

Full Length Research.

Insulin treatment alters some biochemical parameters in potassium adapted streptozotocin-induced diabetic rats.

O. J Owolabi* and E. K .I Omogbai

Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Benin. Benin City, Edo State, Nigeria.

*Corresponding author's: josphineomo@yahoo.com, owolabi@uniben.edu
Phone no: +2348034120318

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Insulin is the main drug for type 1 and 2 diabetes mellitus who are non responsive to oral hypoglycaemic drugs. This study is geared towards assessing the outcome of treating potassium adapted and non-adapted diabetic rats with insulin. The diabetic and non-diabetic rats (potassium adapted and non-adapted) were treated with insulin (5, 10, 20 and 40 i.u S.C). Thereafter the rats were transferred to metabolic cages and urine volumes, levels of plasma glucose, plasma and urine creatinine/electrolytes/urea, creatinine clearance and lipid profile were determined 24 hours after drug administration. In the potassium adapted diabetic rats, resistance to lower doses of insulin (5, 10 i.u/kg) was observed, suggesting insulin resistance by potassium adaptation. A reduction in the blood glucose level of the potassium-adapted diabetic rats were only possible with the higher doses (20 and 40 i.u/kg) of insulin used. A significant reduction ($p < 0.05$) of the LDL and triglycerides levels was noted in the potassium adapted diabetic rats treated with the different doses of insulin. All the doses of insulin administered increased the creatinine clearance in both potassium adapted normal and diabetic rats, in comparison with those not treated with insulin. It can be concluded that potassium-adaptation induces resistance to hyperglycaemic treatment, as seen with a higher blood glucose level that was non-responsive to treatment with lower doses of insulin.

Keywords: Blood glucose, Diabetes, Hypoglycaemia, Insulin, Potassium adaptation, Streptozotocin.

Introduction

Insulin is the mainstay for the treatment of type 1 diabetes mellitus and for type 2 patients, where control is poor with diet and oral hypoglycemic agents. Insulin is also useful in patients with gestational and postpancreatectomy diabetes. In addition it plays an important role in the management of diabetic ketoacidosis, hyperglycemic nonketotic coma and in the perioperative management of both type 1 and 2 diabetes (Jackson, 2001). In all diabetic patients the goal of insulin therapy is normalization of blood glucose and other aspects of metabolism. Optimal treatment requires a coordinated approach to diet, exercise and administration of insulin. Multiple daily doses of insulin should be able to achieve a fasting blood glucose concentration between 90 and 120 mg/dl (5 to 6.7 mmol/l) and a 2 hour postprandial value below 150 mg/dl (8.3mmol/l).

Potassium depletion inhibits insulin secretion and is associated with glucose intolerance, whereas potassium infusion and hyperkalemia increase the secretory rate of insulin by changing the membrane potential of pancreatic beta cells (Rowe *et al.*, 1980;

Dluhy *et al.*, 1972). Insulin is also known to stimulate extra renal potassium disposal by enhancing potassium uptake into the cells (Allon *et al.*, 1997). Since insulin can enhance potassium uptake, and potassium increase appears to enhance insulin secretion, the effect of adaptation to potassium on insulin therapy in diabetes was thus investigated via assessment of some biochemical parameters.

Experiments were thus designed with the following objective: to investigate the effect of insulin treatment with different doses on potassium adapted diabetic as well as in non-adapted diabetic rats.

Experimental

Drugs and Chemicals

Insulin (Sigma-Aldrich, UK), Streptozotocin (Sigma-Aldrich ,UK), Potassium Chloride (Wells Brand Nigeria), Total Cholesterol kit (Randox UK), Triglyceride kit (Randox UK), High density lipoprotein kit (Randox UK),

Glucose oxidase kit (Randox UK), Creatinine kit (Randox UK), Urea kit (Randox UK).

Stock solutions of drugs were stored in a refrigerator at 4°C. All chemicals were of analytical reagent grade.

Animals

Albino rats were obtained from the Animal house, Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Benin, Edo State. Animals were age matched and weighed between 200 and 300 g. They were allowed free access to water or a particular solution and fed on standard diet (Bendel Feed and Flour Mills Ewu, Nigeria). Depending on the group, 5 animals were housed in a cage with a 12 hr light-dark cycle prior to the experimental protocols.

Animals were handled according to the standard protocols for the use of laboratory animals. (National Institute of Health, USA: Public Health Service Policy on Humane care and use of Laboratory animals, 2002). Approval for the work was obtained from the Faculty of Pharmacy Ethical Committee on the use of Animals for experiments.

