PAPERS AND ORIGINALS

Hypothermia: a complication of diabetic ketoacidosis

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Summary and conclusions

During 1969-77, 20 episodes of severe hypothermia occurred in 19 diabetic patients in Nottingham. Thirteen were associated with ketotic hyperosmolar coma, two with lactic acidosis, and one with hypoglycaemia, while in four there was no loss of diabetic control. Ketoacidosis accounted for 11.8% of all admissions for severe accidental hypothermia and was a commoner cause than hypothyroidism (8%). Patients with ketoacidosis were younger and developed hypothermia as often during the summer as during the winter. The metabolic disturbance was characteristic, with severe acidosis (mean pH 7.04), a high blood glucose concentration (mean 56.6 mmol/l; 1020 mg/100 ml), and high plasma osmolality (mean 379.7 mmol (mosmol)/kg). Eight of the 13 episodes proved fatal.

Hypothermia may aggravate ketoacidosis and complicate treatment and should be sought in all patients with severe diabetic coma.

Introduction

Many patients admitted to this hospital with accidental hypothermia have been diabetics with ketoacidosis, and not all have been old. In several cases the clinical features suggested that the hypothermia was a direct consequence of the metabolic disturbance. We believe that insufficient attention has been given to this potentially dangerous complication of diabetic coma and have therefore reviewed all cases seen at this hospital during 1969-76.

Materials and methods

We used the Hospital Activity Analysis (HAA) index to review the notes of all patients admitted to this hospital during 1969-76 with diabetes, hypothermia, or hypothyroidism. Severe hypothermia was defined as a rectal temperature of 33°C or below.

Results

During the seven years 72 patients were admitted on 75 occasions for accidental hypothermia. Fifteen diabetics were responsible for 16 (21%) of these admissions, and on nine occasions (11.8%) the patient had ketoacidosis. In 1977 four other patients presented with diabetic ketoacidosis and hypothermia and are included here.

ACCIDENTAL HYPOTHERMIA IN NON-DIABETICS

During 1969-76, 57 non-diabetic patients (43 women, 14 men) were admitted on 59 occasions because of hypothermia. The mean age was 75.6 years (range 22-99); only two patients were under 55. Forty-eight admissions (81%) occurred during October to March. Of the 55 elderly patients, 45 lived alone, nine lived with other old people, and only one lived with younger relatives. In 24 instances hypothermia developed as a direct result of poor social circumstances, and in 33 the precipitating factors were sometimes multiple, the most common being hypothyroidism (8 cases), heart failure (8), mental confusion (7), drugs or poisoning (7), and stroke (4). The two younger patients had suffered severe exposure.

Thirty-four patients died (57.6% of admissions), which is comparable to the incidence in other series.¹ Mortality in men was very high: all 12 over the age of 55 died. In contrast only 21 of the 43 women died (49%).

HYPOTHERMIA IN DIABETICS

Four of the 19 diabetics developed hypothermia without an appreciable metabolic upset. In each case there was a clear precipitating cause (stroke, chlorpromazine treatment, barbiturate overdose, and isolation with dementia). All were elderly women with established diabetes receiving diet alone (one) or diet and chlorpropamide (three); three died. In the other 15 patients hypothermia was associated with a metabolic disturbance (tables I and II). One of these (case 16), a 68-year-old woman who lived alone and had a

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TABLE I—Clinical details and necropsy findings in diabetic patients admitted with hypothermia and metabolic derangement

Case No	Age and sex	Month of admission	Duration of diabetes	Clinical features	Duration of survival	Necropsy findings
1	73 F	May	2 weeks	Uncontrolled diabetes	8 days	Bronchopneumonia, fat necrosis
2	28 F	Nov	4 years	Omitted insulin	4 days	Bronchopneumonia, cerebral softening, fat necrosis
3	81 F	Jan	10 years	Fracture of neck of femur	14 days	Bronchopneumonia
4	75 F	Oct	2 weeks	Uncontrolled diabetes	8 hours	Fat necrosis
5*	54 M	Dec	5 years	Alcohol intoxication and exposure	Survived	
6*	56 M	June	7 years	Omitted insulin	Survived	
7	81 F	Oct	1 week	Uncontrolled diabetes, confusion	Survived	
8	76 F	July	12 years	Dementia. Found on floor	Survived	
9	65 M	July	25 years	Isolation and neglect	8 weeks	Necropsy not performed
10	43 F	May	8 years	Uncontrolled diabetes, boil on neck	Survived	
11	72 F	April	2 years	Found unconscious on floor	8 hours	Pulmonary embolism
12	65 F	Dec	At presentation	Isolation and neglect	16 hours	Fat necrosis
13	62 F	Feb	24 years	Vomiting, uncontrolled diabetes	24 hours	Pulmonary oedema
14	65 F	Dec	10 years	Phenformin-induced lactic acidosis	11 hours	No appreciable abnormality
15	65 M	May	14 years	Phenformin-induced lactic acidosis	24 hours	Bronchopneumonia
16	68 F	Dec	13 years	Insulin-induced hypoglycaemia	Survived	

