Effectiveness of pre-emptive hemodialysis with high-flux membranes for the treatment of life-threatening alcohol poisoning

R. Peces[1], R. Fernández[2], C. Peces[3], E. González[1], E. Olivas[1], F. Renjel[1], M. Jiménez[2], O. Costero[1], A. Montero[1] and R. Selgas[1]

[1]Servicio de Nefrología. Hospital Universitario La Paz. Madrid. [2]Unidad de Cuidados Intensivos. Hospital Universitario La Paz. Madrid. [3]Área de Tecnología de la Información. SESCAM. Toledo.

Nefrología 2008; 28 **(4)** 413-418

SUMMARY

Alcohol intoxication (methanol, ethanol and ethylene glycol) may result in metabolic acidosis with increased anion gap, increased serum osmolal gap, and neurologic abnormalities ranging from drunkenness to coma, and death. The mortality and morbidity rates remain very high despite intensive care therapy. The toxicity of methanol and ethylene glycol is clearly correlated to the degree of metabolic acidosis. The established treatment of severe methanol and ethylene glycol intoxication is ethanol administration and hemodialysis (HD). By inhibiting the main metabolic pathway of methanol and ethylene glycol (alcohol dehydrogenase), ethanol prevents the formation of major toxic metabolites (formic acid, glycolic acid and oxalic acid). Conventional HD can reduce serum methanol, ethanol and ethylene glycol and its metabolites rapidly, but high-flux membranes should be capable of removing more toxic per hour of HD. In this report, we describe 14 cases of life-threatening alcohol intoxication (11 methanol, 1 ethanol, and 2 ethylene glycol) who were treated successfully with supportive care, ethanol infusion (methanol and ethylene glycol), and early HD with a high-flux dialyser. The median pH was 7.04 ± 0.06 (range 6.60-7.33), median bicarbonate 9.9 ± 1.9 mmol/l (range 1.4-25), and median base deficit 18.4 ± 2.6 mmol/l (range 2-33). The median anion gap was 29.1 ± 2.3 mmol/l (range 16-45) and the median osmolal gap was 119 ± 47 mOsm/l (range 16-402). On admission there was an excellent linear correlation between the serum toxic alcohol concentrations and the osmolal gaps (R^2 = 0.98, p = 0.0006). In all cases early HD corrected metabolic acidosis and osmolal abnormalities. The mortality was 7% (1 from 14). We conclude that pre-emptive HD should be performed in severe intoxications to remove both the parent compound and its metabolites. The HD prescription should include a large surface area dialyser with high-flux membrane, a blood flow rate in excess of 250 ml/min, a modified bicarbonate bath enriched with phosphorus and potassium, and a long time session. The phosphorus and potassium-enriched bicarbonate-based dialysis solution used in patients with normal phosphorus and potassium serum levels avoided HD-induced hypophosphatemia and hypopotassemia. HD as implemented in these cases is a safe and very effective approach to the management of alcohol poisoning.

Key words: *Anion gap. Ethanol. Ethylene glycol. Hemodialysis. High-flux membranes. Metabolic acidosis. Methanol. Osmolal gap.*

