Diagnosis and treatment of organotin poisoned patients

Feng Guo, Xiao-wei Lu, Qiu-ping Xu

ICU, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, China (Guo F, Xu QP); Emergency Department, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, China (Lu XW)

Corresponding Author: Qiu-ping Xu, Email: xqp8866@sina.com

BACKGROUND: With the development of industry and agriculture, organotin compounds have been widely used in China. Organotin compounds cause a common occupational poisoning. The toxicity of organotin was reported in animal studies; however the reports about human organotin intoxication are very rare. In this study we retrospectively analyzed the clinical manifestations of 15 organotin-poisoned patients who had been treated at our hospital from 2002 through 2007.

METHODS: Fifteen patients with organotin poisoning were admitted to Sir Run Run Shaw Hospital Affiliated to Zhejiang University School of Medicine from 2002 to 2007. They were 9 males and 6 females, aged from 25 to 52 years. Clinical manifestations and Glasgow Coma Scales showed that the poisoning was mild in 4 patients, moderate in 6 and severe in 5. The severe patients were given glucocorticoid after hospitalization by intravenous guttae of 500 mg methylprednisolone for the first day, followed by 160 mg methylprednisolone per day for three days, and then 80 mg methylprednisolone per day for another three days. Potassium glutamate and sodium glutamate were intravenously dripped to reduce blood ammonia; intravenous guttae plus oral administration of potassium 9 g/day was used to correct intractable hypokalemia; sodium bicarbonate was used to correct metabolic acidosis, and sedatives were used to control spasm and twitch; mechanical ventilators were used in 4 patients with dyspnea.

RESULTS: Most of the patients showed elevated level of blood ammonia, decreased level of blood potassium and metabolic acidosis, but some had demyelination changes shown by CT and MRI. Treatments included correction of metabolic acids, blood potassium and ammonia, and mechanical ventilation when necessary. For patients with injuries of the nervous system, glucocorticoids were given immediately after hospitalization. These patients showed intractable hypokalemia and metabolic acidosis during the treatment. Fourteen patients recovered completely without long-term side-effect. One patient in the aphasic stage restored the linguistic capacity during a 6-month follow-up.

CONCLUSIONS: Elevated level of blood ammonia, decreased level of blood potassium, and metabolic acidosis are common in patients with organotin poisoning. Demyelination can be observed in patients with severe poisoning. The abnormalities of the patients are reversible after suitable treatments.

KEY WORDS: Organotin; Poisoning; Blood ammonia; Demyelination

INTRODUCTION

Organotin compounds are used as heat stabilizers in polyvinyl chloride polymers, industrial and agricultural biocides, and industrial catalysts in chemical reactions. With the development of industry and agriculture in China, organotin compounds have been widely used and become a common source of occupational poisoning.

Studies have shown that organotin is toxic to the liver, kidneys, and the central nervous system. Its toxicity in animal studies has also been documented, but rarely in clinical studies. This study aimed to summarize the clinical manifestations and results of 15 organotin poisoned patients who had been treated at Sir Run Run Shaw Hospital Affiliated to Zhejiang University School...
of Medicine from 2002 to 2007.

METHODS

Patients

In the 15 patients 9 were males and 6 females, aged between 25 and 52 years. They met the Diagnostic Criteria and Principles of Management of Occupational acute organotin poisoning (GBZ26-2002), and the concentration of organotin they exposed to was much higher than the international standards TWA 0.1 mg/m$^3$ and STEL 0.2 mg/m$^3$. Their clinical manifestations and Glasgow Coma Scale showed that organotin poisoning was mild in 4 patients, medium in 6 and severe in 5. All of the patients who were workers of leather or plastic factories suffered from occupational poisoning without signs of alcoholic and drug poisoning. They had a history of respiratory tract inhalation of organotin and 5 of them also had skin exposure to organotin. Symptoms and signs, liver function, blood ammonia, blood potassium, and results of blood gas analysis, electroencephalography, skull CT and MRI were closely monitored in these patients.

Treatment

The severe patients were administered with an adequate dose of glucocorticoid after hospitalization: intravenous guttae of 500 mg methylprednisolone for the first day, followed by 160 mg methylprednisolone per day for three days, and then 80 mg methylprednisolone per day for another three days. Potassium glutamate and sodium glutamate were intravenously dripped to reduce blood ammonia; intravenous guttae plus oral administration of potassium 9 g per day was used to correct intractable hypokalemia; sodium bicarbonate was used to correct metabolic acidosis, and sedatives were used to control spasm and twitch; mechanical ventilators were used in 4 patients with dyspnea.

