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Use of Continuous Vein-Venous Hemodiafiltration and On-Line Hemodiafiltration in Four Cases of Acute Arsine Gas Poisoning

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Abstract

Introduction: Extensive hemolysis resulting in anuric renal failure is the main clinical sign of acute arsine poisoning. Plasmapheresis and exchange transfusion are recommended for patients with massive hemolysis. We report four cases of arsine exposure which demonstrate the effectiveness of continuous vein-venous hemodiafiltration and on-line hemodiafiltration for arsenic removal.

Method: Blood samples were obtained from four males admitted to Poisoning Treatment Centre during 2014–2015. The arsenic concentration was measured by a hydride atomic absorption analysis using ZeeNit 600 atomic absorption analyzer.

Results: Three of the patients developed acute renal failure and underwent dialysis over 35 to 38 days. In two cases of on-line hemodiafiltration- (on-line HDF) arsenic blood concentration decreased for 57 and 16%, total amount of arsenic removed was 98.7 mg and 43.3 mg, average arsenic clearance was 79.8 ± 30.0 ml/min. During continuous vein-venous hemodiafiltration (CVVHDF) arsenic blood concentration decreased for 99% arsenic clearance was 121.6 and 200 ml/min. Renal arsenic clearance was 75.6 ml/min. Arsenic half-life noticeably reduced during both reported procedures.

Conclusion: Both on-line HDF and CVVHDF were effective for arsenic removal in cases reported in this study. The reducing of arsenic blood concentration did not prevent acute renal failure.

Key Words: Arsine poisoning, continuous vein-venous hemodiafiltration, on-line hemodiafiltration

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Introduction

Although rare, arsine gas poisonings can occur in the color metals industry. The toxicity of arsine was recognized 200 years ago. Since then hundreds cases of poisonings resulting in extensive hemolysis and acute renal failure (ARF) have been reported [1, 2]. The precise mechanisms of hemolysis and renal damage are not fully understood [3-6]. Multiorgan dysfunction including coagulopathy, liver and brain damage, pulmonary edema and circulatory failure are reported in severe cases [5] but the mechanisms of multiple organ damage are also unclear. The mechanisms of toxicity of arsine may be through oxidative stress and glutathione depletion, [4] and interactions with sulfhydryl groups [4]. It is postulated that arsenic-hemoglobin-haptoglobin complex should be removed as soon as possible after arsine exposition to prevent renal damage [1, 7]. Traditionally plasmapheresis and exchange transfusion are recommended for patients with massive hemolysis [1, 5, 7] and renal replacement therapy is implicated for ARF treatment. Several recent publications advocate arsenic removal by hemodialysis (HD) and hemodiafiltration (HDF) [8-10].

We describe four cases of arsine exposure aimed to evaluate the effectiveness of extracorporeal arsenic removal in acute arsine gas poisoning.

Method

Four patients with acute arsine gas poisoning were admitted to the Sverdlovsk Regional Poisoning Treatment Centre during 2014–2015, three of them were involved into the same exposure. Arsenic concentrations were measured at the chemical toxicological laboratory of Sverdlovsk Regional Poisoning Treatment Centre. Microwave mineralization with 6% nitric acid was used for samples preparation. Arsenic concentration in samples was measured by means of a hydride atomic absorption analysis using ZeeNit 600 atomic absorption analyzer.

Fresenius 4008S machine was used for intermittent on-line hemodiafiltration and hemodialysis with blood flow 200–250 ml/min, dialisate flow 500 ml/min; high-flux dialyzer ELISIO 17H was used for HDF. MultiFiltrat machine with AV1000 hemofilter was used for continuous vein-venous hemodiafiltration (CVVHDF).

Elimination half-life ($t_{1/2}$) was calculated from the ratio of arsenic concentration versus time.

The dialyzer clearance (D) was calculated from the standard formula: D= (Q × (A-V)) /A, where Q=Blood flow (ml/min), A=Blood arsenic concentration on the inlet side, V=Blood arsenic concentration on the outlet side of the dialyzer.

The renal clearance (R) was calculated from the formula: R= (U/B) × A × T, where U=Urine arsenic concentration, B=Blood arsenic concentration, A=Urine amount (ml), T=Time for urine collection (min).

The total amount of arsenic removed during hemodiafiltration (A) was calculated from the formula: A= $(q_1+q_2+q_3)$ /3 × (D+S), where q=Dialisate arsenic concentration (microg/ml), D=Amount of dialisate outflowed (ml), S=Amount of substitute (ml).