RESUMEN

La intoxicación por alcoholes (metanol, etanol y etilenglicol) origina acidosis metabólica severa con hiato aniónico y osmolal elevados, alteraciones neurológicas que van desde la obnubilación al coma profundo, amaurosis y muerte. A pesar de la terapia intensiva la morbilidad y la mortalidad siguen siendo muy elevadas. En la intoxicación por etilenglicol, además, puede ocurrir la precipitación masiva de oxalato en los tejidos, sobre todo en el riñón, produciendo un fracaso renal agudo. El tratamiento establecido, en las intoxicaciones por metanol y etilenglicol, es la administración de etanol y la hemodiálisis (HD) precoz. La HD convencional puede reducir rápidamente los niveles de metanol, etanol y etilenglicol, así como los de sus metabolitos tóxicos, corrigiendo también los trastornos electrolíticos y ácido-base. Las membranas de alto flujo son capaces de eliminar más cantidad de tóxico por hora de HD pudiendo ser más eficaces en el tratamiento. En este estudio se presentan 14 casos de intoxicación por alcoholes (11 metanol, 1 etanol y 2 etilenglicol) tratados precozmente con bicarbonato, infusión de etanol (para metanol y etilenglicol) y HD con membranas de alto flujo. Al ingreso el pH medio fue 7,04 ± 0,06 (rango 6,60-7,33), el bicarbonato medio de 9,9 ± 1,9 mmol/l (rango 1,4-25) y el déficit de bases medio de 18,4 ± 2,6 mmol/l (rango 2-33). El hiato aniónico inicial fue de 29,1 ± 2,3 mmol/l (rango 16-45) y el hiato osmolal de 119 ± 47 mOsm/l (rango 16-402). Existió una excelente correlación lineal entre los niveles séricos iniciales del alcohol tóxico y el hiato osmolal (R^2 = 0,98, p = 0,0006). En todos los casos, el tratamiento precoz con HD corrigió la acidosis metabólica y el hiato osmolal. De los 14 casos, 11 sobrevivieron sin secuelas, 2 quedaron con amaurosis y 1 falleció (mortalidad 7%). Se concluye que en las intoxicaciones severas por alcoholes la HD debe instaurarse precozmente. La infusión de etanol, al frenar el me-

Correspondence: *R. Peces*
Servicio de Nefrología
Hospital Universitario La Paz
Paseo de la Castellana, 261
28046 Madrid
cpeces@varnet.com

tabolismo del metanol y del etilenglicol, permite la eliminación rápida por HD de los alcoholes y sus metabolitos tóxicos. La prescripción de HD debe incluir un dializador de alto flujo y gran superficie, un flujo sanguíneo elevado, un baño de bicarbonato con concentraciones normales de potasio y fósforo, y debe prolongarse el tiempo necesario. La modificación del baño de HD evita la hipofosfatemia y la hipopotasemia. La HD según fue implementada en estos casos es una forma segura y efectiva de tratamiento de la intoxicación grave por alcoholes.

Palabras clave: Acidosis metabólica. Etanol. Etilenglicol. Hemodiálisis de alto flujo. Hiato aniónico. Hiato osmolar. Metanol.

INTRODUCTION

Poisoning induced by alcohols (methanol, ethanol, and ethylene glycol) may cause neurological changes ranging from confusion to deep coma, amaurosis, and death. Despite intensive treatment, morbidity and mortality continue to be very high, mainly because of the delay in diagnosis and treatment.[1-6] Toxicity from methanol, ethanol, and ethylene glycol is related to the degree of metabolic acidosis and the increase in plasma osmolality induced.[1-3] By inhibiting the main metabolic pathway of methanol and ethylene glycol, alcohol dehydrogenase (ADH), ethanol, and fomepizole prevent the formation of the main toxic metabolites, formic acid from methanol and glycolic and oxalic acids from ethylene glycol.[7] The established treatment for severe poisoning by methanol and ethylene glycol is administration of ethanol and pre-emptive HD.[1-7] Conventional HD treatment may rapidly decrease levels of methanol, ethanol, and ethylene glycol, as well as their metabolites, and also correct electrolyte and acid-base disorders, but high-flux membranes may remove a greater amount of toxic per hour of HD, increasing its efficacy [8]. The study objective was to prospectively analyze the effectiveness of therapeutic measures, including dialysis, in cases of poisoning by these alcohols where an early treatment protocol including bicarbonate administration, ethanol infusion, HD using high-flux membranes, and a modified bath to prevent hypophosphatemia and hypokalemia was used.

MATERIALS AND METHODS

Data from 14 patients admitted to our hospital in the past 3 years for poisoning with methanol (11), ethanol (1), and ethylene glycol (2) are reported. Initial diagnosis was made based on a clinical history with sufficient evidence of intake of toxic alcohols (statements from patients themselves or witnesses, and containers brought with residues of toxics ingested), as well as the presence of metabolic acidosis with elevation of the anion and/or osmolal gaps. In addition, whenever possible, serum levels (as well as urinary and gastric juice levels in some cases) of the corresponding toxic alcohols were measured by gas chromatography (National Institute of Toxicology and Forensic Science, Ministry of Justice, Madrid). Routine procedures were used to test all other biochemical parameters such as electrolytes, osmolality, arterial blood gases, etc. on arrival to the emergency room, before the start and at the end of dialysis treatment, and throughout the course. Anion gap was calculated using the standard formula $(Na^+ + K^+) - (Cl^- + HCO_3^-)$, and osmolal gap by subtracting from the osmolality measured (osmometer) the osmolality calculated with the standard formula. Calculated serum osmolality (mOsm/L) = 2 x Na + Urea (mg/dL)/6 + glucose (mg/dL)/18.