Procedure for Potassium Adaptation

The potassium adapted rats received potassium chloride (0.75 %) via oral administration for 5 weeks in place of tap water (Ozolua *et al.*, 2002).

Induction of diabetes

Experimental diabetes mellitus was induced in adult Wistar rats weighing 200–300 grams using Streptozotocin (60 mg/kg, I.P) in a 0.1 M citrate buffer solution (Frode and Medeiros, 2008).

Experimental protocol

Normal rats, potassium adapted normal rats and diabetic rats fasted over night (n= 5 per group) were divided into 3 groups each. Each of these groups received 5, 10 and 20 i.u/kg of insulin respectively. The potassium adapted diabetic rats were placed in 3 groups of 5 rats each and received 10, 20 and 40 i.u/kg of insulin respectively (Jafari *et al.*, 2004). All administrations were done subcutaneously.

The animals were kept in the metabolic cages separately and their body weight, urine volume, the levels of plasma glucose, plasma and urine creatinine, triglyceride, total cholesterol, HDL, LDL, creatinine clearance and urea in all animals were determined. Plasma and urine electrolytes were also determined.

Blood samples (5 ml) were collected via cardiac puncture, from which plasma was obtained after spinning the blood samples in a centrifuge. This was done after collecting the 24 h urine volumes from the metabolic cages. The plasma obtained was now used

in analysing the lipids, creatinine, urea, creatinine clearance, blood glucose and electrolytes.

Statistics analysis

Data are presented as the mean \pm standard error of the mean (S.E.M) and n represents the number of rats per group.

Comparisons were made where appropriate by One-way ANOVA (GraphPad Prism Software, UK, version 2.05a) with Tukey post hoc.

A value of $p < 0.05$ indicates significant differences in all cases.

Results

Effect on blood glucose

The blood glucose of the diabetic group was significantly ($p < 0.05$) reduced with insulin treatment (5, 10 and 20 i.u/kg) to 192.54, 190.0 and 185.0 mg/dl respectively while that of the potassium adapted group

treated with 5 and 10 i.u/kg of insulin was significantly higher than that of non adapted treated.

The blood glucose of the potassium adapted diabetic group was significantly higher ($p < 0.05$) than that of the diabetics (Figure 1) and was not significantly reduced on treatment with 10 i.u/kg of insulin (277.29 mg/dl). However the 20 and 40 i.u/kg doses of insulin significantly reduced the elevated blood glucose levels to 183.6 and 100.24 mg/dl respectively.

Effect on creatinine and urea

The effect of potassium adaptation on both the creatinine and urea (plasma and urine) of diabetic rats treated with the different doses of insulin (5, 10, 20 and 40 i.u/kg) are presented in Table 1.

The plasma and urine creatinine of the diabetic group treated with insulin at 5 i.u/kg produced no significance in comparison with the untreated diabetics, though the effect of the higher doses, (10 and 20 i.u/kg) was significant.

The urea values are also presented in Table 1. The plasma and urine urea values of the diabetic group treated with insulin (5, 10 and 20 i.u/kg) was not significantly different in comparison with the untreated diabetic group.

Effect on creatinine clearance

The potassium adapted group treated with 10 and 20 i.u/kg of insulin had a significantly ($p < 0.05$) higher creatinine clearance in comparison with the non adapted group, treated with the same doses of insulin (Figure 2). Treatment of potassium adapted diabetic

group with 10 i.u/kg of insulin increased ($p < 0.05$) their creatinine clearance in comparison with the untreated adapted diabetics.

Effect on urine volume

The result on the urine volume is presented in Figure 3. The volume of urine in potassium adapted diabetic group was significantly reduced ($P < 0.05$) with 10, 20 and 40 i.u/kg of insulin.

Effect on lipid profile

LDL and TG of the diabetic group (Table 2) treated with 5 i.u/kg of insulin was significantly different ($p < 0.05$) from the diabetic rats not treated with insulin. The total cholesterol, HDL, triglycerides of potassium-adapted

diabetic group were significantly different ($p < 0.05$) from the diabetic group, with a triglyceride value of 186.0 ± 24.6 mg/dl, almost five times the value of the diabetic group value. The triglyceride value however fell drastically from 186 mg/dl ($p < 0.0001$) following treatment with the different doses of insulin.

Effect on electrolytes

Tables 3 and 4 shows the result on the plasma and urine electrolytes respectively. Though the plasma potassium value of the adapted group was higher than control, it was however not significant. The urine potassium of the potassium adapted diabetic was significantly lower ($p < 0.05$) than that of the diabetic rats.

