

34. EFFECTS OF SODIUM BICARBONATE IN ORGANOPHOSPHATE PESTICIDE POISONING

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INTRODUCTION:

Organophosphate (OP) compounds are widely used as pesticides in many parts of the world. Acute OP pesticide poisoning is a common cause of admission to the clinical toxicology ward of Imam Reza hospital. Insufficient control on the importation, production, storage and safe use of OP pesticides are the main reasons of poisoning (1).

OP compounds have also been manufactured and used as chemical warfare agents. In 1983 & 1984 in Majnoon Island and in the Halabjeh massacre (1988), OP compounds were used as nerve gases by Iraqi troops. Analysis of the environment, urine and blood samples of victims proved Tabun in Majnoon Island and Sarin in Halabjeh (2,3). Terrorist attacks in Matsomoto (1994) and in the Tokyo subway (1995) by Sarin nerve gas caused 18 deaths and thousands of casualties (4,5).

The very well known antidotes of organophosphate (OP) poisoning are atropine sulphate and oximes (6-8). Atropine counteracts the muscarinic effects of OP poisoning, but the therapeutic effects of oximes are controversial and are not the same in different OPs (9-12). In addition, the high cost of pralidoxime and the hepatotoxicity of obidoxime, particularly with high doses, have urged the clinicians and scientists to search for more additional effective treatment (13).

Palacio studied the effects of sodium bicarbonate (NaHCO_3) in OP pesticide poisoning on experimental animal models with a positive outcome (14). It was thus aimed to study the effects of NaHCO_3 in treatment of patients with acute OP pesticide poisoning.

PATIENTS AND METHODS

The patients (aged 14-60 years) were admitted to the hospital between April 1996 and March 1999 with a history of intentional oral ingestion of a known OP pesticide with ingestion – admission interval of less than 6 hours and revealed clinical features of moderate to severe poisoning were studied. The patients were divided into two groups:

The control patients received atropine (A) and the other received treatment as usual. Atropine sulfate was administered by I.V. to control the muscarinic effects and to induce mild to moderate atropinization (dry mouth, tachycardia, flushing and mydriasis) within 30 minutes. Atropine infusion was continued based on clinical responses to maintain the atropinization. Atropine was tapered based on clinical improvement.

The test group was treated just as the controls, but included was an infusion of sodium bicarbonate (AB) initially 3mEq/kg in one hour, followed by 3mEq/kg in 23h and the same amount every day until recovery/death. Arterial blood gas and pH (ABG) were estimated on admission and at certain intervals by a blood gas analyzer (AVL-99). Acetylcholinesterase (AChE) activity was estimated in red blood cells by the modified Ellman method (15). Clinical and paraclinical findings including AChE activity were recorded on pre-designed forms. The results were analyzed by the Chi-square and Student-t tests using a statistical package for social sciences (SPSS). The results are shown as mean and standard deviations.

RESULTS

Over the three years of study, 50 patients (27M and 23F) were studied in the two groups. Age, sex, weight and vital signs of the patients in each group are summarized in Table 1.

There were no statistically significant differences between the groups on the OP types, AChE activity (385 ± 346 U/L in the test and 428 ± 435 U/L in the controls), arterial blood pH (7.36 ± 0.12 , and 7.32 ± 0.12 , respectively) and initial atropine dose (48.0 ± 39.1 and 53.7 ± 35.8 mg, respectively) required for atropinization on admission. However, on admission clinical findings, only cyanosis and respiratory arrest were significantly higher ($p < 0.05$) in the AB group (Table 2).

There were also no statistical significant differences on AChE activity, clinical severity and ABG during treatment, hospitalization days and ICU therapy between the groups.

Maximum arterial blood pH and NaHCO_3 in the test group were 7.47 ± 0.3 and 24.4 ± 2.4 mEq/L, respectively, which were significantly higher than the controls (7.37 ± 0.8 and 19.5 ± 4.5 mEq/L, respectively, $p < 0.01$) as shown in Table 3. Three patients of the control and only one of the test group died. However, the differences in arterial blood pH and NaHCO_3 were not statistically significant.

DISCUSSION

The severity of intoxication on admission based on clinical findings except for the cyanosis and respiratory arrest, which was higher in the AB group, were similar. Paraclinical findings on admission were also similar in the groups. Thus, the test group had similar and even higher severity of intoxication on admission. Sodium bicarbonate was also used to correct the metabolic acidosis. However, the amount of sodium bicarbonate administered was not enough to induce alkalosis as judged by the arterial pH and bicarbonate of the two groups during treatment. Even the maximum arterial pH and bicarbonate which were significantly higher in the AB group, were lower than the results achieved by Placcio in his animal experiment (14).

It is thus recommended to administer more sodium bicarbonate to achieve an arterial pH of 7.50 to 7.55. Alkalinization of the blood to pH of more than 7.50 by sodium bicarbonate facilitates destruction of OP molecules. Moreover, OPs are ester of phosphoric acid and hydrolysis of the molecules increase with higher pH (16). However, different chemical structures of OPs may reveal different stabilities in acid solution and react differently in alkali solution. Dimethoate, methyl parathion, malathion and trichlorfos in particular were more stable in acid solution whilst diazinon was less stable in acid solution (17). This could suggest that sodium bicarbonate therapy might be successful in the management of intoxication with some OPs like dimethoate, methyl parathion, malathion and dichlorfos. It is thus very important to study the effects of sodium bicarbonate in each OP separately.

CONCLUSIONS

The sodium bicarbonate doses used in this study were not big enough to produce significant alkalinization. Due to the different chemical structures of OPs, and their different stabilities in acid solution, further study is recommended with higher doses of sodium bicarbonate in each OP separately.