To correct metabolic acidosis, 100 to 300 mL of 1 M sodium bicarbonate and 1,000 mL of isotonic saline were initially infused to all patients. Repeat infusion of 1 M sodium bicarbonate was required in some cases to maintain bicarbonate levels at safe levels until HD was started. As fomepizole was not available, ethanol infusion was used to inhibit ADH in patients with methanol and ethylene glycol poisoning. Treatment was started with a loading dose of ethanol (750 mL of a 10% solution in 5% glucose) over 30 minutes. A 10% ethanol infusion at 100 mL/h was subsequently administered. During the HD session, ethanol infusion was increased to 150-200 mL/h, and in some cases the 100 mL/h infusion was continued for 8-24 hours. In patients intoxicated by methanol, folic acid was administered IV at a dose of 20 mg/8 h to accelerate formate metabolism. In cases of ethylene glycol poisoning, pyridoxine (50 mg/6 h IM) was administered to convert glyoxylate into glycine, and thiamine (100 mg/6 h IM) to convert glycolic acid into α-hydroxy-β-ketoadipate. A certain proportion of alcohols and their metabolites is excreted by the kidney (20% of ethylene glycol, 2%-5% of ethanol, and 1%-2% of methanol), so that a forced diuresis at 200 mL/hour was maintained in all patients showing no renal failure.

For HD, a dual lumen femoral catheter, a dialyzer with a high permeability polysulfone or polyamide membrane 1.6 to 2.1 m^2 in surface area, a blood flow of 250-350 mL/min, and a bicarbonate batch with a flow rate of 500 mL/min were used. During HD (4 to 6 hours), ultrafiltrate volume was replaced by isotonic saline (2,000 to 3,000 mL). In order to prevent hypophosphatemia and hypokalemia, patients with normal renal function and normal serum levels of phosphorus and potassium were dialyzed with a HD solution of bicarbonate enriched with phosphorus and potassium.[9,10] The commercial HD bicarbonate solution (Gambro 290®) was modified by mixing water with the base and acid concentrate, adding 1 M monopotassium phosphate (KH_2PO_4), 1 M dipotassium phosphate

Table I. Electrolyte composition of a modified commercial hemodialysis solution

	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)	P (mg/dL)	Ca (mg/dL)	Mg (mg/dL)
Commercial HD solution	138	2	108.5	0	5	1
Modified HD solution	139 ± 0.3	3.9 ± 0.1	110 + 0.4	3.1 ± 0.1	4.9 ± 0.1	1.1 ± 0.02

(X ± SEM, n = 32).

Table II. Clinical data of patients intoxicated by methanol (M), ethanol (E), and ethylene glycol (EG)

Case	Age	Sex	GCS	Toxic levels (mg/dL)	Treatment	Mechanical ventilation	Prognosis
1	44	V	3	(M) 130	Ethanol + HD	Yes	Recovery
2	43	V	12	(M) ND	HD	No	Recovery
3	25	M	14	(M) < 10 (post-HD)	Ethanol + HD	No	Recovery
4	24	V	14	(M) < 10 (post-HD)	Ethanol + HD	No	Recovery
5	44	V	12	(M) < 10 (post-HD)	Ethanol + HD HDF	No	ARF, amaurosis, recovery
6	56	V	3	(M) 500	Ethanol + HD	Yes	ARF, death
7	44	V	8	(EG) ND	Ethanol + HD	Yes	ARF recovery
8	47	V	4	(EG) ND	HD	Yes	Recovery
9	28	M	14	(M) 19	Ethanol + HD	No	Recovery
10	26	M	14	(M) 34	Ethanol + HD	No	Recovery
11	32	M	14	(M) ND	Ethanol	No	Recovery
12	40	M	3	(E) 284	HD	Yes	Recovery
13	47	M	12	(M) 54	Ethanol + HD	No	Recovery
14	39	M	3	(M) 900	Ethanol + HD	Yes	Amaurosis recovery

GCS = Glasgow Coma Scale; HDF = Hemodiafiltration; ND = Not done; ARF = Acute renal failure.

