

PODOPHYLLIN POISONING

A Case Report

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Podophyllin is extracted from *Podophyllum peltatum* resin and used in medicine because of its cytotoxic and cathartic effects. It is often used in dermatology as a topical application for treatment of *condylomata acuminata* (venereal wart) and warts of the skin (*verruca vulgaris*). The patient whose case is presented here showed evidence of severe intoxication after ingestion of 350 mg of podophyllin contained in Bilaks tablets.*** This medication is used as a cathartic and each tablet contains phenolphthalein, 0.10 gm; extract of rhubarb, 0.03 gm; extract of belladonna, 0.02 gm; and podophyllin, 0.05 gm.

Case Report

T. S., a two year old girl, ingested about seven Bilaks tablets, unknown to her parents. Three hours after ingestion, she began vomiting and her parents brought her to Hacettepe Medical Center. Her stomach was washed with a saline solution and she was admitted for observation. Past medical histories of the patient and her family were non-contributory.

Physical Examination (on admission) : Temperature, 37°C (R); pulse, 80 per minute; blood pressure, 100/50 mm Hg. She appeared to be a healthy child in no obvious distress. Examination of the systems were all within normal limits. She was given 5 % D/W intravenously on admission and after a few hours was given fluids orally which she retained well.

Eight to nine hours after ingestion of the pills, the patient became restless and had visual hallucinations, and pupils were slightly dilated. Drowsiness and spasticity of the extremities occurred a few hours later. At this time eye grounds were normal and her temperature, which had reached 39 C, was reduced to 36 - 36.5 C by continuous applications of alcohol to the inguinal and axillary regions.

Twenty-four hours after ingestion of the pills, cyanosis and hematemesis occurred and the patient began to have generalized convulsions. Her respira-

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*** Bilaks produced by Diler Laboratories, Istanbul, Turkey.

tion rate dropped to 12 per minute and blood pressure (by the flush method) was 50 mm Hg. Levophed[®] (leveterenol bitartrate, Winthrop Laboratories) was administered intravenously and blood pressure returned to normal (90 mm Hg).

Neurological examination on the fourth hospital day revealed that her pupils were equal and reacted to light, and the eyegrounds were still normal. Although she was unconscious, her eyelids moved spontaneously, and her extremities responded to stimulation. Both extremities were hypotonic and were kept in semiflexion position. Deep tendon reflexes and abdominal skin reflexes were not responsive. Convulsions were controlled by intravenous sodium pentathol, and alcohol sponging was necessary to keep her temperature down.

The patient remained unconscious and convulsions continued until the twelfth hospital day. At this time her respiration became regular and convulsions occurred less frequently. Oral feeding was begun, and phenobarbital and Dilantin[®] (diphenylhydantoin, Parke-Davis) were administered. On the fifteenth hospital day convulsions again became frequent and slight left facial paralysis was noted. However, her condition improved thereafter and she was started on physical therapy after the 20th day. She was discharged from the hospital on the 33rd day after admission.

Laboratory Examination: Hemoglobin level was 12.75 gm per 100 ml on admission and 8.45 gm per 100 ml on the tenth hospital day. Leucocytosis was evident throughout the entire period of hospitalization, ranging from 13,000 to 32,000 per mm³.

Several urinalyses were negative for protein and sugar. Microscopic examination of urinary sediments were also negative for cells and casts, except on the third hospital day when leucocyte clumps and slight pyuria were noted (8 to 10 leucocytes). Cultures from urine and blood were positive for *E. coli* on two occasions.

Additional laboratory tests yielded the following values: NRN, 30 to 40 mg %; CO₂, 19.80 to 20 mEq/l; Cl, 103 to 110 mEq/l; Na, 135 to 140 mEq/l; K, 3.3 to 4.9 mEq/l; serum calcium, 7 mg % (3rd hospital day) and 10.2 mg % (5th hospital day). SGOT was 24 to 25 units, measured on two different occasions. A lumbar puncture was traumatic but cultures from spinal fluid were negative. Spinal fluid sugar was .92 mg %, and protein was 52 mg %. Lung x-ray on the 14th hospital day revealed bilateral emphysema. EKG was normal. EEG showed generalized but slight cortical and subcortical dysrhythmia.

Discussion

This cathartic drug contains phenolphthalein, extract of rhubarb, extract of belladonna, and powder of podophyllin. Phenolphthalein is a well-known cathartic and has been used for many years because of its stimulant action on the large bowel. It is not a toxic drug, and it has been reported⁶ that no harmful effects were suffered by a child who had ingested 6 grams of the drug. However, it is also recognized that, in susceptible people, ingestion may cause severe diarrhea, various types of skin eruptions, and even collapse.

Extract of rhubarb is also used for its cathartic action and is known to cause nausea and vomiting, severe headache, and skin eruptions,¹ in some sensitive people. Extract of belladonna is used with podophyllin because the latter alone often causes severe abdominal cramps. Children, however, are especially sensitive to belladonna and an overdosage often causes dryness of the mouth, thirst, photophobia, skin eruptions, hallucinations, and elevation of the body temperature.

The effective agent in podophyllin is podophyllotoxin. Ten milligrams of podophyllin resin produces watery feces and is a cathartic.² Podophyllotoxin is an irritant and has a cytotoxic effect on the bowels as well.

The patient's initial pupillary dilatation, restlessness, and elevated body temperature (39 C) were probably due to the toxic effect of belladonna. Nausea, vomiting and diarrhea could be caused by any toxic drug. Our patient had symptoms of peripheral collapse during the first 24 hours of hospitalization, frequently seen in cases of podophyllin poisoning. Gastro-intestinal bleeding, cyanosis, hypotension, and bradypnea followed the initial symptoms. Our patient evidenced all the classical symptoms of podophyllin poisoning. Spasticity and convulsions were probably caused by the cytotoxic action of the drug on the central nervous system. Generalized dysrhythmia on the EEG might also be evidence of this toxic effect.

Clinical and laboratory examinations revealed no indications of severe damage to the heart or liver. The patient's sudden deterioration on the 15th hospital day we felt to be the result of *E. coli sepsis*. The hypocalcemic condition encountered on the third hospital day was probably caused by oxalates in the rhubarb which bind serum calcium as calcium oxalate which is then excreted by the kidneys. After the fifth hospital day serum calcium levels were normal and not related to the patient's convulsions.

The patient was discharged 33 days after admission. She was seen for a check-up six months after discharge and although her general health was good, we noted a slight foot drop of the left side which might have been caused by some central nervous system damage. Otherwise she acted normally and talked very well for her age.

Conclusion

Podophyllin is a highly toxic drug which should not be used as a cathartic. There is no specific antidote for the drug and therapy in cases of drug poisoning is purely supportive. Gastric lavage

should be done at the earliest possible moment and the patient should be closely observed in the hospital for signs of drug poisoning. It is reported that local application of this drug can cause illness,⁴ and death has also been reported.⁵

Peripheral collapse should be watched for and treated promptly. Body fluids and electrolytes lost through vomiting and diarrhea can be replaced by intravenous feedings. Tests should be made to determine whether there is any gastro-intestinal bleeding or infection.

Summary

The case of a child with podophyllin poisoning is presented, and the treatment discussed. The patient recovered after severe peripheral collapse but possible cerebral cortical damage is evidenced by slight ataxia of the left leg noted six months after discharge from the hospital. The patient had ingested 350 mg of podophyllin contained in Bilaks tablets.

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