RESULTS

Clinical manifestations

In the present study, manifestations of mild poisoning included headache, dizziness, hypodynamia, restlessness, inappetence, nausea, somniphathy, tinnitus and amblyacusia; those of medium poisoning included extreme hypodynamia, vomiting, mental confusion, hypersomnia and addictive disturbance; and those of severe poisoning included coma, twitch, mental symptoms and epileptic attack. Glasgow coma scale scores showed specific measures designated in three aspects: open eyes, speech and movement. Scores in these three categories indicated the degrees of conscious disturbance: the maximum value was 15, indicating clear awareness; the score below 8 indicated coma; the minimum score was 3. We divided the patients into three groups according to Glasgow coma scale: mild >12, moderate 8-12, and severe < 8.

Laboratory examinations

Urine tin test was conducted on the first day of hospitalization. Patients' urine was diluted by diammonium phosphate and measured under 286.3 nm wavelength by a graphite oven atomic absorption spectrum method. Twelve patients were found positive in urine tin test, 13 had increased levels of ALT (45-221) U/L, 15 had decreased blood potassium levels (2.2-3.47) mmol/L, 12 had increased blood ammonia levels (42-220) μmol/L, and 12 had metabolic acidosis. Moreover diffuse electroencephalogram abnormality was found in 3 patients, mild abnormality in 7 and normality in 5. In the patients with severe poisoning, pathological changes of demyelination were observed in the skull by CT and MRI.

Treatment results

The treatment period ranged from 5 to 45 days, with 9.7 days on average. The 10 patients with mild and medium poisoning were discharged from the hospital within 14 days. After treatment they didn't complain of any discomfort or abnormal physical signs. And laboratory examinations of these patients showed nothing abnormal. After treatment the 5 patients with severe poisoning showed normal results of laboratory and additional examinations except one patient who had demyelination in the skull shown by CT. Follow-up for 6 months found that the 10 patients with mild and medium poisoning had returned to work while 3 of them still suffered from somniphathy. Four of the 5 patients with severe poisoning recovered at home, and the rest one with aphasic disease restored the linguistic ability.

DISCUSSION

RnSnX is the general formula of organotin which can be absorbed by the skin, digestive tract and respiratory tract. In the present study all patients had respiratory inhalation, and the 5 patients of the severe group had extra skin exposure. Therefore, the protection of both respiratory tract and skin is necessary.
Organotin is metabolically degraded by dealkylation and de-arylation through liver microsomes, and is mainly discharged via the kidney, digestive tract, saliva and breast milk. Tetraethyl tin also can be discharged via the mucous membrane of the respiratory tract.

The pathogenesis of organotin intoxication varies. Trialkyltin targets the central nervous system and often causes demyelination. It can also cause acute toxic encephalopathy with delayed toxic effects including expansion and hyperemia of blood vessels in alba, interstitial brain edema, neurotransmitter change, inhibition of dopamine and muscarinic receptor binding to restrain adenosine triphosphatase activity, malfunction of brain calcium pumps, limited functions of adenosine triphosphatase, and functional change of potassium pumps, which leads to changes of cell permeability as well as edema of astrocytes and axons. Organotin also acts on the limbic system and cerebellum, it disturbs the metabolism of the brain glutamate and γ-aminobutyric acid and causes hyperphrenia. Dialkyl is found poisonous to the biliary duct and liver.

In this study, T1 weighted images of MRI in patients with severe organotin poisoning showed low signal areas with a speckle shape in alba around the lateral ventricle. T2 weighted images showed high signal areas with a speckle shape in alba around the lateral ventricle, which was clearly larger than cinerea with a clear edge and no signs of occupation. T2 weighted images were more distinct than T1 weighted images, and diffusion weighted images were similar to T2 weighted images.