(K_2HPO_4), and 2 M potassium chloride (KCl). After addition of the phosphorus and potassium preparation, the mix was vigorously shaken to ensure that no precipitation occurred. The final HD solution had the following theoretical composition: potassium 4 mmol/L and phosphorus 3 mg/dL. Samples of the final HD solution were analyzed. Table I shows the composition of the commercial and modified HD solutions used in patients with normal kidney function and normal phosphorus and potassium levels.

In some patients with methanol poisoning, the theoretical duration of HD required was retrospectively calculated using the Hirsch formula:[11,12] Time (hours) = -V ln (5/C)/0.06 k, where V is the volume of H_2O in liters, C is the initial methanol concentration in mmol/L, and k represents 80% of the urea clearance of the dialyzer used. Values are given as mean ± SEM, and statistical analysis was performed using the linear regression method.

RESULTS

Table II shows the clinical characteristics, therapeutic measures, and prognosis of the study patients. Sex distribution was 7 males and 7 females. Six of the 14 patients (43%) experienced coma and required mechanical ventilation, 3 patients (21%) had acute renal failure, and 13 patients (93%) were treated with HD. Table III gives the laboratory test results on admission of intoxicated patients. Several patients (11 out of 14) were admitted to hospital several hours (up to 24) after poisoning, when they already had a marked metabolic acidosis. On admission, mean pH was 7.04 ± 0.06 (range 6.60-7.33), mean bicarbonate levels were 9.9 ± 1.9 mmol/L (range 1.4-25), and mean base deficit was 18.4 ± 2.6 mmol/L (range 2-33). Mean initial anion gap was 29.1 ± 2.3 mmol/L (range 16-45), and mean initial osmolal gap was 119 ± 47 mOsm/L (range 16-402). An excellent linear correlation was found between initial serum levels of the toxic alcohol and osmolal gap (R^2 = 0.98, p = 0.0006) (fig. 1). In several cases, mental or visual changes appeared within 6 to 24 hours of toxic intake. In some patients, concomitant intake of large amounts of ethanol (Cases 2, 3, 4, 9, 10, and 11) resulted in less toxic effects, that were delayed for up to 24-36 hours from intake to hospital arrival Except for Case 6, who showed at hospital admission a grade 3 coma, multiorgan failure, profound acidosis, a high osmolal gap, and very high methanol levels (500 mg/dL) and died, 11 patients survived without sequelae and 2 patients with amaurosis (7% mortality) (Tables II and III). Most patients, except for the one who died, Case 7 with renal failure and Case 14, required a single HD session. In Case 5, HDF was performed for some hours after the HD session. Case 7, who experienced acute renal failure, required regular HD sessions for 14 days until recovery of kidney function. Case 14 received three consecutive HD sessions because of the extreme severity of poisoning, and required mechanical ventilation and intensive therapy for 4 weeks after experiencing bronchial aspiration. This patient, diagnosed of schizophrenia, already had amaurosis as a result of a prior episode of methanol poisoning. Table IV gives the data of patients in whom the theoretical HD time required to achieve methanol serum levels lower than 16 mg/dL was calculated according to the Hirsch formula,[11,12] as well as the actual HD duration.

DISCUSSION

If there is no history of alcohol intake (methanol, ethanol, or ethylene glycol), initial diagnosis is difficult. Measurement of serum levels of these alcohols is helpful, but is not always available. Diagnosis depends on an obvious epidemiological context and on the finding of metabolic acidosis with an elevated anion gap and/or osmolal gap.[13-15] Osmolal gap may overestimate in some cases the amount of alcohol present in serum. However, the discrepancies between the measured and calculated osmolalities are approximately 32, 21, and 17 mOsm/L per 100 mg/dL increase in methanol, ethanol, and ethylene glycol concentrations respectively.[1,2] These data allow for indirect estimation of toxic alcohol levels when direct estimation of such levels is not initially available.

