Blood Glucose Profile in Nigerian Chronic Renal Patients on Haemodialysis

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ABSTRACT
Glucose derangements are recognized features of end stage renal disease. Hypoglycaemia, when encountered in patients with chronic renal failure carries a poor prognosis. This study was designed to assess the magnitude of hypoglycaemia in chronic renal failure patients on haemodialysis.

Twenty non-diabetic chronic renal failure patients on haemodialysis with glucose-free bicarbonate dialysate were studied. Body mass index and serum albumin were recorded. Venous blood glucose was assessed before commencement of haemodialysis and hourly for 4 hours during dialysis. 12 of the initial study group had blood glucose estimation on a day they were not undergoing dialysis.

Blood glucose levels of <3.9mmol/l was regarded as hypoglycaemia and <2.5mmol/l as severe hypoglycaemia.

Blood glucose of subjects in the dialysis and post-dialysis period were globally low but hypoglycaemia was more prevalent during dialysis. In the haemodialysis period blood glucose was <3.9mmol/l in 85% and <2.5mmol/l in 50% of subjects. Blood glucose decreased with increasing duration of haemodialysis. Symptoms of hypoglycaemia were uncommon and only encountered in 15% of subjects. Malnutrition was prevalent in the study population.

Chronic renal failure patients have low levels of blood glucose and during haemodialysis they commonly develop hypoglycaemia. which in most cases, passes unnoticed. Malnutrition may be a contributory factor to the development of hypoglycaemia in subjects studied. We advocate the use of glucose-containing dialysate fluids for haemodialysis in non-diabetic chronic renal failure patients. Glucose drinks during haemodialysis may also be of help. Adequate nutrition should also be encouraged in patients with chronic renal failure.

Key words: Chronic renal failure, Haemodialysis, Hypoglycaemia.

INTRODUCTION
Glucose derangement, in the form of hyperglycaemia or hypoglycaemia, is part of the metabolic abnormalities associated with end stage kidney disease (ESKD) [1]. After insulin therapy, renal insufficiency is the second most common cause of hypoglycaemia accounting for 50% of hypoglycaemia in hospitalized cases [2, 3]. Also of note is the fact that hypoglycaemia in chronic renal failure (CRF) patients undergoing haemodialysis (HD) tends to be asymptomatic, is a serious complication and is associated with a high mortality rate [4, 5].

The pathogenesis of hypoglycaemia in CRF is complex involving several factors and mechanisms. Glucose unavailability due to reduced substrate is thought to be the most important factor with poor appetite, also nausea and vomiting all contributing to the reduction in substrate [1]. Drug-induced hypoglycaemia ranks second in the genesis of hypoglycaemia in renal failure. With deterioration in renal function, there is a progressive decrease in insulin metabolism and excretion leading to hyperinsulinaemia and consequently hypoglycaemia. Alcohol, sulphonylureas, non-selective β-adrenergic blockers, salicylates are examples of other drugs that are not effectively eliminated because of renal failure and which can contribute to the hypoglycaemia in CRF [6]. Inadequate hepatic glycogenolysis and gluconeogenesis, depression in sympathetic counter-regulatory response has also been shown to play a part in the development of hypoglycaemia in CRF [3].

Despite the magnitude of the problem, it is under-diagnosed because of insufficient awareness [1]. The aims of this study, therefore, were to assess the blood glucose profile and to determine
the prevalence of hypoglycaemia in CRF patients on HD in our center. To our knowledge no such study has been done in our environment.

PATIENTS AND METHOD

The study was carried out in the Renal Unit of the University of Benin Teaching Hospital over a five-month period. Following informed consent 22 non-diabetic CRF patients on haemodialysis were recruited. Subjects on B-Blockers, with history of significant alcohol intake or chronic liver disease, pre-dialysis blood glucose <3.9mmol/l were excluded. Patients were allowed their usual meals on morning of HD. Biodata, aetiology of CRF and serum albumin were retrieved from case records in all patients. All patients were in Stage 5 chronic kidney disease with signs and symptoms of CRF, renal ultrasonographic findings of two shrunken kidneys and a creatinine clearance <15mls/minute. Aetiology of CRF was considered to be hypertension in patients aged >40 years, who had been hypertensive for >5 years with features of longstanding hypertension; chronic glomerulonephritis in those with urinary findings of proteinuria, haematuria and red blood cell or granular casts in urine while diagnosis was taken to be toxic nephropathy in patients with history of prolonged and significant exposure to nephrotoxins such as herbal medications and skin lightening products. No renal biopsy was done in any patient because all had bilaterally shrunken kidneys. Body weight (kg) and height (m) were measured for calculation of body mass index (BMI). BMI and serum albumin were used to assess nutritional status of subjects. BMI <20 and/or a serum albumin <3.2 gm/dl were taken as evidence of malnutrition.

