CLINICAL EXPERIENCE WITH HYPEROSMOLAR NON-KETOTIC DIABETIC COMA

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SYNOPSIS

Analysis of experience with 12 cases of non-ketotic hyperosmolar diabetic coma reveals that all the patients except one were over 40 years of age, and all had evidence of infection at the time of diagnosis. Half of them had a history of, or symptoms consistent with, diabetes mellitus and subsequent follow-up of survivors revealed three more patients with diabetes mellitus. Evidence of liver impairment was present in 3 patients and renal insufficiency (blood urea exceeding 250 mg./100 ml.) in 4 patients. Prior to diagnosis, 2 patients received hydrocortisone (600 mg. and 1000 mg.) and 2, large intravenous glucose load. All but 2 patients had varying degrees of depression of the sensorium but only 5 were clinically dehydrated. Blood sugar ranged from 165 mg./100 ml. to 1420 mg./100 ml., 9 patients had values in excess of 700 mg./100 ml. Acetonuria was uniformly absent and serum osmolality values lay between 321 and 431 m.osm./kg. H_2O. Hypernatraemia ($Na<150$ meq./L) was seen in only 6 out of 10 cases in whom serum sodium was measured.

Five patients perished, 3 of whom had received hypertonic (4·2%) $NaHCO_3$ solution (500 ml., 600 ml., 1600 ml.) and 1 had received 1.5 litres normal saline prior to diagnosis. For the survivors, half strength normal saline administered ranged from 1.5 to 10 litres, supplemented by water orally. Only 12 to 272 units of soluble insulin were required to bring hyperglycaemia under control.

INTRODUCTION

Hyperosmolar non-ketotic diabetic coma is a condition that has received increasing attention since Sament and Schwartz published their case in 1957. This condition is characterised by plasma hyperosmolality, hyperglycaemia and absence of ketosis and is associated with a high mortality (Jackson, 1969). In this paper we report a retrospective analysis of our experience with this condition.

MATERIALS AND RESULTS

Twelve patients with non-ketotic hyperosmolar diabetic state were seen in a general medical unit (Medical Unit II, Department of Medicine) from 1969 to 1973. There were seven males and five females. All but one were over 40 years of age. Three patients were actually septuagenarians.

A clear-cut history of diabetes mellitus was present in 3 patients; they were mild, non-ketosis-prone, maturity-onset diabetics. A further 3 patients, while not known to be diabetic, had had polyuria and polydipsia for variable periods prior to diagnosis of the hyperosmolar state.

As shown in Table I all patients had evidence of infection. Chest infection and urinary tract infection each accounted for three. Two had leptospirosis. Cholangitis, infected (diabetic) gangrene and infected skin (following trauma) were seen among the others. Other noteworthy concomitant conditions include chronic renal insufficiency (present in 4 patients) had liver dysfunction (present in 3 patients).

Additionally two patients had received massive intravenous doses of hydrocortisone (600 mg., 1000 mg.) for septicaemia and one had peritoneal dialysis with hypertonic (4·25% glucose) dialysate. One patient interestingly passed from classical diabetic ketoacidosis, with treatment, to hyperosmolar state. Dilantin (phenytoin) had been used as an anti-arrhythmic drug in a patient who had chronic renal insufficiency.

The prominent clinical features specific to the hyperosmolar state are depression of the sensorium and dehydration. Varying degress of altered state of consciousness, from mental confusion to deep coma, were present in all but

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TABLE I

AETIOLOGICAL FACTORS OF PATIENTS WITH HYPEROSMOLAR NON-KETOTIC DIABETIC COMA

Case	History or Symptoms of Diabetes Mellitus	Infection	Liver Impairment	Renal Impairment	History of Glucose Loading	Hydrocortisone	Dilantin
1*	+	+					
2		+	+	+	+		
3		+	+			+	
4	+	+					
5*		+					
6*	+	+		+	+		+
7	+	+		+			
8		+		+			
9*	+	+					
10	+	+					
11		+					
12*		+	+		+	+	

*Patients died eventually.

two patients. Five patients were overtly dehydrated (skin turgor, blood pressure), but all had oliguria and raised blood urea.