All alcohols have a low molecular weight, protein binding, and distribution volume, and may therefore be efficiently re-

Table III. Laboratory test results on admission in patients with methanol, ethanol, and ethylene glycol poisoning

Case	Na mmol/L	K mmol/L	Cl mmol/L	HCO_3 mmol/L	Anion gap mmol/L	Osmolal gap mOsm/L	pH	PCO_2 mmHg	Base deficit mmol/L	Urea mg/dL	Glucose mg/dL
1	141	5.9	99	4.8	43	79	6.80	29	25	16	288
2	132	7.6	102	2.3	35	16	6.99	10	27	24	112
3	133	4.7	103	5.3	29	34	7.07	18.5	23	30	106
4	136	4.7	106	10.6	24	65	7.21	27.2	17	24	122
5	141	4.4	105	4.1	36	ND	7.11	13.2	23	23	144
6	139	4.3	107	7.1	29	231	6.60	–	–	85	150
7*	146	6.2	106	1.4	45	ND	6.70	9.3	33	73	189
8*	144	3	105	14.5	28	ND	6.93	10	18	24	489
9	131	3.7	104	9.2	22	ND	7.27	20.6	15.4	18	132
10	137	5.1	103	7.8	31	ND	7.05	29	22	38	135
11	138	3.6	103	20	19	ND	7.33	39	5	14	87
12•	142	3.1	109	20	16	100	7.33	40	5	13	97
13	138	4.6	106	6.3	31	23	7.01	26	23.7	24	159
14	145	3.4	103	25	20	402	7.29	54	2	28	231

*Ethylene glycol; •Ethanol.

moved by HD.[16-18] HD may also remove organic acid anions such as formate, glycolate, and glyoxylate. Intermittent HD is the most efficient method for rapidly decreasing serum levels of toxic alcohols or for removing organic acid anions. While less effective, continuous therapies have also been occasionally used.[19] However, some toxicokinetic studies have confirmed the superiority of HD over continuous procedures for clearance of methanol and ethylene glycol, and also for rapid correction of the associated biochemical changes.[19,20] HD may achieve clearances of 200-250 mL/min for ethylene glycol, 200 mL/min for methanol, 170 mL/min for glycolate, and 223 mL/min for formate.[21-23] On the other hand, high-flux membranes are able to remove a greater amount of toxic per hour of HD, thus increasing its efficacy.[8]

All our patients developed a severe degree of poisoning as demonstrated by the clinical signs, the degree of metabolic acidosis, and the elevations in anion gap and/or osmolal gap they had upon arrival. All patients initially received bicarbonate and volume expansion with isotonic saline to correct acidosis and promote diuresis. Most patients with methanol or ethylene glycol poisoning (11 of 13) were treated with an ethanol infusion to inhibit metabolism of alcohols into their toxic metabolites. Patients intoxicated by methanol were also given folic acid to promote catalase-mediated metabolism of formic acid, while those with ethylene glycol poisoning received thiamine and pyridoxine to promote conversion of glyoxylate into metabolites less toxic than oxalate, such as glycine.[4,5,23,24] In some cases, ethanol infusion was continued during the HD session and prolonged for several hours (8 to 20) after the end of the session. Most patients (13 out of 14) underwent HD for 4 to 6 hours. In several patients this resulted in restoration of consciousness, disappearance of visual disturbances, and normalization of water, electrolyte, and acid-base disorders. The only case of ethanol poisoning, who was treated with a HD session, occurred in a 40-year-old woman in the first weeks of pregnancy with acute ethanol intoxication complicated by deep coma requiring mechanical ventilation associated to metabolic acidosis and elevated osmolal gap. HD was also indicated in this patient in an attempt to prevent lesions in the embryo, including the fetal alcoholic syndrome.[25,26] Despite the severe involvement, all patients completely recovered from biochemical changes, as well as neurological changes and visual disorders, and mortality was only 7%. This low mortality is in contrast to the death rates of

Table IV. HD duration estimated based on initial toxic levels and actual HD duration

Case	Toxic levels (mmol/L)	Estimated HD duration (hours)	Actual HD duration (hours)
1	41	9.6	4
3	3 (post-HD)	NP	4
4	3 (post-HD)	NP	5
5	3 (post-HD)	NP	4 + HDF (FRA)
6	156	10.7	6 (FRA)
9	6	0.4	6
10	11	1.7	6
12	(E) 64	5.6	4
13	17	2.7	6
14	281	9	5 + 6 + 4

E = Ethanol, NA = Not applicable; HDF = Hemodiafiltration; ARF = Acute renal failure.