Urine bicarbonate of the potassium-adapted and diabetic groups were significantly different ($p < 0.05$) from controls.

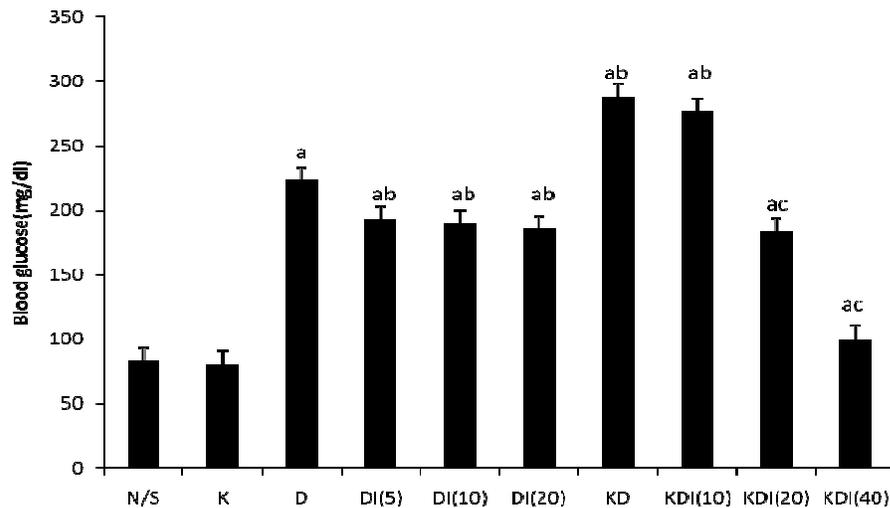


Fig 1: Effect of potassium adaptation on the blood glucose of streptozotocin- induced diabetic rats treated with insulin

Values are mean \pm SEM.

(n=5 per group).

^a $P < 0.0001$ significantly different from the control, ^{ab} $P < 0.05$ significantly different from the diabetic group, ^{ac} $P < 0.05$ significantly different from the potassium adapted diabetic group.

N/S : Normal saline group

I : group treated with insulin

K: group adapted to potassium.

D: diabetic group

DI: Diabetic group treated with insulin

KD: Potassium adapted diabetic group

KDI: Potassium adapted diabetic group treated with insulin

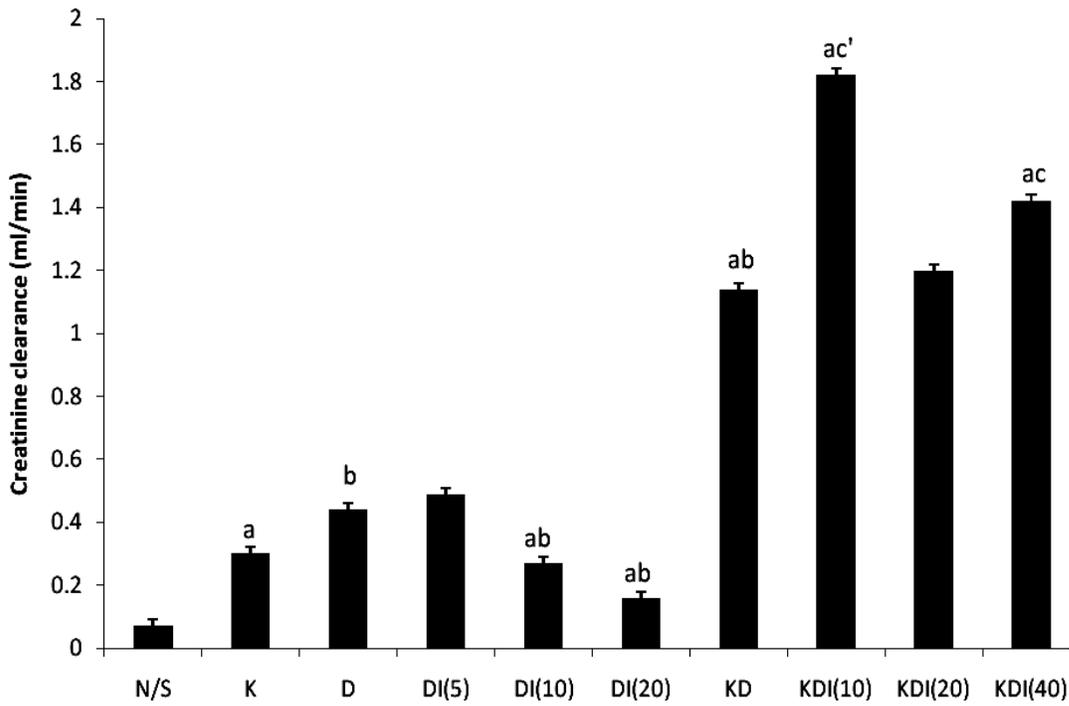


Fig 2: Effect of potassium adaptation on creatinine clearance of streptozotocin-induced diabetic rats treated with insulin

(n=5 per group).