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REFERENCES

1. Balali-Mood, M., Shariat, M. Pattern of acute poisoning in Mashed. M.J. Nabz, 1995; 5: 13-19.
2. Foroutan, A. Report of the specialist appointed by the Secretary-General of the United Nation to investigate allegation by the Islamic Republic of Iran concerning the use of chemical weapons, proceeding of the First World Congress on Biological and Chemical Warfare, Ghent, May 21-23, 1984; 302-310.
3. Hendrickx, B. Report and conclusion of the biological samples of men, intoxicated by was gases, send to the department of toxicology of the state university of Ghent, for toxicological investigation proceeding of the Second World Congress on Biological Chemical Warfare, Ghent, August 24-27, 1986; pp.: 553-582.
4. Okudera, H., Morita, H., Iwashita, T., et al. Unexpected nerve gas exposure in the city of Matsumoto: Report of rescue activity in the first sarin gas terrorism. *Am J Emerg Med*, 1997; 15: 526-530.
5. Nagao, M., Takatori, T., Matsuda, Y., et al. Definitive evidence for the acute sarin poisoning diagnosis in the Tokyo subway. *Toxicol Appl Pharmacol*, 1997; 144:198-203.
6. Vale, J.A., Meredith, T.J., Heath, A. High dose atropine in organophosphorus poisoning. *Postgrad Med J* 1990;66:878-881.
7. de Kort, wlam, Kienstra, S.H., Sangster, B. The use of atropine and oximes in organophosphate intoxications: a modified approach. *Clin Toxicol* 1988;26:199-208.
8. Marrs, T.C. Toxicology of oximes used in treatment of organophosphate poisoning. *Adverse Drug React Toxicol Rev* 1991;10:61-72.
9. Farrar, H.G., Kearns, G.L., Use of continuous infusion of pralidoxime for treatment of organophosphate poisoning in children. *J Pediatr* 1990;116:648-661.
10. Johnson, M.K., Vale, J.A., Marrs, T.C., Meredith, T.J. Pralidoxime for organophosphorus poisoning. *Lancet* 1992;340:6.
11. Balali-Mood, M., Shariar, M., Effects of oximes in acute Organophosphate pesticide poisoning - a retrospective study, Proceeding of the Chemical and Biological Medical Treatment Symposium, Switzerland, 1996, pp. 119-124.
12. De Silva, H.J., Wikewickerma, R., Senanyake, N., Does pralidoxime affect outcome of management in acute organophosphate poisoning, *Lancet* 339 1992; 1136-1138.
13. Balali-Mood, M., & Shariat, M. Treatment of organophosphate poisoning Experience of nerve agents and acute pesticide poisoning on the effects of oximes. *J. Physiology (Paris)*, 1998; 92:375-378.
14. Placcio, D.C. New approach to treatment of OP poisoning, *Ant. Med. Medelin* 1982; 31:1-2.

15. George, P.M., Abernethy, M.H. Improved Ellman procedure for erythrocyte cholinesterase. Clin Chem 1983; 29: 365-368.
16. Cordoba, D., et al. Organophosphate poisoning – Modification of acid-base equilibrium and use of sodium bicarbonate as an aid in the treatment of toxicity in dogs. Vet Human Toxicol 1983; 25:1.
17. Garcia-Repetto, R., Martinez, D., Repetto, M. The influence of pH on the degradation kinetics of some organophosphate pesticide in aqueous solution. Vet Human Toxicol 1994; 36:202-204.

FIGURES AND TABLES

Table 1. Patients and their Vital Signs on Admission

	Control (Atropine)	Atropine + Bicarb.
1. Age (year)	24.9± 10.8	23.5 ± 9.7
2. Sex	15M± 11F	12M ± 12F
3. Weight(kg)	63.4 ± 14.5	59.8 ± 12.3
4. Systolic B.P.(mmHg)	113.6± 26.0	110 ± 12.1
5. Diastolic B.P. (mmHg)	67.1 ± 16.7	71.3 ± 13.2
6. Pulse (min)	90.5 ± 25.0	86.8 ± 25.8
7. Resp. rate(min)	20.3 ± 8.5	22.0 ± 9.9
8. Temperat. (C)	36.9 ± 0.7	37.2 ± 0.3

Table 2. Clinical Findings (%) on Admission and During Treatment.

Clinical Findings	Control (Atropine)		Atropine + Bicarb	
	On Admis.	Treatment	On Admis.	Treatment
1. Nausea/ Vomit	76	0	70	12
2. Diarrhea	26	15	20	8
3. Abd. Pain	53	11	45	20
4. Miosis	84	0	62	0
5. Hypersecr	69	40	76	8
6. Sweating	34	0	41	0
7. Rale/crackle	26	0	20	4
8. Pulm. Edema	11	0	8	0
9. Cyanosis	7.5	0	16*	4
10. Resp. arrest	7.5	7.5	20*	4
11. Agitation	30	3.7	33	12
12. Confusion	34	7.5	25	4
13. Coma	46	11	34	8
14. Twitching	42	3.7	37	12
15. Convulsions	8	0	12	0
16. Cardiac Arrhyt.	0	0	8	0
17. Cardiac Arrest.	7.5	3.7	0	0

*P<0.05

Table 3. Arterial pH, Bicarbonate and Gases

ABG	Control (Atropine)		Atropine + Bicarb	
	On Admis:	Treatment	On Admis	Treatment
pH	7.3 0.1	7.32 0.05	7.36 0.1	7.46 0.15
pH(max)	-	7.37 0.08	-	*7.47 0.03
Bicarb	19.7 3.9	17.2 3.8	18.1 4.0	20.5 5.8
PO2	93.9 45.3	92.1 42.3	82.4 28.5	87.4 37.8
PCO2	34.7 7.4	35.2 8.5	34.8 7.0	36.7 5.9

*P<0.01