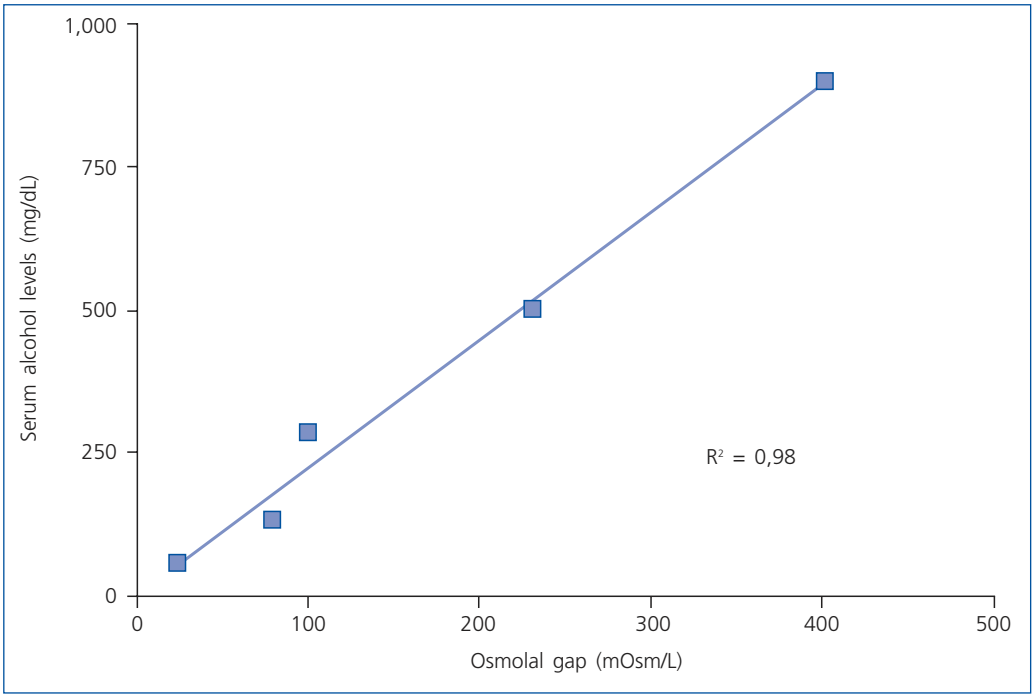

Figure 1. Baseline serum levels of the toxic alcohol *versus* osmolal gap in 5 intoxicated patients.

19% and 46% respectively reported by other studies [27,28]. In 2 large series of patients with methanol poisoning recently reported in Northern Europe, the mortality rates were 18% and 44% respectively.[29,30] Effectiveness of the procedure in our patients may have been due to early diagnosis and treatment, and to use of long HD with high-flux dialyzers that allowed for rapid correction of all changes. In addition, use for HD of a bicarbonate batch enriched with phosphorus and potassium[31] prevented the occurrence of hypokalemia and hypophosphatemia as side effects from HD.

Use of a simple formula that would allow for predicting and prescribing the HD duration required using only the initial levels of the toxic has recently been advocated.[12] When this formula was used in some of our patients (table IV), the theoretical time of HD required was found out to be highly variable, and the calculated values differed from the actual HD duration in some of the patients. Since toxic alcohol levels are not usually known until many hours or days later, prescription of HD duration should be based on the clinical course of coma, pH and bicarbonate correction and, above all, on normalization of osmolal gap[32-37] which, as confirmed by our results, showed an excellent correlation with serum levels of toxic alcohols (fig. 1).

