Hyperosmolar non-ketotic diabetic coma as a cause of emergency hyperglycaemic admission to Baragwanath Hospital

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There were 136 emergency hyperglycaemic admissions to Baragwanath Hospital over a 6-month period during 1992 - 1993, representing 1,2% of the total number of medical admissions; 24 (18%) patients died. Diabetic keto-acidosis (DKA) accounted for 88 (65%) admissions (mortality rate 9%) while 16 admissions (12%) were as a result of hyperosmolar non-ketotic coma (HNKC), defined as hyperglycaemia, dehydration and an altered level of consciousness with a plasma osmolality $\geq$ 330 and an arterial pH $\geq$ 7,30, with absent or minimal ketonuria. Of these 16 patients, 9 (56%) were known to have diabetes mellitus. Patients with HNKC were significantly older than those with DKA ($P < 0,001$) and other patients with non-ketotic hyperglycaemia ($P < 0,05$). The overall mortality rate was 44%; prophylactic low-molecular-weight heparin appeared of benefit ($P < 0,05$).

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Hyperosmolar non-ketotic diabetic coma (HNKC) was first described in a 32-year-old black man admitted to Baragwanath Hospital, Johannesburg.[1] This 3 400-bed hospital serves between 2 and 3 million people. Diabetes mellitus is a common medical problem in this population; some 150 - 200 patients attend the weekly specialist clinic at Baragwanath Hospital, with an unknown number attending the twelve community health clinics situated around Soweto. There is an average of 1 600 admissions annually for diabetes-related problems, representing around 5% of the total number of medical admissions. HNKC is regarded by local physicians as a relatively common cause of emergency admission of diabetic patients, but no formal studies on its prevalence have been undertaken. The objective of this study was to assess the importance of HNKC as a cause of morbidity and mortality in diabetic patients admitted as emergencies to Baragwanath Hospital and to make recommendations for improved management of such patients, if necessary.

Patients and methods

Patients who require admission to Baragwanath Hospital are first seen in the emergency medical ward. Severely ill patients may stay there for several days or be transferred to the intensive care unit; the majority, however, are transferred to one of six medical units within 24 hours. Data were collected on all patients admitted to the emergency ward with a diagnosis of diabetes mellitus over a 6-month period, from September 1992 to February 1993. Patients were entered into the study if they were regarded as a hyperglycaemic emergency, i.e if they required intravenous saline and insulin.[2] A form was completed for each patient with details of age, sex, previous history of diabetes, current drug treatment and possible precipitating factors for the recent illness. The level of consciousness at presentation was assessed together with pulse, blood pressure, degree of dehydration and other physical findings. Haematological and biochemical data were recorded with special attention paid to the arterial pH and presence of ketonuria. Plasma osmolality (mOsm/l) was calculated from the formula 2 (sodium + potassium) + blood urea nitrogen + blood glucose (mmol/l). Diabetic keto-acidosis (DKA) was defined as hyperglycaemia in the presence of ketonuria ≥ 1 +, arterial pH < 7,30, and plasma bicarbonate < 15 mmol/l. HNKC was arbitrarily defined as an altered level of consciousness in a patient with hyperglycaemia, and dehydration with absent or 1 + ketonuria, arterial pH ≥ 7,30, plasma bicarbonate ≥ 15 mmol/l and a plasma osmolality ≥ 330 mOsm/l.

The progress and outcome of each patient's illness was followed in each medical unit, and body mass index (BMI) (kg/m^2) recorded upon recovery.

Statistical analysis was by means of Student's *t*-test or the χ^2-test, with Yates correction, as appropriate.

Results

There were some 11 800 admissions to the medical wards during the 6-month study period; of these, 136 (1,2%) were hyperglycaemic emergencies (Table I) and 24 (18%) patients died.