^aP<0.0001 and ^bP<0.05 significantly different from the control, ^{ab}P<0.05 significantly different from the diabetic group,

^{ac'}P<0.0001 and ^{ac}P<0.05 significantly different from the potassium adapted diabetic.

N/S : Normal saline group

I : group treated with insulin

K: group adapted to potassium.

D: diabetic group

DI: Diabetic group treated with insulin

KD: Potassium adapted diabetic group

KDI: Potassium adapted diabetic group treated with insulin

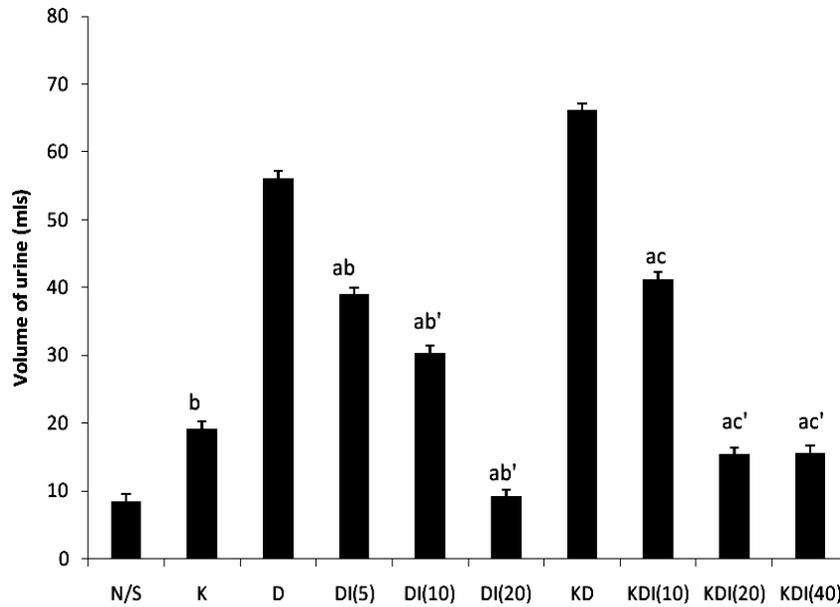


Fig 3: Effect of potassium adaptation on 24 h urine output of streptozotocin- induced diabetic rats treated with insulin

Values are mean \pm SEM.

(n=5 per group).

^bP<0.05 significantly different from the control, ^{ab}P<0.05 and ^{ab'}P<0.0001 significantly different from the diabetic group, ^{ac}P<0.05 and ^{ac'}P<0.0001 significantly different from the potassium adapted diabetic group.

N/S : Normal saline group

I : group treated with insulin

K: group adapted to potassium.

D: diabetic group

DI: Diabetic group treated with insulin

KD: Potassium adapted diabetic group

KDI: Potassium adapted diabetic group treated with insulin

Table 1 : Effect of potassium adaptation on creatinine and urea of streptozotocin- induced diabetic rats treated with insulin

Treatment (i.u/kg)	Creatinine		Urea	
	Plasma	urine	plasma	urine
N/S (2ml/kg)	0.21 \pm 0.03	2.67 \pm 0.62	9.27 \pm 0.37	785.85 \pm 116.90
K ⁺	0.09 \pm 0.01 ^b	1.77 \pm 0.13	9.44 \pm 0.42	469.39 \pm 62.26 ^b
D	0.26 \pm 0.03 ^{ab}	2.64 \pm 0.46	11.23 \pm 0.49 ^b	473.33 \pm 81.50 ^b
D + Ins (5)	0.15 \pm 0.02	2.48 \pm 0.40	14.46 \pm 1.89	588.52 \pm 93.50
D + Ins (10)	0.32 \pm 0.03	4.36 \pm 0.37 ^{ab}	11.61 \pm 4.84	239.4 \pm 44.25 ^{ab}

Table 1 continues

D + Ins (20)	0.41 ± 0.01 ^{ab}	10.35 ± 0.23 ^{ab}	15.7 ± 0.71 ^{ab}	70.66 ± 16.09 ^{ab}
K ⁺ + D	0.45±0.03 ^{ab}	10.97±1.14 ^{ab}	12.47±2.35	319.2±51.15
K ⁺ + D + Ins (10)	0.22 ± 0.01 ^{ac}	28.69 ±3.84 ^{ac}	39.93 ±0.49 ^{ac}	166.3 ± 10.84 ^{ac}
K ⁺ + D + Ins (20)	0.14± 0.03 ^{ac}	9.89± 1.09	35.54 ± 4.62 ^{ac}	196.18± 34.33
K ⁺ + D + Ins (40)	0.18± 0.02 ^{ac}	24.25± 2.55 ^{ac}	33.18 ± 1.57 ^{ac}	315.88± 43.98

Values are mean ± SEM.

