

A Case Report: Convulsion After Poisoning of a herbicide containing Pyrazolate and Propyrisulfuron

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ABSTRACT

Introduction: There have been no reports on poisoning with pyrazolate and propyrisulfuron (Pyr/Pro), a type of herbicide. In this report, we present a case with severe Pyr/Pro poisoning signs, in particular, sustained convulsions.

Case presentation: A 47-year-old man was transferred to emergency room in comatose state after he ingested the most possible amount of 500 ml of herbicide which contained 136.5 mg of Pyr and 8 mg of Pro. Twelve hours after his admission, he suddenly developed generalized convulsions, which lasted for 2 days. Given no abnormal findings on his brain images or laboratory data, convulsions were considered to be caused by Pyr/Pro poisoning. His convulsions were well controlled under benzodiazepine treatments and he was able to be discharged without any complications.

Discussion: This case report suggests that Pyr/Pro poisoning has a higher risk for developing sustained convulsions and loss of consciousness.

Conclusion: We recommend managing signs of central nervous system, including convulsion, in cases with Pyr/Pro poisoning.

Keywords: Pyrazolate; Propyrisulfuron; Herbicide intoxication; Convulsion; Benzodiazepine.

INTRODUCTION

Self-poisoning with agricultural chemicals is still common and associated with suicidal behaviors in most cases. Accumulating case reports have provided knowledge about managements of certain kinds of herbicides such as organophosphate, glyphosate and glufosinate containing herbicides [1]. However, there have been no reports on poisoning with herbicide containing pyrazolate and propyrisulfuron (Pyr/Pro), which has become widely used in Japan. Although Pyr/Pro has been considered to be safe on animals, the actual effects on human bodies have not been investigated. We herein present a case with severe Pyr/Pro poisoning, who developed severe and persistent convulsions.

CASE DESCRIPTION

A 47-year-old man was transferred to the emergency room after taking most possible amount of Pyr (136.5 mg), Pro (8 mg) and water and surfactants (approximately 350 mg) containing

herbicide. We had structured and systematic diagnostic approaches, which revealed no clear evidence on causes of his altered mental status other than herbicide intoxication. On arrival, he was in comatose and vital signs were normal except for his tachycardia: HR 119 /min, BP 135/81 mmHg, BT 36.7, SpO₂ 99% (room air). Blood glucose level was normal with 92 mg/dL. He was of average built with relatively well-nourished and had no evidence of trauma. Given his deep coma status, mechanical ventilation was administered to avoid airway obstruction. Decontamination and injection of activated charcoal were declined because one hour had already passed after ingesting the herbicide [1]. Physical examinations and laboratory examinations including renal, liver, thyroid, coagulation functions, levels of ammonia, and electrolytes were all within normal limits. Drug test using his urine (Triage DOA®) revealed no evidence of substance that could have altered the mental status. He had no history of alcohol abuse. Whole head and body CT scan was normal. He was diagnosed

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as having disturbance of consciousness due to Pyr/Pro poisoning and was hospitalized in intensive care unit.

12 hours after his arrival, he suddenly developed generalized tonic and clonic convulsions. He had no medical history and never had convulsions before according to his family. The convulsions lasted about two minutes and were suppressed by intravenous administration of 10 mg of diazepam. Magnetic resonance imaging of his head revealed no remarkable findings. Electroencephalogram showed diffuse slow wave (5 to 6 Hz) without apparent epileptic discharge or spike and wave complex. Cerebrospinal fluid (CSF) test was normal. CSF culture for bacteria and polymerase chain reaction for herpes simplex virus were found negative later. Interleukin 6 level was 3.0 pg/mL and this value was insufficient to prove inflammatory responses had occurred in his central nervous system.

Midazolam was administered at the rate of 0.04 mg/kg/hour. He, however, intermittently developed convulsions every two hours which began with rapid contractions of extremities and face muscles, followed by generalized tonic-clonic convulsions. Each convulsion was treated by 3 mg of midazolam. Over 2 days, convulsions were gradually controlled by continuous administration of midazolam and then his coma status improved afterwards. Mechanical ventilator was removed on 5 hospital days and he was transferred to the psychiatric unit. After he had psychiatric treatments, then he was able to be discharged on 29 hospital days with no complications.

