70.9 % of persons undergoing dialysis.

The questionnaire required centres to provide

Table V. Persons undergoing dialysis and measurement of aluminium body burden

Member State	Number of persons undergoing dialysis tested	% persons dialysed any time 1984
European Community	24,747	34.3
Belgium	1,721	65.9
Denmark	163	27.6
Eire	52	20.0
Federal Republic of Germany	5,846	29.8
France	7,925	58.9
Greece	40	2.0
Italy	1,648	11.2
Luxembourg	2	2.0
Netherlands	1,259	56.6
Portugal	470	24.9
Spain	1,209	12.4
United Kingdom	3,812	70.9

information on the highest aluminium level measured in body fluids during 1984 in individual patients. The forms gave ranges of aluminium measurements, and the centres were asked to record the numbers of persons undergoing dialysis who fell into each of the ranges. Table VI summarizes the results. The final column of the table gives the number of persons undergoing dialysis in whom information on aluminium levels was given in each of the countries, and the first three columns the proportion of these persons undergoing dialysis with maximum aluminium measurements during 1984 in the ranges shown. Overall, 79.5 % of persons undergoing dialysis in whom information on aluminium levels was provided, had measurements below 100 µg/l in body fluids. 6 % of patients had measurements in excess of 200 µg/l in body fluids during 1984.

The questionnaire also requested data on total number of analyses carried out in 1984 on body fluids, raw water and dialysis fluid. The total number of analyses performed in raw water, dialysis fluid and body fluids in the twelve Member States of the European Communities during 1984 is shown in table VII. A total of 16,159 analyses on raw water were carried out, with an additional 22,782 performed on dialysis fluid. In excess of 70,000 analyses were performed on body fluids during the year. From tables V and VII it is possible to estimate roughly the number of analyses on body fluids performed per persons undergoing dialysis in each country during 1984; this varies from 1 to 4 analyses per persons undergoing dialysis.

Question 7 of the questionnaire asked the centre to indicate whether it collaborated in any quality control programme for aluminium analysis. Out of the 569

Table VI. Proportional distribution of aluminium measured in body fluids during 1984

Member State	Al measured in body fluid 1984 (%)			Number of persons undergoing dialysis tested
	<100 µg/l	100-200 µg/l	>200 µg/l	
European Community	79.5	14.5	6.0	22,985
Belgium	89.7	8.4	1.9	1,658
Denmark	81.8	15.9	2.3	44
Eire	88.0	12.0	0	50
Federal Republic of Germany	75.9	19.1	5.0	5,480
France	78.5	12.9	8.5	7,925
Greece	87.5	12.5	0	40
Italy	82.8	12.6	4.6	1,294
Luxembourg	0	0	0	0
Netherlands	70.5	23.7	5.8	1,259
Portugal	96.4	3.6	0	470
Spain	74.2	14.0	11.8	1,122
United Kingdom	83.8	12.7	3.5	3,643

Table VII. Total number of aluminium analyses carried out in 1984

Member States	Analyses in 1984 (n)		
	Raw water	Dialysis fluids	Body fluids
European Community	16,159	22,782	70,274
Belgium	89	8,176	3,355
Denmark	13	13	185
Eire	113	10	52
Federal Republic of Germany	800	1,506	14,475
France	2,351	4,864	25,563
Greece	4	3	40
Italy	757	1,310	3,138
Luxembourg	43	44	2
Netherlands	84	115	2,826
Portugal	28	67	1,126
Spain	268	430	2,809
United Kingdom	11,529	6,244	16,703

Table VIII. Centres participation in quality assurance programmes for aluminium analysis in 1984

Member State	Quality Assurance Programme		
	Participate	Don't participate	Total
European Community	109	444	553
Belgium	16	22	38
Denmark	4	5	9
Eire	0	3	3
Federal Republic of Germany	20	144	164
France	14	131	145
Greece	0	2	2
Italy	14	42	56
Luxembourg	1	2	3
Netherlands	6	17	23
Portugal	0	9	9
Spain	12	51	63
United Kingdom	22	16	38

centres with access to aluminium analysis, 553 provided an answer to this question. Among these, 109 reported participation in a quality assurance programme (table VIII). The vast majority, 444 or 80.3 % reported no participation in a quality control programme, but a keen interest in participating in a Community Quality Control Programme if available.

Conclusions

Although the draft directive on aluminium has not been adopted as yet by the Council, the actions taken by the Commission in this area over the past years have greatly contributed to stimulate the interest of the people directly concerned by involving them in a common effort to help solving the problems related with the aluminium intoxication of the persons with total renal failure under dialysis treatment.

As already mentioned there are 1406 known dialysis centres in the twelve Member States of the European Communities and these take care of about 72,000 persons undergoing dialysis.

The response rate of 62.6 % to the present survey as opposed to that of 1982, when only 42 % of the dialysis centres to whom the questionnaire was sent returned it, is a possible sign of an increased concern towards aluminium toxicity in persons undergoing dialysis.

With regards to the reference levels of aluminium in serum of the proposal for a Directive the number of persons undergoing dialysis with high levels of aluminium body burden is still elevated (6 % over 200 µg/l overall, with some Member States exceeding 11 %); the number of persons undergoing dialysis in whom the aluminium level in serum or plasma does not seem to be analysed is also very high. This is an indication that the health problems related to aluminium exposure and absorption of persons undergoing dialysis might be underestimated.

If this is true for the dialysis centres which have returned the CEC-EDTA questionnaire, and are, no doubt, concerned with the problem, it may be implied

that within the centres which did not reply, the problems of aluminium exposure and absorption are even less taken into consideration.

This study has also shown that, although only a minority of the dialysis centres having replied participate in quality control programmes, most of them would be interested in participating should one be set up.

Following the results of this survey a list of more than 200 laboratories performing aluminium analysis has been drawn, and have been requested to participate if they wished, in a European Quality Assurance Programme. More than 100 of these laboratories have answered positively and the programme which is coordinated by the University of Guildford (UK), which carries out already a similar programme on an international scale, will be starting soon.

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