*Same patient.

TABLE II—Consciousness level and biochemical details of diabetic patients admitted with hypothermia and metabolic derangement

Case No	Level of consciousness	Temperature (°C)	Blood glucose (mmol/l)	Plasma osmolality (mmol/kg)	Blood urea (mmol/l)	Venous bicarbonate (mmol/l)	Arterial pH†
1	Unconscious	29.2	27.2	334	15.0	5	
2	Drowsy	32.6	72.2	408	19.0	5	
3	Unconscious	30.0	38.0	366	26.2	9	6.85
4	Unconscious	26.8	90.0	410	33.3	11	7.18
5*	Unconscious	24.0	71.0	354	19.1	5	6.89
6*	Unconscious	31.0	67.5	365	21.7	5	6.95
7	Unconscious	33.0	55.0	440	38.3	8	7.24
8	Drowsy	32.0	50.0	379	36.6	9	7.13
9	Unconscious	33.0	60.9	365	40.0	8	7.26
10	Unconscious	33.0	39.0	343	23.4	5	6.85
11	Unconscious	25.0	43.9	423	40.8	7	6.99
12	Unconscious	25.0	57.7	367	20.0	4	
13	Drowsy	31.0	63.5	382	34.0	5	7.04
14	Unconscious	30.8	9.3	369	48.0	5	6.88
15	Drowsy	32.9	42.7	370	27.2	5	6.81
16	Unconscious	32.4	2.5	292	7.5	25	

*Same patient.

†Corrected for temperature.

Conversion: SI to traditional units—Blood glucose: 1 mmol/l $\approx$ 18 mg/100 ml. Plasma osmolality: 1 mmol/kg = 1 mosmol/kg. Blood urea: 1 mmol/l $\approx$ 6 mg/100 ml. Venous bicarbonate: 1 mmol/l = 1 mEq/l.

13-year history of diabetes, was admitted in December with insulin-induced hypoglycaemia. Two patients (cases 14 and 15) had phenformin-induced lactic acidosis, and have been described.²

Diabetic ketoacidosis and hypothermia

Thirteen episodes of hypothermia occurred in 12 patients with ketoacidosis. Two were men, and 10 women. Nine were known diabetics (duration 2–25 years), two were recently diagnosed, and one presented in diabetic coma. Seven of the established diabetics were taking insulin, and three chlorpropamide. Hypothermia and ketoacidosis occurred twice in one patient (cases 5 and 6), and another patient (case 11) had been admitted before 1969 with ketoacidosis and a rectal temperature of 34.4°C. The 12 patients had a lower mean age than the non-diabetics (63.9 compared with 75.6 years). Six of the 13 episodes occurred between April and September, while only 11 (19%) of the episodes in the non-diabetics were in this period.

All diabetic patients admitted with hypothermia and metabolic disturbance had impaired consciousness (table II); 10 were in coma. Shivering was seen in only one case, and several showed absence of Kussmaul breathing, an ominous prognostic sign.³ One patient (case 2) had abdominal tenderness. Isolation and neglect contributed to the condition in seven patients (cases 1, 3, 7, 8, 9, 11, and 12), one of whom lay on the floor for 24 hours with a fractured femur (table I). Another (case 5) developed hypothermia once after alcohol intoxication and exposure and again 18 months later in June, when no cause was found other than diabetic ketoacidosis (case 6). In four cases (2, 4, 10, and 13) uncontrolled diabetes also appeared to be a direct cause.