Table I. Hyperglycaemic emergency admissions

	No.	Deaths	(%)
DKA	88	8	(9)
Alcoholic-starvation ketosis	1	1	
HNKC	16	7	(44)
Hyperglycaemia, non-ketotic	31	6	(19)
Total	136	24	(18)

HNKC

Sixteen (12%) patients (11 women, 5 men) were diagnosed as having HNKC (Table II); 7 (44%) of these patients died (4 women, 3 men). Of the 16 patients, 9 (56%) were known to have had non-insulin dependent diabetes (3 deaths), while 7 (44%) were newly diagnosed (4 deaths). The mean BMI of survivors was 27,0 ± 5,3 (*N* = 5). Five of the known diabetic patients had defaulted from treatment (2 deaths). Five (31%) patients were receiving treatment for hypertension, but only 1 was known to be taking diuretics. There was no significant difference in age, mean osmolality or electrolyte concentration between those who died and those who survived. Five patients were hyponatraemic (Na < 130 mmol/l) at presentation, 4 had hypernatraemia (Na > 150 mmol/l), 3 hypokalaemia (K < 3,0 mmol/l) and 3 hyperkalaemia (K > 5,5 mmol/l). Patients with HNKC were significantly older than patients with DKA (mean difference 27 years, 95% confidence interval (CI) 18,7 - 35,3 years; t = 6,38, df = 100, P < 0,001) and other patients with non-ketotic hyperglycaemia (mean difference 7,8 years, 95% CI 0,8 - 14,8 years; t = 2,19, df = 45, P < 0,05). Levels of consciousness varied at presentation from obtundation to deep coma (4 patients, 3 deaths). Of the 9 survivors, 3 had focal neurological signs, which persisted in 1 patient, 3 had infections, 1 renal failure and in 2 there were no obvious precipitating factors. Of the 7 patients who died, 2 had focal neurological signs, 2 had septicaemia, 1 meningitis, 1 had a large subdural haematoma, while 1 patient died suddenly from probable metabolic causes. There was no obvious difference in treatment between those who died and those who survived, although 6 survivors received prophylactic subcutaneous heparin compared with none of those who died (χ^2 = 4,89; P < 0,05). The mean time between admission and death was 3 days (range 1 - 8 days).

Table II. Mean age (years), plasma osmolality (mOsm/l) and initial electrolyte concentrations (mmol/l) in patients with HNKC

	Survived (*N* = 9)	Died (*N* = 7)	Total (*N* = 16)
Age (range)	67,7 ± 10,9 (54 - 82)	64,3 ± 11,5 (45 - 78)	66,2 ± 11,3
Osmolality (range)	353 ± 15 (330 - 381)	360 ± 32 (330 - 433)	356 ± 24
Blood glucose concentration (range)	49,9 ± 14,0 (28,0 - 81,1)	50,5 ± 16,5 (21,4 - 72,0)	50,2 ± 15,1
Blood urea concentration (range)	19,1 ± 14,6 (6,3 - 54,0)	20,4 ± 6,3 (8,5 - 29,8)	19,7 ± 11,7
Plasma Na concentration (range)	138,9 ± 11,5 (115 - 158)	140,0 ± 17,7 (116 - 168)	139,4 ± 14,5
Plasma K concentration (range)	4,0 ± 1,4 (2,5 - 6,6)	4,8 ± 1,0 (3,3 - 6,4)	4,4 ± 1,3

DKA

There were 88 admissions (86 patients: 52 women, 34 men) with DKA; in 14 patients (10 women, 4 men) this was their initial presentation with diabetes. Their mean age was 39,2 ± 16,2 years (range 12 - 74 years); 8(9%) patients died (7 women, 1 man). They were significantly older (mean difference 15,9 years, 95% CI 4,4 - 27,4; $t = 2,71$, df = 84, $P < 0,01$) than the survivors. The mean BMI ($N = 73$) was 23,3 ± 3,9 kg/m², range 15,4 - 36,6; there was no significant difference between men and women. Of the 8 deaths, 4 were known diabetic patients, 3 were new presentations and in 1 patient this information was missing. Precipitating factors in episodes of DKA were non-compliance or inadequate insulin (40 patients: 21 women, 19 men), infection (21 patients: 17 women, 4 men), alcohol abuse (7 patients: 1 woman, 6 men), stroke (1 woman), and were unknown in 14 patients (11 women, 3 men). The mean plasma osmolality of all patients with DKA was 317 ± 20 mOsm/l (range 287 - 373); 21(26%) patients had a plasma osmolality greater than 330 mOsm/l, and there were 3 deaths. They were also markedly acidotic with a mean arterial pH of 7,08 ± 0,14.