DISCUSSION

Pyr/Pro containing substance is one of the most frequently used herbicides in Japan in recent years. Characteristics of Pyr/Pro intoxication, however, have been still unknown. According to an animal experiment by its developers, Pyr is a wide spectrum herbicide with excellent selectivity in paddy rice and low toxicity to mammals, fishes and soli microflora. Pyr is easily hydrolyzed to destosyl pyrazolate; active body of pyrazolate, which has no bioaccumulative potential and p-toluenesulfonic acid, which is rapidly secreted into urine without metabolized when taking orally [2]. Likewise, Pro is considered to be safe because it has an oral and dermal lethal dose 50% value when taken an amount of higher than 2000 mg/kg in rat study [3]. In our case, the estimated amount of Pro is approximately 0.11 mg/kg, which, in theory, is safe for his body. On the contrary, our case revealed Pyr/Pro may have substantial effects on our body, in particular, inducing sustained convulsions and loss of consciousness.

Glufosinate, a herbicide, has the highest risk for developing convulsions among the herbicides because of its chemical structure, which bounds the N-methyl-D-aspartate receptor and induces epileptogenic changes in central nervous system [4]. However, Pyr/Pro has no structural similarities to excitatory neurotransmitters such as glutamate, acetylcholine, catecholamine, and serotonin, which might alter neural

circumstance of human central nervous system. One potential mechanism might be that Pyr/Pro may lower the threshold of convulsions because our careful inspections including taking history, head MRI, electroencephalogram, blood test, and CSF studies revealed no evidence of apparent causes of convulsions; i.e., alcohol or benzodiazepine medications withdrawal, vascular disease, CNS infection, metabolic diseases, demyelination diseases, brain edema, trauma and so on.

Our case shows that benzodiazepine is effective in treatments for convulsions by Pyr/Pro poisoning, similar to by other herbicides, especially by glufosinate [5]. Instead of an intermittent administration of diazepam 10 mg, continuous infusion of midazolam had an adequate anticonvulsant effect. Clinical course in our case suggested that sustained epileptogenic change had occurred in patient's nervous system and treatment with benzodiazepine is required to suppress convulsions induced by Pyr/Pro.

This case report includes several limitations. Firstly, it is difficult to rule out a possibility that containing surfactant may have caused convulsions as a result of cerebral edema owing to its related vasodilatation function. Surfactants are believed to be responsible for various complications, however, convulsion is thought to be rare complication [6]. Second, levels of Pyr/Pro and surfactants in serum and CSF were not examined. Lastly, this is just one case report and a number of cases need to be included for further discussion.

CONCLUSION

This present case suggested that Pyr/Pro poisoning might have a higher risk for developing sustained convulsions. It is highly recommended to pay attention for CNS signs and symptoms when managing patients with Pyr/Pro poisoning.

REFERENCES

1. Simpson Jr WM, Schuman SH. Recognition and management of acute pesticide poisoning. *Am Fam Physician*.2002;65(8):1599.
2. Nakagawa M, Yanai T, Tanizawa K, Yamaoka K. Development of a New Herbicide, Pyrazolate. *J Pest Sci*.1988;13(2):363-373.
3. Ikeda H, Ito S, Okada Y, Mikata K, Endo M, Komoto I. Development of a novel paddyrice herbicide propyrisulfuron (Zeta-One). R&D Report, Sumitomo Kagaku. 2011;2.
4. Matsumura N, Takeuchi C, Hishikawa K, Fujii T, Nakaki T. Glufosinate ammonium induces convulsion through N-methyl-D-aspartate receptors in mice. *Neurosci Lett*.2001;304(1-2):123-125.
5. Calas AG, Perche O, Richard O, Perche A, Pâris A, Lauga F, et al. Characterization of seizures induced by acute exposure to an organophosphate herbicide, glufosinate-ammonium. *Neuroreport*. 2016;27(7):532-541.
6. Seok SJ, Park JS, Hong JR, Gil HW, Yang JO, Lee EY, et al. Surfactant volume is an essential element in human toxicity in acute glyphosate herbicide intoxication. *Clin Toxicol*.2011;49(10): 892-899.