In the patients with severe organotin poisoning, an adequate dose of glucocorticoid was given immediately after their hospitalization so as to minimize the damage to the central nervous system. Four patients with demyelination recovered, and one showed a delayed recovery due to misdiagnosis. Long-term follow-up showed no side effect of acute organotin poisoning. These results of the patients with severe organotin poisoning indicated that the injury of the central nervous system can be reversed by timely treatment with an adequate dose of glucocorticoid. Glucocorticoid is produced by suprarenal gland zona fasiculata, and is a collective name of a group of steroid hormones. It is mainly used to adjust glycometabolism, including hydrocortisone (hydrocortisone), cortine (cortisone) and corticosterone. Glucocorticoid affects metabolism of sugar, protein and fat. Under certain physiological conditions, bioactive peptides (such as corticotropin releasing factor, CRF) are produced by hypothalamus; CRF then passes through the hypophyseal portal vessels and stimulates hypophysis to produce adrenocorticotropic hormone (ACTH), which sensitively acts on the adrenal cortex to produce glucocorticoid. Glucocorticoid also can activate a series of physiological responses such as increasing blood sugar level and heart rate. Hypothalamus, hypophysis and adrenal gland constitute the HPA (hypothalamic-pituitary-adrenal) axis. CRF, ACTH and glucocorticoid maintain a stable state via physiological feedback and exert normal physiological functions via their receptors. Glucocorticoid has multiple functions including stabilizing cell membrane and lysosome membrane, reducing permeability of the blood-brain barrier, and restraining immune response. It has nonspecific restraining effects on inflammation which caused by pathogens, chemical and physical causative agents. The main mechanisms are as follows: 1) improving functions of the blood-brain barrier and controlling the formation and expansion of vasogenic brain edema; 2) preventing the release of a large mount of stress-responding vasoconstrictor substances such as 5-HT and noradrenaline; 3) preventing cytotoxic brain edema; and 4) removing oxygen-free radicals.

We found that in around 80% of patients with liver injuries the levels of blood ammonia were higher than normal values. Even in patients with mild liver injury, the level of blood ammonia was elevated. This may be due to the interruption to the urea synthesis from ammonia in the liver; however, the exact mechanism is still unclear. In case of hepatic failure, normal metabolism in the liver is disrupted, resulting in the increase of non-esterified fatty acid, thiol, phenol, cholic acid and aromatic amino acid, which may contribute to the damage of the central nervous system. In this research, however, all patients had minor functional abnormalities of the liver with a maximum level of glutamic-pyruvic transaminase of only 120 U/L. The liver injury was not serious enough to cause symptoms in the nervous system. And some patients with neural injuries did not show any malfunction of the liver. CT and MRI of the patients with severe organotin poisoning showed pathological changes in the brain, suggesting that the symptoms of the nervous system were caused directly by organotin poisoning instead of damage to the liver function.

Hypokalemia in our patients may be due to a number of causes. Firstly organotin impairs the function of the digestive tract, interferes the assimilation and the absorption of potassium. Secondly, poisoning of the central nervous system, especially hypothalamus, causes hypothalamic-pituitary-adrenal axis disorder and
excessive release of adrenocorticotrophic hormone, which stimulate the secretion of adrenocorticotrophic hormone from the adrenal cortex. Adrenocorticotrophic hormone leads to excessive discharge of potassium by the kidney, and causes low blood potassium. Thirdly, animal tests have shown that organotin impairs uriniferous tubule function and increases potassium discharge, leading to a low level of blood potassium. All abnormalities appeared within the first week after the poisoning. With an effective treatment, all indicators began to normalize on the 10th day, and became completely normal in most patients on the 14th day. After 45 days of treatment, all patients recovered except one who is still showing brain demyelination. We conclude that the treatment of organotin poisoning has three stages: acute stage, 1-7 days after the poisoning, with such main manifestations as refractory acidosis, hypokalemia, hyperammonemia, and liver damage; paracmasis stage, 7-14 days after the poisoning, during which all indicators turn to be normal in most cases; and recovery stage, 14-45 days after the poisoning, during which patients with demyelination changes recover gradually. The treatment is focused on the acute stage to correct metabolic acidosis and hypokalemia, protect liver function, lower the level of blood ammonia, control hydrocephalus and epileptic seizure, and on the sufficient use of glucocorticoid in the treatment of severe poisoning as well as mechanical ventilation in patients with dyspnea.

Funding: None.
Ethical approval: Not needed.
Conflicts of interest: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.
Contributors: Guo F wrote the first draft. All authors contributed to the design and interpretation of the study and to further drafts.

REFERENCES


Received March 25, 2010
Accepted after revision July 20, 2010

www.wjem.org