The biochemical changes are set out in Table II. Acetonuria was uniformly absent at diagnosis. Blood sugar was greater than 700 mg.% in 9 patients while hypernatraemia (>150 mEq./L) was present in 6 patients. (Serum sodium estimation was not done in 2 patients). Serum osmolality ranged between 321 and 431 mOsm./kgH_2O. There was a tendency towards hyperkalaemia although hypokalaemia was actually present in 2 patients. Serum alkali reserve was low in 4 patients.

Treatment with 0·45% normal saline (1·5 to 10 litres), soluble insulin (12—272 units) and water by mouth was applied to all cases after diagnosis. However 5 of the 12 patients died. It is interesting to note that of the 5 patients who died, 3 received large doses of hypertonic (4·2%) $NaHCO_3$ (400 ml.—1600 ml.) and one had received 1·5 litres normal saline prior to diagnosis. The other died of fulminant septicaemia. Of the 7 survivors, follow-up re-

TABLE II

LABORATORY DATA OF PATIENTS

Case	Osmolality mOsm/kgH_2O	Alk. Reserve vol.%	S. Na+ mEq/L	S. K+ mEq/L	Urea mg%	Blood Sugar mg%	Urine Acetone
1	334	28	—	—	86	1088	Nil
2	414	—	151	5·4	204	1420	Nil
3	377	65	167	—	—	780	Nil
4	321	62	—	—	62	920	Nil
5	341	—	146	5·4	190	370	Nil
6	398	75	170	3·5	460	688	Nil
7	377	—	170	6·9	376	165	Nil
8	387	—	174	4·7	408	454	Nil
9	431	36	181	2·7	122	708	Nil
10	368	31	130	3·5	105	1600	Nil
11	406	28	127	6·0	252	1600	Nil
12	368	—	130	2·4	174	1280	Nil

vealed normal G.T.T. in 2 patients, one of whom, however, had abnormal cortisone-G.T.T. Four had mild diabetes mellitus (one patient was lost to follow-up).

DISCUSSION

The aetiology of this condition remains a subject of speculation. The majority of our cases were either mild or previously undiagnosed diabetes, as is also the experience of Sheldon and Pyke (1968), Halmos, Nelson and Lowry (1966), Schwartz and Apfelbaum (1965). Six patients had either past history or symptoms suggestive of diabetes mellitus, and follow-up of the seven survivors revealed associated diabetes mellitus (clinical and latent) in three more patients.

Precipitating factors such as infection, stress or large ingestion of carbohydrate, had been reported (Schwartz and Apfelbaum, 1965; DiBenedetto, Crocco and Soscia, 1965). All our patients had evidence of infection. Liver and renal impairment were frequently present, which could have impaired glucose tolerance (Boukaert and De Duve, 1947; Pyke, 1968; Hutchings, Hegstron and Beinstein, 1966). Glucose loading (including peritoneal dialysis with 4·25% glucose dialysate) and large doses of hydrocortisone probably contributed significantly to hyperglycaemia (Boyer, Gill and Epstein, 1967). Goldberg and Sanbar (1969) reported an aetiological role for "Dilantin" particularly in the presence of renal insufficiency. This was seen in one of our patients.

Although alkali reserve was low in 4 patients, none of the patients had ketonuria or were clinically acidotic. Most of the patients with low alkali reserve actually had concomitant renal insufficiency. Coexistence of lactic acidosis could not be ruled out.

The mistaken administration of hypertonic $NaHCO_3$ solution was closely associated with fatal outcome. This occurred in the earlier cases and had significantly contributed to the high mortality (five out of twelve) in our experience. The small dosage of insulin required to control hyperglycaemia is in sharp control to that conventionally and for diabetic ketoacidosis (Sheldon and Pyke, 1968).

The cornerstone of management is to effectively correct hyperosmolality with rapid infusion of half-strength normal saline and generous intake of water by mouth.

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