A Fatal Case of Opioid Intoxication After Raw Poppy Plant Ingestion

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Abstract

Papaver somniferum contains many opioids and is frequently used in agriculture. Both the intoxication and the withdrawal of opioids have a wide range of symptoms such as coma, depressed respiration and agitation. Here, a fatal case of opioid intoxication will be presented. A four-year-old female patient was admitted to the pediatric intensive care unit after ingesting raw poppy plants. She had shallow respiration, tachycardia, hypertension and muscle cramps. A high plasma opioid level was measured and bolus intravenous naloxone was administered which resulted in a brief gain of consciousness. She was intubated after a sudden respiratory depression and loss of consciousness 10 hours later. Naloxone infusion was started and continued for two days. She developed disseminated intravascular coagulation and was lost on day twelve. Raw plant ingestion proves difficult to treat since there is less information about the ingredients. Having no consensus on naloxone dosage and intrinsic complications such as hypo- and hypertension, redistribution, rhabdomyolysis and dysmotility disrupts naloxone administration. Ingestion of opioids as plants brings out different complications for the treatment course while deciding on naloxone dosage proves opioid intoxication difficult to treat.

Introduction

Since poppy seed has an economic value as an industrial plant, it is frequently grown in Turkey as well as in different regions of the world. Papaver somniferum subsp. anatolicum var. nigrum (blind poppy) is the variant that is mostly used in agriculture. It consists of 99 kinds of alkaloids [1]. Ones that are found in the highest concentrations are morphine, codeine, thebaine, noscapine, and papaverin [2]. Alkaloid concentrations change according to harvest timing. Phenanthrene alkaloids in poppy seeds can cause severe addiction. While opioid intoxication causes bradycardia, coma, decreased gastrointestinal system (GIS) motility, depressed mental state, depressed respiration, hypotension, hypothermia and myosis, opioid withdrawal may present with agitation, diarrhea, diaphoresis, hypertension, cramps, midriasis, piloretraction, tachycardia, tachypnea, vomiting, and yawning [3]. Although naloxone has been used as a specific antidote for opioid intoxication since 1960, suggested dosing and administration routes vary widely in different sources [4]. Here, a fatal case of opioid intoxication will be presented.

Case Presentation

A four-year-old female patient was brought to the pediatric emergency department after her parents could not wake her up. Her family were occupied as poppy seed farm workers in Afyon province of Turkey and reported that they all ate raw poppy plants approximately 12 hours prior. The patient was unconscious and not wakeable. She was quickly admitted to the Pediatric Intensive Care Unit. Non-invasive mechanical ventilation was started. She had tachycardia and hypertension. Neurological examination revealed no response to painful stimuli and hyperactive deep tendon reflexes. PRISM III score was 20 and the expected mortality rate was 29.8%. Intravenous (IV) naloxone at 0.1 mg/kg/dose was administered after plasma opioid level was reported to be 1196 ng/mL. She had a brief gain of consciousness. She was intubated after a sudden change according to harvest timing. Phenanthrene alkaloids in poppy seeds can cause severe addiction. While opioid intoxication causes bradycardia, coma, decreased gastrointestinal system (GIS) motility, depressed mental state, depressed respiration, hypotension, hypothermia and myosis, opioid withdrawal may present with agitation, diarrhea, diaphoresis, hypertension, cramps, midriasis, piloretraction, tachycardia, tachypnea, vomiting, and yawning [3]. Although naloxone has been used as a specific antidote for opioid intoxication since 1960, suggested dosing and administration routes vary widely in different sources [4]. Here, a fatal case of opioid intoxication will be presented.

Keywords: naloxone, opioids, papaver somniferum, plant alkaloids, poppy

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position of the endotracheal tube. IV of 0.0025 mg/kg/hour naloxone infusion was initiated as the patient lost her consciousness again (GCS: 3). After one dose of 20 ml/kg bolus saline, IV 5 mcg/kg/min dopamine infusion was initiated since the patient was hypotensive, the dose was gradually increased, dobutamine and adrenaline were added. While the initial vasoactive-inotrope score was 0, it increased to 5 at the 12th hour, and to a maximum of 60 at the 24th hour. Inotropic agents were gradually stopped after hypertension developed under naloxone infusion. IV hydration was decreased to 2000 ml/m2/day. Naloxone infusion was gradually stopped after plasma opiate levels of <70 ng/mL were detected on the second day of her care. IV 0.3 mcg/kg/day desmopressin acetate was administered after detecting that urine output was 9.6 ml/kg/hour and plasma sodium (Na) level was 169 mEq/L and further investigations (urine Na, plasma and urine osmolarity) were done and a diagnosis of diabetes insipidus was made. Brain computerized tomography (CT) showed edema in bilateral infratentorial region in both cerebellar hemispheres (Figure 1).