In cases 1–13, hypothermia (mean temperature 29.7°C) was associated with ketotic hyperosmolar coma (table II). Plasma tested with Ketostix or Acetest gave positive results in eight patients, and ketonuria of ++ or above was recorded in the rest. The metabolic disorder was uniformly severe, with a mean plasma glucose concen-

tration of 56.6 mmol/l (1020 mg/100 ml), range of 27.2–90.0 mmol/l (490–1620 mg/100 ml); osmolality 379.7 mmol(mosmol)/kg, range 334–440 mmol/kg; and urea 28.2 mmol/l (169 mg/100 ml), range 15.0–40.8 mmol/l (90–246 mg/100 ml).

Outcome

Despite treatment with fluids, insulin, and passive rewarming, eight of the 13 episodes proved fatal (table I). Four patients (cases 4, 11, 12, and 13) died within 48 hours of admission, two in asystole and two in ventricular fibrillation (due to hyperkalaemia in case 4). Three died two days to two weeks after admission, two from bronchopneumonia and one from cerebral oedema. The remaining patient (case 9) died in a convalescent home from bronchopneumonia eight weeks after admission.

Necropsy was performed in seven cases. Three showed bronchopneumonia, and four localised areas of intraperitoneal fat necrosis. The pancreas was macroscopically normal in all cases. One patient had a deep vein thrombosis and a small pulmonary embolus. Death was ascribed to bronchopneumonia in three and to metabolic causes in the other four.

Discussion

Body temperature may be subnormal during diabetic coma, even when infection is present,³ and Kussmaul commented on the cool, dry skin and cold extremities of his patients.⁴ Foster, in 1925,⁵ described a patient with a temperature of 33.6°C, but since then there have been few accounts of associated severe hypothermia. Rees⁶ described a woman of 44 admitted in diabetic coma with a temperature of 32.2°C on a day when the air temperature was 15°C, and Matz,⁷ who reported on two

patients admitted in April with diabetic coma and hypothermia, referred to eight others seen over five years. Severe hypothermia complicating ketoacidosis has recently been described in three patients aged below 30,^{8,9} and our experience of 13 admissions in eight years suggests that the association may not be uncommon. In contrast, hypothermia is a well-recognised complication of hypoglycaemia¹⁰ and may also occur in lactic acidosis.²

In our series diabetic patients accounted for one-fifth of all episodes of severe accidental hypothermia, whereas the many published reports show no excess of diabetics. We believe that there are two explanations for this. Most of our patients were identified retrospectively from a diagnostic index by consulting the categories of accidental hypothermia, diabetes, and hypothyroidism. This inevitably creates bias in favour of the second two conditions, since a secondary diagnosis such as hypothermia may be overlooked by coding clerks once a primary diagnosis—for example, stroke—has been identified. Conversely, other studies of accidental hypothermia may have underestimated the incidence in diabetics, particularly in centres where patients with diabetic metabolic emergencies are admitted direct to specialised units. Our impression is not that accidental hypothermia is more common in stable diabetics than in the rest of the population but rather that it occurs more commonly in the course of diabetic metabolic emergencies than has been recognised.

This impression is reinforced by the differences observed between the patients with ketoacidosis and hypothermia and those in the non-diabetic group. The diabetics were younger, and environmental temperature seems to have contributed less, since six of the 13 episodes occurred between April and September compared with 11 (19%) of the 59 in non-diabetics. The metabolic disturbance in the patients with ketoacidosis was severe and characteristic, very high blood glucose concentrations being associated with a pronounced metabolic acidosis. Hypothermia may aggravate uncontrolled diabetes in several ways: insulin secretion is impaired at low temperatures,¹¹ peripheral utilisation of glucose is reduced, and resistance to exogenous insulin develops.¹² Hypothermia stimulates the release of catecholamines¹³ and cortisol¹⁴ and may thus aggravate the metabolic disturbance. Loss of diabetic control is not inevitable in severe hypothermia, however, and did not occur in four of our patients.

While hypothermia may aggravate uncontrolled diabetes, ketoacidosis may affect temperature regulation. Although studies on patients in diabetic coma^{15,16} have shown a normal mean oral or rectal temperature, some patients in each series had a subnormal temperature, and fever is uncommon even in the presence of infection.¹⁷ Hypothermia may result from a failure of heat production. Oxygen consumption is a direct index of fuel consumption by body tissues and may be impaired in untreated diabetic ketoacidosis. Schecter *et al*¹⁸ compared the peripheral circulatory failure of hypovolaemia with that seen during diabetic coma and found that the arteriovenous oxygen difference was high in the former and low in the latter, suggesting

a failure of oxygen utilisation in the diabetics. This "histotoxic hypoxia" in diabetic ketoacidosis has been confirmed.¹⁹

Severe accidental hypothermia¹ and diabetic coma²⁰ carry a high mortality in the elderly, and the management of patients with both problems is difficult. Insulin may be ineffective at low temperatures,²¹ so that rapid rewarming is probably justified. Fluid and potassium replacement should be given with caution and arterial blood used for biochemical analysis, as stasis and pooling may render venous samples unreliable.²¹ Survivors of hypothermic diabetic coma may be at risk of recurrence, as are survivors of accidental hypothermia in general,²² and attention should be given to potential precipitating factors such as poor housing, alcohol abuse, or treatment with barbiturates or phenothiazines.