In conclusion, alcohol poisoning may cause severe cell damage that may be irreversible, and if left untreated or treated at a late stage, may be associated with high mortality and morbidity. A high suspicion index is therefore required in the presence of metabolic acidosis with increased anion and/or osmolal gaps, acute renal failure, or unexplained visual or neurological changes. When poisoning by these toxic substances is strongly suspected or their serum levels are documented, general supportive measures should be taken, and treatment with ethanol and HD must be started as soon as possible. HD prescription should include a high-flux, large surface area dialyzer, a high blood flow rate, and a bicarbonate bath with normal phosphorus and potassium concentrations, and a prolonged session.

ACKNOWLEDGEMENTS

We thank the National Institute of Toxicology and Forensic Science of the Ministry of Justice (Madrid) for measurements of toxic alcohol levels.

REFERENCES

1. Sivilotti ML, Winchester JF. Methanol and ethylene glycol intoxication. Version 15.3. UpToDate Inc. Wellesley, USA, 2008.
2. Seyffart G: Methyl alcohol; in Seyffart G (ed). Poison index: the treatment of acute intoxication. Lengerich, Pabst Science Publishers, 1997; pp. 457-464.
3. Kraut JA, Kurtz I. Toxic alcohol ingestions: clinical features, diagnosis, and management. *Clin J Am Soc Nephrol* 2008; 3: 208-225.
4. Barceloux DG, Krenzelok EP, Olson K, Watson W. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Ethylene Glycol Poisoning. Ad Hoc Committee. *J Toxicol Clin Toxicol* 1999; 37: 537-560.
5. Barceloux B, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology Practice Guidelines for the Treatment of Methanol Poisoning. *J Toxicol Clin Toxicol* 2002; 40: 415-446.
6. Jacobsen D, McMartin KE. Antidotes for methanol and ethylene glycol poisoning. *J Toxicol Clin Toxicol* 1997; 35: 127-143.
7. Megarbane B, Borron SW, Baud FJ. Current recommendations for treatment of severe toxic alcohol poisonings. *Intensive Care Med* 2005; 31: 189-195.
8. Peces R, Álvarez R. Effectiveness of hemodialysis with high-flux polysulfone membrane in the treatment of life-threatening methanol intoxication. *Nephron* 2002; 90: 216-218.
9. Dorval M, Pichette V, Cardinal J, Geadah D, Ouimet D, Leblanc M. The use of an ethanol- and phosphate-enriched dialysate to maintain stable serum ethanol levels during haemodialysis for methanol intoxication. *Nephrol Dial Transpl* 1999; 14: 1774-1777.