**FIGURE 1:** Brain computerized tomography (CT) showed edema in bilateral infratentorial region in both hemispheres.

IV 1 mg/kg/day dexamethasone treatment was initiated. Total parenteral nutrition was administered since the patient did not improve after two days of IV hydration in hopes for regression of respiratory depression and neurological symptoms after cessation of naloxone infusion. On the sixth day of her care, gastric residue was detected after initiation of enteral feeding via a nasogastric tube. The residue still had poppy seeds in its content. Gastric lavage was repeated. High amounts of poppy seed were extracted. Control opiate level was 78 ng/mL. Daily gastric lavage was continued. Near-infrared spectroscopy (NIRS) and ambulatory electroencephalogram (EEG) monitorization was done. NIRS was between 56-60%. Electrical brain activity was severely reduced in the EEG. Permissive hypercapnia was achieved. A control brain CT that was performed in order to assess progression of brain edema showed continuation of edema. Mannitol treatment was initiated. A d-dimer level of >34 ng/dL was reported while prothrombin time and fibrinogen levels were normal. The patient’s disseminated intravascular coagulation score was 5 and fresh frozen plasma was transfused. No defecation was observed for three consecutive days and a rectal enema was applied. High amounts of poppy seed were observed in the feces on the eighth day of her care. Her general condition had
worsened on the 12th day of her care while thrombocytopenia developed and new infiltrations were observed in her chest x-ray (Figure 2).

Her antibiotherapy was revised as caspofungin, meropenem and linezolid. Hypertension resistant to furosemide, captopril and amlodipine was observed. IV esmolol infusion was initiated. Subsequently, hypotension followed. Esmolol infusion was gradually decreased and stopped. Inotropic agents were administered as the patient was hypotensive and the electrocardiogram showed widespread ST depression. Control plasma opioid level was 20 ng/dL. The patient was bleeding through the endotracheal tube and quickly had a cardiac arrest. She did not respond to cardiopulmonary resuscitation (CPR) and died. The poppy plant (Figure 3) that the patient was thought to have ingested was analyzed and reported to consist of unusually high levels (never before measured as high by the Anatolian University Farmaceutic Toxicology Department) of morphine, codeine, acetylhydrocodeine, papaverine and atropine alkaloids (Table 1).
FIGURE 3: The poppy plant that the patient was thought to have ingested

| Compounds          | Mol. Formula | Expected [M+H]+ | Measured [M+H]+ | Amount (%) |
|--------------------|--------------|-----------------|-----------------|------------|
| Morphine           | C_{17}H_{19}N_{3}O_{3} | 286.1438        | 286.1435        | 55.1       |
| Codeine            | C_{18}H_{21}N_{3}O_{3} | 300.1594        | 300.1606        | 9.4        |
| Thebaine           | C_{19}H_{21}N_{3}O_{3} | 312.1594        | 312.1599        | 16.3       |
| Papaverine         | C_{20}H_{23}N_{3}O_{4} | 340.1543        | 340.1555        | 3.9        |
| Acetyldihydrocodeine | C_{20}H_{25}N_{4}O_{4} | 344.1856        | 344.1859        | 7.0        |
| Salutaridinol      | C_{19}H_{23}N_{4}O_{4} | 330.1700        | 330.1701        | 6.8        |
| Isopavine          | C_{20}H_{23}N_{4}O_{4} | 342.1700        | 342.1709        | 1.5        |

TABLE 1: Alkaloids found in the ingested poppy plant.

**Discussion**

In developed countries, opioid intoxication is generally due to recreational use or suicide and such events
Conclusions

Opioid intoxication can also occur with raw ingestion of the poppy plant or seed or as a tea. Ingestion of opioids as a plant instead of the drug form brings out many different complications for the course of treatment and requires specific research on management. Lack of consensus in naloxone treatment and dealing with side effects in addition to complications of intoxication all contribute to difficulty in treatment. Effects of opioids such as GIS motility dysfunction and rhabdomyolysis should not be forgotten beside the opioid epidemic [13] or withdrawal management in neonatal abstinence syndrome [14].

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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