

Sulfonylurea-induced Hypoglycemia Associated with Unusual Neurological Features

B. Harris, M.B., B.S., and M. S. Knapp, M.D., M.R.C.P., Bristol, England

We have recently treated a patient with sulfonylurea induced hypoglycemia who, when recovering, developed several features resembling Parkinson's disease. We were also able to record the serum insulin level, an observation which has been absent from previous reports of prolonged sulfonylurea induced hypoglycemia.

A sixty-three-year old man was admitted to hospital in a semi-comatose condition. Eight years previously diabetes mellitus had been diagnosed on the basis of glycosuria and a casual blood sugar of 300 mg. per 100 ml. He was treated with tolbutamide 0.5 gm. twice daily. As a result of advice given one month previously he had restricted his calorie intake for the first time (calculated calorie intake 600-700 calories daily). During these four weeks his wife had noticed that he was becoming "withdrawn" and "confused," and two days before admission he was found unconscious on the floor. He was put to bed at home and although he remained unrousable he was not sent to hospital for two days, during which time he received no food and no further tolbutamide. On examination there were no abnormalities in the cardiovascular or respiratory systems or in the abdomen. The pupils were small and did not react to light. There was a diabetic retinopathy but cranial nerves were otherwise normal. In the limbs muscle tone was increased throughout the range of joint movement, especially in the arms. The tendon reflexes were present and equal in the arms but absent in the legs. The plantar responses were absent. Biochemical investigations on admission showed blood glucose, 16 mg. per 100 ml.; blood urea, 19 mg. per cent; blood insulin (double antibody insulin assay), 24 μ U. per 100 ml., liver function tests, normal.

Treatment was commenced with 40 ml. of 50 per cent dextrose, then continued with a 5 per cent dextrose drip and hourly glucose drinks for twenty-four hours, blood glucose being maintained between 80 and 250 mg. per 100 ml. During the first twelve hours of treatment the patient became fully co-operative. A marked tremor of the forearms and hands developed during the

next three days and was present constantly. This was similar to the tremor found in Parkinson's disease and was accompanied by cogwheel rigidity of both upper limbs, dysarthria and a masklike facial expression. Three days after the onset of treatment these features became less marked, and over the course of a week the tremor and cogwheel rigidity disappeared.

There is no satisfactory explanation for the hypoglycemia which occasionally occurs during sulfonylurea therapy. In two patients inadequate degradation of tolbutamide was found (Kreeger¹; Spurney et al.²). Gardner et al.³ who found the half-life of tolbutamide normal in three patients, suggested a disturbance in the ability to respond to hypoglycemia, possibly due to a reduced calorie intake with resulting slow depletion of hepatic glycogen stores. This could have been initially responsible for the hypoglycemia in our patient who suddenly resolved to take a low calorie diet. The usual fall in insulin secretion which accompanies hypoglycemia may not have occurred—indeed the blood level was normal on admission. The relatively high insulin level would then have resulted in a further fall in blood sugar and eventually loss of consciousness. The hypoglycemia continued for at least two days after the last dose of tolbutamide, probably because glycogen stores had been further depleted in the absence of food intake. Abnormal metabolism of tolbutamide with prolonged activity may have been an additional factor in precipitating and prolonging the hypoglycemia.

This type of neurological disturbance has not been previously described in tolbutamide hypoglycemia and was presumably due to temporary brain damage in the region of the substantia nigra. This case illustrates the importance of careful observation when reducing calorie intake in patients taking oral hypoglycemic drugs.

REFERENCES

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- ³ Gardner, P., Goodner, C. J., and Dowling, J. T.: Severe hypoglycemia in elderly patients receiving therapeutic doses of tolbutamide. *JAMA* 186:991, 1963.

From the Bristol Royal Infirmary, University of Bristol, Bristol 2, England.