BRIEF NOTES AND COMMENTS

Attempted Suicide with Phenformin

Harold L. Dobson, M.D., Houston

SUMMARY

Following ingestion of .85 gm. of phenformin, in a suicide attempt, the principal symptoms were violent gastrointestinal cramping, nausea, and vomiting, all of a few hours' duration. This appeared to provide major protection against other toxic effects. There was no significant hematemesis or melena. Blood lactate was normal and no ketonuria was observed. Blood sugars were in the hyperglycemic range. DIABETES *14*:811-12, December 1965.

With the introduction of new therapeutic agents, unique information concerning acute toxicity may be gained from the study of patients who have accidentally or deliberately ingested excessive quantities of the drug. Although the oral hypoglycemic agents have been in use for more than five years, there are few reports of excessive ingestion reported during this period; all reports have involved the sulfonylureas.[1,2] It is the purpose of this report to record a suicide attempt with phenformin, a biguanide compound.

Case report: A.M., a forty-seven-year-old white female, had been diagnosed as diabetic by her private physician four months prior to the acute episode. Her therapeutic program consisted of a diet and phenformin, timed disintegration capsule, (DBI-TD) 50 mg. and phenformin (DBI) 25 mg. daily. On this therapy she felt better and, by history, was in acceptable diabetic control.

Her marriage had been marked by discord for at least fifteen years and the patient had separated from her husband five weeks previously, ostensibly because of financial problems. She experienced increasing depression and anxiety. At 6 a.m. on the day of admission she ingested seventeen capsules (.85 gm.) of phenformin in time disintegration form. This dosage was confirmed by other members of the family and by reference to the date and number of capsules of the most recent refill of the prescription. Within one hour she developed abdominal pain and cramping which progressed rapidly into explosive nausea and vomiting. This subsided only to recur within two hours. Cramps of moderate to marked severity were recurrent during this period. She drank approximately four ounces of orange juice but vomited promptly. Later she retained two to three ounces of a soft drink. There was no diarrhea at any time, and hematemesis was not noted. The patient had no syncope or seizures. To one physician she gave a history of staggering gait, lethargy, and sweating present about four to five hours after ingestion of the drug. Another physician was unable to obtain any significant history of these symptoms.

She was brought to the emergency room of Ben Taub Hospital seven hours after taking the overdose. At that time the blood pressure was 180/110, pulse 120, respirations 18. One episode of vomiting occurred soon after admission. The vomitus contained bile and flecks of blood. The patient was a pallid, obese, white female who appeared to be chronically ill and mildly dehydrated. She was alert and cooperative. Bowel sounds were hyperactive and there was mild diffuse abdominal tenderness with no muscle spasm. Physical examination was otherwise within normal limits. Laboratory data obtained eight hours after the overdose revealed: WBC 11,150; hematocrit 39 vol. per cent; blood sugar (Somogyi-Nelson) 126 mg. per 100 ml.; CO_2 combining power 25.8 mEq./L. and a blood lactic acid 0.9 mM./L. (The patient had been at bed rest for at least one hour.) Urinalysis showed no protein, sugar, or acetone. Chest roentgenogram showed fibrotic scarring of the right upper lobe and discrete calcification in the left hilar region.

The patient was kept at bed rest and 1 liter of 10 per cent glucose in distilled water was given intravenously at the rate of 30 drops/min. followed by 1,000 cc. 5 per cent in distilled water. Liquids by mouth were allowed as tolerated. There was no further vomiting and the nausea subsided. Vital signs were checked every two hours. The blood pressure stabilized at 120/70, the temperature remained normal, the pulse fell to 80 beats/min. by the following morning, and respirations were stable at 16-18 min. Urine was tested every two to three hours and no glycosuria or ketonuria was found.

At 7 a.m. the following morning the CO_2 combining power was 32 mEq./L. and blood sugar was 187 mg. per 100 ml. (AutoAnalyzer). Feces contained no gross blood.

The patient was seen by a psychiatric consultant who felt that the diagnosis of chronic anxiety reaction with acute depression leading to attempted suicide was justified. The patient was discharged to the care of her family. She failed to return for subsequent appointments.

DISCUSSION

The common undesirable effect of phenformin therapy is gastrointestinal distress, which is dose related and may be extreme.[3] In this case, severe gastrointestinal cramps, nausea, and vomiting of six to seven hours' duration were the prin-

From the Metabolic Section, Dept. of Internal Medicine, Baylor University College of Medicine and Ben Taub Hospital, Houston, Texas.

cipal symptoms. Irritation of the gastrointestinal mucosa has been reported.[4] If this report is correct, gross hemorrhage could occur. No significant hematemesis or melena occurred in this patient.

Increase in blood lactate following therapeutic administration of phenformin has been reported and some feel that this drug incites or contributes to lactate acidosis[5] while others hold the relationship to be tenuous.[6] A blood lactate obtained eight hours after ingestion of .85 gm. of phenformin was normal and the CO_2 combining power obtained twenty-five hours after ingestion suggested mild metabolic alkalosis. Ketonuria in the presence of normal or slightly elevated blood sugars has been attributed to phenformin.[5] In this case ketonuria was not detected in urine samples obtained from the seventh to the twenty-seventh hour after ingestion of the excessive dosage.

Phenformin seldom, if ever, lowers blood sugar into the range of significant hypoglycemia.[7,8] Prior to coming to the emergency room, the patient developed vague symptoms suggesting hypoglycemia, but these could have been a manifestation of the gastrointestinal distress. Blood sugar was minimally elevated on admission to the emergency room and was moderately elevated the following morning, after the patient had received intravenous glucose.

These observations, plus the general experience with large therapeutic doses,[3,5] suggest that the irritating effect of phenformin on the gastrointestinal tract is the principal toxic effect of a single massive dose. Under the same circumstances, the three sulfonylureas in use at the present time often produce severe, and at times fatal, hypoglycemia.[9] The absence of the systemic metabolic alterations attributed to phenformin may be explained in at least two ways: (a) prompt expulsion of the drug from the gastrointestinal tract; (b) these metabolic effects do not appear in all patients and may not be dose related. The lack of an adequate method for determination of the level of phenformin in the blood prevented any differentiation between these possibilities.

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EDITORIAL

DIABETOLOGIA, Volume 1, Number 1

The Editors of this Journal have read with interest the first (August 1965) issue of *Diabetologia*,* the publication of the newly-formed European Association for the Study of Diabetes.

We have been aware for some years of the rising tide of research papers coming from various laboratories all over the world. The introduction of new technics of insulin and glucagon assay, the development of hypoglycemic agents, and the proliferation of research laboratories concerned with diabetes and related diseases were bound to increase the need for exchange of information via national and international meetings.

The last meeting of the International Diabetes Federation, held in Toronto in 1964, occupied five days, during which 187 papers were presented. In addition, 166 papers were read by title. This is evidence enough of the large number of reports asking or deserving dissemination.

It was only natural, therefore, that clinicians and laboratory scientists in Europe joined together to create another forum for the publication of acceptable papers and the exchange of ideas of mutual interest.

We welcome their publication as an effort comparable to our own and are impressed with the first number which has a format like ours, including the use of a summary as a foreword. This new journal has a special attraction for English readers since an English summary is supplied for every paper written in a language other than English.

The publisher is to be congratulated for producing an

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