Hypothermia is easily missed and the rectal temperature should be checked with a low-reading thermometer in all patients admitted with severe ketoacidosis.

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References

- Exton-Smith, A N, *British Medical Journal*, 1973, **4**, 727.
- Gale, E A M, and Tattersall, R B, *British Medical Journal*, 1976, **2**, 972.
- Joslin, E P, *et al*, *The Treatment of Diabetes Mellitus*, 10th edn. Philadelphia, Lea and Febiger, 1959.
- Kussmaul, A, in *Classic Descriptions of Disease*, ed R H Major. Springfield, Charles C Thomas, 1945.
- Foster, N B, *Journal of the American Medical Association*, 1925, **84**, 719.
- Rees, J R, *Lancet*, 1958, **1**, 556.
- Matz, R, *Hormones*, 1972, **3**, 36.
- Alberti, K G M M, and Hockaday, T D R, *Clinics in Endocrinology and Metabolism*, 1977, **6**, 421.
- Craig, O, *Diabetes in Childhood*. London, Butterworths, 1977.
- Strauch, B S, *et al*, *Journal of the American Medical Association*, 1969, **210**, 345.
- Baum, D, Dillard, D H, and Porte, D, *New England Journal of Medicine*, 1968, **279**, 1309.
- Wynn, V, *Lancet*, 1954, **2**, 575.
- Young, J B, and Landsberg, L, *Clinics in Endocrinology and Metabolism*, 1977, **6**, 599.
- Sprunt, J G, Maclean, D, and Browning, M C K, *Lancet*, 1970, **1**, 324.
- Zieve, L, and Hill, E, *Archives of Internal Medicine*, 1953, **92**, 51.
- Cohen, A S, *et al*, *Annals of Internal Medicine*, 1960, **52**, 55.
- Greenaway, J M, and Read, J, *Australasian Annals of Medicine*, 1958, **7**, 151.
- Schecter, A E, Wiesel, B H, and Cohn, C, *American Journal of the Medical Sciences*, 1941, **202**, 364.
- Ditzel, J, Anderson, H, and Daugaard, N, *Lancet*, 1972, **2**, 818.
- Fitzgerald, N G, O'Sullivan, D J, and Malins, J M, *British Medical Journal*, 1961, **1**, 247.
- Cooper, K E, in *Recent Advances in Medicine*, ed D N Barron, N Compston, and A M Dawson, 15th edn. London, Churchill, 1968.
- Macmillan, A L, *et al*, *Lancet*, 1967, **2**, 165.

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ONE HUNDRED YEARS AGO Dr W Rubb (*Nashville Journal Med and Surgery*, January 1878) reports the following strange case. The patient in question is the little daughter of Mr Samuel B, who resides in north-east Simpson County, Kentucky. Both parents of the child are healthy, and offer nothing to indicate the hereditary transmission of the disease. The patient was four years old in March 1877, and then weighed one hundred pounds, measuring eighteen inches across the chest and nearly five feet in height. Her mammae were as fully developed as they are at puberty, and she menstruated regularly. Up to February 1876, though she was remarkably developed, she had given no indication of the following strange phenomenon. At that time, her temperature became higher than normal; and

hair soft and downy, in colour like that of her head, commenced growing all over her body. It completely covered her, with the exception of her face, palms of her hands, and soles of her feet; and the skin was entirely hidden from view. The sudoral secretion became constant and profuse, of a very offensive odour, which is noticeable at some distance from her. So profuse is the secretion that, in half an hour after being washed and dressed, her person and clothing will become saturated. The perspiration is of a dark yellow colour, and of greater specific gravity than usual. Her voice is coarse like a man's, and sounds as though she was speaking in a barrel. Her strength is equal to that of a full-grown man. Her intellect is much beyond her years, and her form is perfect. (*British Medical Journal*, 1878.)