Venous blood samples were taken from subjects two hours after breakfast for estimation of pre-dialysis (or zero hour) blood glucose. Two patients were excluded from continuing with the study at this point because of blood glucose <3.9mmol/l. HD commenced using a low flux dialyser (F 5, UF 4.0) and glucose-free bicarbonate dialysate fluid, blood flow rate of 150mls/minute for initial 15-30 minutes and increased to 250-350mls/minute thereafter. Venous blood samples were taken hourly for 4 hours for estimation of glucose using the glucose oxidase method [7]. Blood glucose <3.9mmol/l was regarded as hypoglycaemia and <2.5mmol/l as severe hypoglycaemia. Subjects were closely monitored for symptoms of hypoglycaemia and 100mls of 50% dextrose was administered to any subject with such symptoms and were thereafter discontinued from study.

Four to six (4 – 6) weeks after initial study and on a day when patients were not on HD 12 of the study population were further studied. Venous blood samples were taken at 3 points (2-hours post breakfast for the zero hour sample and hourly for two hours). They were also monitored for symptoms of hypoglycaemia.

Data generated were analysed using SPSS statistical package and presented as means ± standard deviation (SD). Analysis of variance and the Kruskal-Willis test were used to compare the difference between means within groups while Mann-Whitney test was used to compare means between the groups. P value < 0.05 was considered significant.

RESULTS

Twenty (20) CRF patients (10 males, 10 females) aged 21 – 65 years (mean age 38.14 ± 11.95 years) were studied. Aetiology of CRF was hypertension in 11(55%), chronic glomerulonephritis in 8(40%) and toxic nephropathy in 1(5%). Mean BMI was 20.4 ± 2.1 while mean serum albumin was 3.43 ± 0.52gm/dl. Malnutrition was prevalent in the study population with 10(50%) of patients having BMI <20 and mean serum albumin <3.2 gm/dl. 20 patients dialysed for 2 hours. 18 for 3 hours and 16 for 4 hours. At commencement of study 6(30%) patients had blood glucose <4.5mmol/l.

On Haemodialysis

The blood glucose of patients was globally low ranging from 1.7-8.2mmol/l, <3.9mmol/l in 17 (85%) and <2.5mmol/l in 15 (75%) of patients. 6(30%) patients had pre-dialysis blood glucose <4.5mmol/l that reduced to <2.5mmol/l during HD in 4(67%) of them. Despite these low values only 3(15%) patients had symptoms of hypoglycaemia and all such patients had blood glucose <2.5mmol/l. The reported symptoms were weakness and feeling of hunger.

Blood glucose decreased with increasing duration of HD (Table 1 and Fig 1). Mean blood glucose was 5.19 ± 1.15mmol/l at commencement of study (0 hour) 4.09 ± 0.97mmol/l at one hour, 3.77 ± 1.66mmol/l at 2 hours, 3.02 ± 0.69mmol/l at 3 hours and 2.90 ± 0.92mmol/l at 4 hours of HD. This difference in the mean blood glucose between groups (in relation to duration of dialysis) within the HD group was highly significant (p < 0.001). At one hour of HD 8(40%), at 2 hours 14 (70%), at 3 and 4 hours
**Table 1: Mean Blood Glucose of Chronic Renal Failure Subjects**

<table>
<thead>
<tr>
<th>Group</th>
<th>0 hour</th>
<th>1 hour</th>
<th>2 hours</th>
<th>3 hour</th>
<th>4 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>5.19±1.15</td>
<td>4.09±0.97</td>
<td>3.77±1.66</td>
<td>3.02±0.69</td>
<td>2.90±0.92</td>
</tr>
<tr>
<td>N=20</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Post HD</td>
<td>5.12±0.86</td>
<td>5.09±1.08</td>
<td>5.15±1.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=12</td>
<td></td>
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</tbody>
</table>

**Post-dialysis**

Blood glucose values were similarly low in the post-dialysis period with a range of 3.2 – 6.2 mmol/l. The mean blood glucose at zero, one and 2 hours were 5.12 ± 0.86 mmol/l, 5.09 ± 1.08 mmol/l and 5.15 ± 1.01 mmol/l respectively (Table 1). The difference in the means between the groups within the post-dialysis group was not significantly different (P>0.05).