Results

Case 1

A thirty-nine year old male was admitted 48 hours after exposure to arsine gas in his garage where he worked with heated copper nickel alloy which contained arsenic. He complained of weakness, nausea, dry mouth and backache and had developed orange colored diarrhea, red coloured urine and his urine output was decreased. On admission he was conscious, icteric, anuric (20 ml of black urine), with normal vital signs: heart rate 78 per min and blood pressure 130/60 mmHg. Concentration of free hemoglobin in plasma was 8.4 g/l in the blood and 34 g/l in the urine, serum lactate level 8.63 mmol/l. Blood urea nitrogen (BUN) was 24.65 mmol/l and creatinine 0.437 mmol/l. Blood hemoglobin was 105 g/l on admission but fell to 81 g/l on the second day and 61 g/l on the third day. On admission he was given sodium dimercaptopropansulfone 15 g and N-acethylcisteine (ACC) 6.6 g IV. He underwent 18 hours CVVHDF on the first day with follow up dialysis therapy over 38 days (one more CVVHDF, one procedure of on-line HDF- and 17 HD). Two plasmapheresis with 600 ml of plasma exchange each were done on the fifth and sixth day.

On the fifth day the patient became unconscious, was intubated and ventilated for 37 days. The patient was finally discharged on day 65 although his filtration rate was still low at 39.4 ml/min. The main clinical and laboratory data are summarized in the **Table 1.**

On admission arsenic blood concentration was 1600 microg/l (background level in population 10 microg/l). Ten days later it was still high, 880 microg/l ($t_{1/2}$ 275.3 hours) and the second CVVHDF, for 11 hours were given. At 5 hours the blood arsenic concentration decreased to 175 microg/l (clearance 121.6 ml/min) and was 11.5 microg/l on completion (clearance 200 ml/min). Arsenic half-life ($t_{1/2}$) during CVVHDF was 1.8 hours. On day 12 the patient received intermittent hemodialysis for four hours. The blood arsenic concentration was 135 microg/l before and 105 microg/l after procedure ($t_{1/2}$ 11 hours); Dialyzer column (2.1 m^2) clearances were 37.2 and 39.3 ml/min.

Cases 2–4

Three workers 24, 36 and 25 years old were admitted 10 hours after welding lead solder, which also contained other elements including arsenic, during their six hour shifts. All of them complained of weakness, nausea, vomiting and red-colored urine. One patient (case 3) complained of flank pain and another (case 4) of back pain. They were conscious with normal vital signs but two of them were anuric (cases 3 and 4). These patients underwent on-line HDF for 12 hours after hospital admission while the patient with normal urine output received IV fluids 7600 ml/20 hours. All three patients were treated with full 21-hours dose of ACC.

Arsenic kinetic parameters in cases 3 and 4 during on-line HDF are presented in the **Table 2** Average arsenic clearance was 79.8 ± 30.0 ml/min. The total amount of arsenic removed was 98.7 mg in case 3 and 43.3 mg in case 4. Renal clearance was calculated 75.6 ml/min only for case 2 as the rest were anuric on admission. The amount of arsenic excreted in the urine in case 2 was 26.3 mg during the first eight hours of treatment.

Blood arsenic level decreased in the second case to 176.4 microg/l during the first 168 hours ($t_{1/2}$ 82.5 hours), in the third case to 30.4 microg/l during the first 144 hours ($t_{1/2}$ 22 hours) and in the fourth case to 65.2 microg/l during the first 144 hours ($t_{1/2}$ 27.6 hours).

Discussion

Exchange transfusion is considered to be the method of choice for arsenic-hemoglobin complex removal [1, 7]. Some authors [ý2, ý5] emphasize the value of plasmapheresis in removing arsenic and the patient's rapid recovery in severe acute arsine poisoning. Significant decrease of arsenic blood and urine concentrations after plasmapheresis has been reported [5]. Measured total arsenic removed was 55.4–177.4 in different cases [5].

Hemodialysis does not effective for arsenic-hemoglobin complex removal [1, 2] as this complex is too large. In our first case we also found low arsenic clearance using an ordinary dialyzer. The value of other methods of renal replacement therapy for arsenic removal such as hemofiltration and high-flux dialysis is questionable. Recent publication reported the use of plasma exchange and continuous vein-venous hemodiafiltration in the management of arsine poisoning [10] and the therapeutic benefits

Table 1 Clinical and laboratory data of patients admitted to poison treatment center.

Case	1 – male 39 yo	2 – male 24 yo	3 – male 36 yo	4 - male 25 yo
Free plasma Hb, g/l	8.4	0.1	6.8	6.4
Free urine HB, g/l	34	0.17	16.7	3.1
Blood Hb min, g/l	61	76	75	70
Total bilirubin max, micromol/l	46.9	141.3	46.2	40.3
LDH max, ME/l	6759	841	3745	2760
Initial blood As level, microg/l	1610	724.1	2847	2411
Initial urine As level, microg/l	-	7971	12230	12000
Anuric period duration, days	32	0	27	24
Renal replacement therapy period, days	38	0	37	35
Volume of blood cells transfusion, ml	2450	2040	1730	2700
In hospital days	64	14	49	49
Urine As level before discharging, mg/24 h	-	0.13	1.73	0.8
Filtration rate before discharging, ml/min	39.4	157.1	93.5	61.1

Table 2 Arsenic kinetic parameters in cases 3 and 4 during on-line HDF.

