Decrease in Butyrylcholinesterase Accompanied by Intermediate-like Syndrome after Massive Ingestion of a Glyphosate-surfactant

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Abstract:
An 86-year-old woman intentionally drank approximately 300 ml of a glyphosate-surfactant. She was found with consciousness disturbance and experienced several vomiting episodes. On arrival, serum biochemistry revealed a decreased level of butyrylcholinesterase (B-CHE) (11 [normal range: 180-450] IU/L). Later, her B-CHE level further decreased to single-digit values, and she became comatose with involuntary movement and an increase in muscle tone. Her consciousness level and muscle tone improved with the recovery of her B-CHE level. Physicians should be alert for the occurrence of intermediate syndrome when the B-CHE levels of patients who have consumed a massive amount of glyphosate-surfactant show a prolonged decrease.

Key words: glyphosate-surfactant, intermediate syndrome, butyrylcholinesterase

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Introduction

Glyphosate-surfactants are commonly used pesticides that are thought to be safer than paraquat. When used normally, these agents do not induce adverse effects on the development or on the reproductive or endocrine systems in humans or other animals (1).

Paraquat has not been sold since 1999, and glyphosate-surfactant can be purchased without any regulations in Japan. A hospital-based survey of clinical cases of pesticide acute poisoning revealed glyphosate-surfactant to be the most frequent cause among 137 cases (2). Acute poisoning symptoms induced by a glyphosate-surfactant include gastrointestinal symptoms, respiratory distress, hypotension, altered consciousness and renal insufficiency (3-5). However, no studies have reported the induction of a decrease in the butyrylcholinesterase (B-CHE) level or intermediate syndrome (typical symptoms of organophosphate poisoning) by glyphosate-surfactants.

We herein report the case of a patient with a transient decrease in her B-CHE level, which was accompanied by intermediate-like syndrome, following the ingestion of a massive amount of a glyphosate-surfactant.

Case Report

An 86-year-old woman intentionally drank approximately 300 ml of a glyphosate-surfactant, which had been bought for her kitchen garden, after a quarrel with her daughter. She was found by her daughter with consciousness disturbance, after several vomiting episodes. She was brought to our hospital by a physician-staffed helicopter.

Upon arrival, her vital signs were as follows: Glasgow Coma Scale (GCS), E3 V3 M6; blood pressure, 108/76 mmHg; pulse rate, 66 beats per minute; respiratory rate, 30 breaths per minute; saturation of peripheral oxygen with oxygen of 10 L per minute, 100%. Her pupils were 2 mm in size with prompt light reflex. The physiological findings on muscle tone, chest roentgenography and electrocardiography studies were negative. Serum biochemistry revealed a decreased level of B-CHE (11 [normal range: 180-450] IU/L). The patient underwent cathartic and activated charcoal

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Figure. Time course of B-CHE, GCS and muscle tone. The improvement in the GCS score was correlated with the recovery of the patient’s B-CHE level. The patient’s muscle tone also improved after the recovery of her B-CHE level. B-CHE: butyrylcholinesterase, GCS: Glasgow Coma Scale

treatment after gastric lavage. She was admitted to our hospital, and her cardio-respiratory function was continuously monitored. Figure shows the time course in her B-CHE level, GCS and muscle tone.

On the second day, she complained of pain with delirium, but her physical and laboratory findings showed no remarkable changes. On the third day, she became alert and was able to drink water. Her peripheral oxygen improved to the normal range under room air. On the fourth and fifth days, her B-CHE levels further decreased to single-digit values; however, she was asymptomatic. On the sixth day, she developed consciousness disturbance and involuntary movement with an increase in muscle tone. Urgent head magnetic resonance imaging and electroencephalography showed negative findings. She temporarily showed apnea with reduced peripheral oxygen but obtained spontaneous respiration. On the seventh day, she became comatose. On the ninth day, her GCS score improved, but she displayed catalepsy-like movement. On the 13th day, she showed convulsions, which were treated by levetiracetam.

Her consciousness level and muscle tone improved according to the recovery of her B-CHE level. Her symptoms improved further the next day, and she was eventually able to feed herself and walk. As the patient’s condition was complicated by depression, she was transported to a psychiatric hospital.

Discussion

This is the first case of glyphosate-surfactant poisoning to be accompanied by a transient decrease in the B-CHE level and intermediate-like syndrome. There have been no clinical reports describing cases in which the ingestion of a large amount of glyphosate-surfactant resulted in a severe and prolonged decrease in a patient’s B-CHE level. Accordingly, we were unable to clarify whether or not this severe effect on the B-CHE level after the ingestion of a large amount of glyphosate-surfactant occurs in all humans.

In normal use, glyphosate-surfactant does not alter the levels of B-CHE (6). However, in some species, glyphosate-surfactant can reduce the level of acetylcholinesterase (A-CHE) in erythrocytes, brain and muscle (7). Glyphosate-surfactant can also reduce the level of B-CHE in massive doses (8). B-CHE can act as a backup for acetylcholinesterase and as a scavenger for poisons that might inhibit acetylcholinesterase activity (9). In organophosphate-induced neurotoxicity, A-CHE and/or B-CHE inhibition was found to be correlated with the occurrence of intermediate syndrome (10). In addition, Yilmaz et al. prospectively performed therapeutic plasma exchange for patients who developed intermediate syndrome during follow-up for organophosphate intoxication (11). As a result, a statistically significant increase was detected in the plasma B-CHE levels of patients after therapeutic plasma exchange. Thirteen of 17 patients showed clinical improvement and were discharged after therapeutic plasma exchange. These results suggested that low levels of B-CHE have the potential to induce intermediate syndrome. Accordingly, the ingestion of a massive amount of glyphosate-surfactant may reduce the level of B-CHE, even in humans, which has the potential to induce intermediate syndrome, similarly to organophosphate poisoning.

Conclusion

Physicians should pay attention to the occurrence of intermediate syndrome when the B-CHE levels of patients who have ingested a massive amount of glyphosate-surfactant are decreased for a prolonged period of time.

The authors state that they have no Conflict of Interest (COI).
**Table. Results of the Blood Analyses on Arrival.**

| Parameter                          | Value                  |
|------------------------------------|------------------------|
| pH                                 | 7.406                  |
| PCO₂                               | 41.0 mmHg              |
| HCO₃⁻                              | 25.3 mmol/L base excess|
| PO₂                                 | 75.6 mmHg              |

**Blood gas analysis:** (on 10 L min⁻¹ of oxygen)

| Parameter                          | Value                  |
|------------------------------------|------------------------|
| Cell blood count and biochemical analysis |                        |
| white blood cells                  | 16.0x10⁹ /µL           |
| platelets                          | 20.1x10⁴ /µL           |
| total protein                      | 7.4 g/dL               |
| aspartate aminotransferase         | 20 IU/L                |
| alkaline phosphatase               | 157 IU/L               |
| creatine phosphokinase             | 54 IU/L                |
| blood urea nitrogen                | 18.6 mg/dL             |
| glucose                            | 182 mg/dL              |
| potassium                          | 3.1 mEq/L              |
| C-reactive protein                 | 0.3 mg/dL              |
| activated partial thromboplastin time | 19.2 (24.9) sec       |
| prothrombin time                   | 10.7 (11.7) sec        |
| fibrinogen degradation products    | 5.2 µg/mL              |

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