As shown in Table 2 at zero hour the mean blood glucose of 5.12 ± 0.86 mmol/l and 5.19 ± 1.15 mmol/l in the post-dialysis and HD groups respectively were similar (P < 0.05) while the mean blood glucose of 5.09 ± 1.08 mmol/l at one hour and 5.15 ± 1.01 mmol/l at 2 hours post-dialysis were low but were significantly higher than values of 4.09 ± 0.97 mmol/l (p < 0.05) and 3.77 ± 1.66 mmol/l (p < 0.01) at same points during HD. 2(17%) patients had blood glucose < 3.9 mmol/L in the post-dialysis period.

**DISCUSSION**

The findings of this study show that CRF patients run low levels of blood glucose and hypoglycaemia is commonly encountered in them when they undergo HD. 30% of patients had blood glucose < 4.5 mmol/l at commencement of study while 85% and 45% had blood glucose levels < 3.9 mmol/l and < 2.5 mmol/l respectively intradialysis. The causes and mechanisms of hypoglycaemia in CRF are multifactorial. Diminished glucose availability due to reduction of substrate is thought to be the most important mechanism leading to hypoglycaemia; poor appetite, nausea, vomiting, and inadequate dietary intake all result in calorie deprivation [1]. Also there is depression of sympathetic counter-regulatory response and this contributes to hypoglycaemia through inadequacy of hepatic glycogenolysis and gluconeogenesis[3, 8]. All these lead to chronic...
malnutrition in CRF patients. Indeed, malnutrition was prevalent in patients studied as 50% of the study population was malnourished and this is comparable to reports of 38% and 43.2% malnutrition rates in CRF patients [9, 10]. The high rate of malnutrition, no doubt, contributed to the common occurrence of hypoglycaemia, during dialysis and to the decreasing blood glucose levels with increasing duration of HD. The use of glucose-containing dialysate fluid for HD in non-diabetic patients will go a long way to correcting hypoglycaemia in this group of patients. Where this is not available, patients can be encouraged to take snacks or glucose drinks during HD and parenteral glucose given where necessary.

Despite the magnitude of hypoglycaemia observed in subjects with 50% having blood glucose levels <2.5mmol/l intra-dialysis, symptoms of hypoglycaemia were few and far between. Symptoms were observed in only 15% of subjects. This observation agrees with earlier reports that patients on HD may develop hypoglycaemia and not be aware of it and this has been attributed to blunting of sympathetic symptoms[4,5]. The sympathetic symptoms of hypoglycaemia are present at higher plasma glucose levels of between 2.8 – 3.9mmol/l compared to the neuroglycopenic symptoms, which manifest at lower blood glucose levels [11]. The sympathetic symptoms of hypoglycaemia are thought to be blunted for two reasons. First is the fact that the fasting state and under nutrition in CRF patients inhibit the sympathetic system; second is the presence of autonomic neuropathy with lack of sympathetic counter regulations in ESRD patients[1]. Thus impaired sympathetic counter-regulatory response in CRF patients plays a dual role of contributing to hypoglycaemia and also to the paucity of hypoglycaemic symptoms. The use of drugs like the non-selective β-blockers (such as propanolol, pindolol) cause hypoglycaemia by diminishing counter-regulatory response to hypoglycaemia. To combat this, addition of glucose to dialysate has been found to reduce the risk of hypoglycaemia in patients receiving such drugs during HD[3]. As part of exclusion criteria patients on β-blockers were excluded from study and they can be assumed not to have played any role on the degree of hypoglycaemia observed from results of this study.

The results of this study show that malnutrition and hypoglycaemia are commonly encountered in Nigerian patients with CRF. Hypoglycaemia, in majority of these patients, is asymptomatic. To reduce the high mortality associated with them, efforts should be made to diagnose and tackle hypoglycaemia in our population of CRF patients. Proper nutrition, adequate calorie-intake should be ensured in this group of patients. Blood glucose evaluation should be done more routinely in non-diabetic CRF patients. Glucose containing dialysate fluid should be used in HD patients and where this is not feasible glucose drinks should be given to non-diabetics during HD.

REFERENCES