Case	kinetic parameters	5 min HDF	2 hours HDF	4 hours HDF
3 – male 36 yo	As blood level, microg/l	4394	5161	1886
	As outflow dialysate level, microg/l	2296	1388	1253
	As clearance, ml/min	99.7	115.4	-
	$t_{1/2}$, hours		4.9	
4 - male 25 yo	As blood level, microg/l	3188	2529	2688
	As outflow dialysate level, microg/l	1314	799	54
	As clearance, ml/min	83.6	58.5	41.5
	$t_{1/2}$, hours		16.3	

of continuous venovenous hemodialysis, hemoperfusion, plasma adsorption and plasma exchange have been compared [8]. Reductions in arsenic blood and urine concentrations with rapid clinical improvement were observed in three children treated with combined chelating therapy and hemodiafiltration [9].

The present case series showed high arsenic clearance calculated during CVVHDF (case 1) and on-line HDF (cases 3 and 4). Amount of arsenic measured in the dialisate outflow during on-line HDF were comparable with its blood level. Arsenic half-life noticeably reduced during both procedures. In another case description [6] the estimated half-life was also high, 59.2 h.

Despite the effective arsenic removal, all patients who underwent CVVHDF and on-line HDF developed renal failure with prolonged anuric periods and required renal replacement therapy for between 35 and 38 days. Only one patient (case 2) did not develop renal damage. Severe complications developed in case 1 which might be due to the long period of time between the arsine gas exposure and hospital admission. Other patients who were admitted on the first day post exposure did not have any signs of brain damage or multiorgan dysfunction.

Limitations

There are several limitations to be mentioned: plasmapheresis was used only in case 1 even not during the 1st day after exposure and with small amount of plasma exchanged. Also only total arsenic blood and urine concentrations were measured while arsenic compounds were not. Arsenic concentration in outflow dialisate was measured only during on-line HDF procedures but not measured during CVVHDF.

Conclusion

Both on-line HDF and CVVHDF were effective for arsenic removal in the cases reported. It was confirmed by high dialysing clearance, high amount of arsenic removed to outflow dialisate during on-line HDF and the reduction in arsenic half-life. The reduction of arsenic blood concentration did not prevent acute renal failure. A comparative study of plasma exchange and hemodiafiltration should be undertaken to examine the value of these methods in the management of arsine poisoning.

Declaration of Interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

References

1 Hesdorffer CS, Milne FJ, Terblanche J, Meyers AM (1986) Arsine gas poisoning: the importance of exchange transfusions in severe cases. Br J Ind Med 43: 353-355.

2 Pullen-James S, Woods SE (2006) Occupational Arsine Gas Exposure. J Natl Med Assoc 98: 1998-2001.

3 Fowler BA, Weissberg JB (1974) Arsine Poisoning. N Engl J Med 291: 1171-1174.

4 Leonard T, Rael TL, Fierro FA, Bar-Or R, Carter DE, et al. (2006) Interaction of Arsine with Hemoglobin in Arsine-Induced Hemolysis. Toxicological Sciences 90: 142–148.

5 Song Y, Wang D, Li H, Hao F, Ma J, et al. (2007) Severe acute arsine poisoning treated by plasma exchange. Clin Toxicol (Phila) 45: 721-7.

6 Yoshimura Y, Endo Y, Shimoda Y, Yamanaka K, Endo G (2011) Acute arsine poisoning confirmed by speciation analysis of arsenic compounds in the plasma and urine by HPLC-ICP-MS. J Occup Health 53: 45-49.

7 Teitelbaum DT, Kier LC (1969) Arsine poisoning. A report of five cases in the petroleum industry and a discussion of the indications for exchange transfusions and haemodialysis. Arch Environ Health 19: 133-43.

8 Huang C, Zhang P, Liu H, Li Y, Yu Y, et al. (2015) Treatment for acute arsine poisoning with blood purification. Intensive Care Med 41: 549-50.

9 Luzhnikov EA, Sukhodolova GN, Ostapenko YN, Kovalenko LA, Kovalchuk AS (2014) Rare occurrence of arsenic hydride poisoning in children. Clin Toxicol (Phila) 52: 424-425.

10 Tang WX, Wu WH, Cui TL, Qin W, Fu P, et al. (2012) Application of hybrid blood purification treatment for severe acute arsine poisoning. Int J Artif Organs 35: 208-16.