10. Chebrolu SB, Hariman A, Eggert CH, Patel S, Kjellstrand CM, Ing TS. Phosphorus-enriched hemodialysis for the treatment of patients with severe methanol intoxication. *Int J Artif Organs* 2005; 28: 270-274.
11. Hirsch DJ, Jindal KK, Wong P, Fraser AD. A simple method to estimate the required dialysis time for cases of alcohol poisoning. *Kidney Int* 2001; 60: 2021-2024.
12. Youssef GM, Hirsch DJ. Validation of a method to predict required dialysis time for cases of methanol and ethylene glycol poisoning. *Am J Kidney Dis* 2005; 46: 509-511.
13. Haviv YS, Rubinger D, Zamir E, Safadi R. Pseudo-normal osmolal and anion gaps following simultaneous ethanol and methanol ingestion. *Am J Nephrol* 1998; 18: 436-438.
14. Meatherall R, Krahn J. Excess serum osmolality gap after ingestion of methanol. *Clin Chem* 1990; 36: 2004-2007.
15. Ammar KA, Heckerling PS. Ethylene glycol poisoning with a normal anion gap caused by concurrent ethanol ingestion: importance of the osmolal gap. *Am J Kidney Dis* 1996; 27: 130-133.
16. Wadgymar A, Wu GG. Treatment of acute methanol intoxication with hemodialysis. *Am J Kidney Dis* 1998; 31: 897.
17. Garella S. Extracorporeal techniques in the treatment of exogenous intoxications. *Kidney Int* 1988; 33: 735-754.
18. Peterson CD, Collins AJ, Himes JM et al. Ethylene glycol poisoning: pharmacokinetics during therapy with ethanol and hemodialysis. *N Engl J Med* 1981; 304: 21-23.
19. Kan G, Jenkins I, Rangan G, Woodroffe A, Rhodes H, Joyce D. Continuous haemodiafiltration compared with intermittent haemodialysis in the treatment of methanol poisoning. *Nephrol Dial Transplant* 2003; 18: 2665-2667.
20. Christiansson LK, Kaspersson KE, Kulling PE, Ovrebo S. Treatment of severe ethylene glycol intoxication with continuous arteriovenous hemofiltration dialysis. *J Toxicol Clin Toxicol* 1995; 33: 267-270.
21. Abramson S, Singh AK. Treatment of the alcohol intoxications: ethylene glycol, methanol and isopropanol. *Curr Opin Nephrol Hypertens* 2000; 9: 695-701.
22. Moreau CL, Kerns W, Tomaszewski CA, McMartin KE, Rose SR, Ford MD, Brent J. Glycolate kinetics and hemodialysis clearance in ethylene glycol poisoning. *J Toxicol Clin Toxicol* 1998; 36: 659-666.
23. Kerns W, Tomaszewski C, McMartin K, Ford M, Brent J. Formate kinetics in methanol poisoning. *J Toxicol Clin Toxicol* 2002; 40: 137-143.
24. Brent J. Current management of ethylene glycol poisoning. *Drugs* 2001; 61: 979-988.
25. Rubert G, Miñana R, Pascual M, Guerri C. Ethanol exposure during embryogenesis decreases the radial glial progenitor pool and affects the generation of neurons and astrocytes. *J Neurosci Res* 2006; 84: 483-496.
26. Fischer D, Solbach C, Kitz R, Ahr A, Veldman A. Acute ethanol intoxication during pregnancy and consecutive fetal cardiac arrest: a case report. *J Perinat Med* 2003; 31: 343-344.
27. Nolla-Salas J, Nogué Xarau S, Marruecos Sant L, Palomar Martínez M, Martínez Pérez J. Methanol and ethylene glycol poisoning. Study of 18 cases. *Med Clin (Barc)* 1995; 104: 121-125.
28. Brahmi N, Blel Y, Abidi N, Kouraichi N, Thabet H, Hedhili A, Amamou M. Methanol poisoning in Tunisia: report of 16 cases. *Clin Toxicol (Phila)* 2007; 45: 717-720.
29. Hovda KE, Hunderi OH, Tafjord AB, Dunlop O, Rudberg N, Jacobsen D. Methanol outbreak in Norway 2002-2004: Epidemiology, clinical features and prognostic signs. *J Intern Med* 2005; 258: 181-190.
30. Paasma R, Hovda KE, Tikkerberi A, Jacobsen D. Methanol mass poisoning in Estonia: Outbreak in 154 patients. *Clin Toxicol* 2007; 45: 152-157.
31. Chow MT, Silvestro VA, Yung CY, Nawab ZM, Leehey DJ, Ing TS. Treatment of acute methanol intoxication with hemodialysis using an ethanol-enriched, bicarbonate-based dialysate. *Am J Kidney Dis* 1997; 30: 568-570.
32. Hovda KE, Hunderi OH, Rudberg N, Froyshov S, Jacobsen D. Anion and osmolal gaps in the diagnosis of methanol poisoning: clinical study in 28 patients. *Intensive Care Med* 2004; 30: 1842-1846.
33. Hunderi OH, Hovda KE, Jacobsen D. Use of the osmolal gap to guide the start and duration of dialysis in methanol poisoning. *Scand J Urol Nephrol* 2006; 40: 70-74.
34. Hassanian-Moghaddam H, Pajoumand A, Dadgar SM, Shadnia Sh. Prognostic factors in methanol poisoning. *Hum Exp Toxicol* 2007; 26: 583-586.
35. Liu JJ, Daya MR, Carrasquillo O, Kales SN. Prognostic factors in patients with methanol poisoning. *J Toxicol Clin Toxicol* 1998; 36: 175-181.
36. Elwell RJ, Darouian P, Bailie GR. Delayed absorption and postdialysis rebound in a case of acute methanol poisoning. *Am J Emerg Med* 2004; 22: 126-127.
37. Hantson P, Haufroid V, Wallemacq P. Formate kinetics in methanol poisoning. *Hum Exp Toxicol* 2005; 24: 55-59.