Others

There were 31 patients (22 women, 9 men) admitted with non-ketotic hyperglycaemia, who were not considered hyperosmolar. Their mean age was 58,4 ± 11,7 years (range 40 - 85 years) with women being significantly older than men (mean difference in age 11,7 years, 95% CI 3,5 - 19,9 years; $t = 2,81$, df = 29, $P < 0,01$). The mean BMI was 27,4 ± 4,6 kg/m² ($N = 19$), range 18,8 - 35,7. Seven (23%) admissions were new presentations of diabetes (4 women, 3 men). Of the remainder, the precipitating factors identified were infections (10 patients: 8 women, 2 men), defaulting treatment (9 patients: 6 women, 3 men), stroke (2 women) and seizures (1 man). There were 6 (19%) deaths (5 women, 1 man). Two deaths were in patients whose osmolality was close to the arbitrarily defined level of 330 mOsm/l; 1 patient (326 mOsm/l) had septicaemia and renal emphysema and the other (327 mOsm/l) died abruptly from probable metabolic causes.

Discussion

This study confirms that HNKC is relatively common in this black diabetic population, accounting for 12% of all emergency diabetic admissions. Therefore, physicians at Baragwanath Hospital can expect to see 2 or 3 cases each month and each medical unit can expect about 5 or 6 patients annually. Nearly half the patients had not previously been diagnosed as suffering from diabetes mellitus, while defaulting treatment was a major factor in known diabetic patients. No patients were taking drugs, such as steroids, phenytoin, chlorpromazine or propanalol, which can precipitate HNKC,[3] and only 1 patient was known to be taking a diuretic for the treatment of hypertension. Glucose-rich carbonated drinks taken to alleviate the thirst of hyperglycaemia may occasionally be a factor leading to HNKC;[4] although they are popular in Soweto no information was available on their consumption by patients in this series.

Patients with HNKC should be managed along similar lines to those with DKA.[5] Normal saline should be rapidly infused initially, unless the plasma sodium concentration exceeds 150 mmol/l, when hypotonic saline should be used,[4] but after 1 - 2 litres it is preferable to switch to half normal saline as water losses exceed those of solute. Khardori and Soler[3] found no relationship between the volume and type of fluid used in the treatment of HNKC and the final outcome; it would seem desirable, however, to attempt to reverse the severe biochemical abnormalities with a simple scientific approach. Small quantities of neutral insulin should be given hourly until the blood glucose concentration is about 12 - 15 mmol/l. The intravenous route should be used as absorption may be erratic from other sites in the severely dehydrated patient. Potassium supplementation is essential and may need to be prolonged.[5] Infection, which may not appear clinically severe should be vigorously treated. Prophylactic heparin has been reported not to reduce mortality in HNKC,[4] but in view of the high risk of thrombosis of major vessels we believe that prophylactic low-molecular-weight heparin should be given; this study provides some statistical support for this.

Focal neurological signs and seizures are common in HNKC,[4] and affected 31% of patients in the present series. They may be secondary to cerebral thrombosis or cerebral dehydration, but hyperosmolality *per se* may activate epileptogenic foci[7] or cause widespread demyelination of the central nervous system.[8]

Of concern was the observation that some patients, who were not hyperosmolar initially, became so after some days in hospital. This was likely to be related to the excessive use of intravenous normal saline, and perhaps also failure to continue insulin treatment in sick non-insulin-dependent patients. A quarter of patients admitted with DKA also exhibited hyperosmolality; these patients with a mixed picture may have a poorer prognosis, and should be carefully monitored.

The high mortality rate (25%) of hyperglycaemic emergencies seen at Baragwanath Hospital in previous years[9] has been reduced, but much remains to be done. Public education on the signs and symptoms of diabetes, and greater awareness of the possibility of diabetes in older patients attending Soweto polyclinics, should lead to an earlier diagnosis, while the diabetic nursing services have a major role to play in stressing the importance of compliance. A failure of diagnosis and defaulting on treatment were significant correctable factors in this series.

The management of patients with HNKC presents a considerable challenge to clinicians. It may not be possible to reduce the high mortality rate significantly as most patients are elderly, with advanced disease, and the cause of death is usually multifactorial. In this population rigorous treatment of infection, careful monitoring of the metabolic milieu, avoidance of excessive use of normal saline and prophylactic low-molecular-weight heparin may be important factors leading to a successful outcome.

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