(n=5 per group).

^aP<0.0001, ^bP<0.05 significantly different from the control, ^{ab}P<0.05 significantly different from the diabetic group ^{ac}P<0.0001 significantly different from

the potassium adapted diabetic group and ^{ad}P<0.05 significantly different from the potassium adapted group.

N/S: Normal saline group

Ins: group treated with Insulin

K⁺: group adapted to potassium

D: diabetic group induced with streptozotocin

Table 2 : Effect of potassium adaptation on the lipid profile of streptozotocin- induced diabetic rats treated with insulin.

Treatment (i.u/kg)	Lipids (mg/dl)			
	Total cholesterol	HDL (mg/dl)	LDL (mg/dl)	Triglyceride
N/S (2ml/kg)	61.81± 3.52	28.59± 3.42	22.86± 2.47	75.20± 10.93
K ⁺	44.32± 5.95 ^b	47.68± 1.75 ^b	12.07± 2.80 ^b	26.82± 6.94 ^b
D	60.13± 6.35	20.12± 2.89 ^b	33.10± 3.42 ^b	46.55± 7.87
D + Ins (5)	47.19± 1.00	15.53± 1.91	16.27± 2.43 ^{ab}	76.96± 9.04 ^{ab}
D + Ins (10)	76.20± 5.84	39.60± 2.87 ^{ab}	15.13± 5.67 ^{ab}	144.3± 15.33 ^{ab}
D + Ins (20)	62.00± 1.83	8.00± 1.08 ^{ab}	32.40± 2.77	108.00± 4.24 ^{ab}
K ⁺ + D	31.78± 2.54 ^{ab}	26.14± 2.50	0.66± 0.46 ^{ab}	186.0± 24.60 ^{ab}
K ⁺ + D + Ins (10)	52.60± 1.54 ^{ac}	34.60± 3.12	10.54± 1.79 ^{ac}	34.00± 1.09 ^{ac}
K ⁺ + D + Ins (20)	75.00± 2.41 ^{ac}	18.40± 5.59	46.64± 5.00 ^{ac}	53.40± 8.14 ^{ac}
K ⁺ + D + Ins (40)	57.80± 4.28 ^{ac}	25.60± 1.03	23.74± 2.31 ^{ac}	78.52± 9.83 ^{ac}

Values are mean ± SEM.

(n=5 per group).

^aP<0.0001 and ^bP<0.05 significantly different from the control, ^{ab}P<0.05 significantly different from the diabetic group, ^{ac}P<0.0001 significantly different from the potassium adapted diabetic group and ^{ad}P<0.05 significantly different from the potassium adapted group.

N/S : Normal saline group

Ins: group treated with insulin

K⁺ group adapted to potassium.

D: diabetic group

Table 3: Effect of potassium adaptation on plasma electrolyte of streptozotocin- induced diabetic rats treated with insulin.

Treatment (i.u/kg)	Plasma electrolyte (mmol/l)			
	Na ⁺	K ⁺	HCO ₃ ⁻	Cl ⁻
N/S (2ml/kg)	139.0±2.08	4.8±0.15	26.2±1.16	104.3±1.50
K ⁺	146.0±1.09 ^b	5.3±0.36	24.4±0.40	105.2±1.50
D	140.8±1.08	4.6±0.12	24.2±0.54	108.7±0.67 ^b
D + Ins (5)	139.2±1.07	7.1±0.45 ^{ab}	4.4±0.19 ^{ab}	105.1±2.24
D + Ins (10)	118.6± 1.33 ^{ab}	3.2 ± 0.26 ^{ab}	42.2 ± 2.82 ^{ab}	83.2 ± 4.32 ^{ab}
D + Ins (20)	122.5± 0.65 ^{ab}	3.4 ± 0.14 ^{ab}	38.5 ± 0.65 ^{ab}	93.5 ± 2.90 ^{ab}
K ⁺ + D	143.2±1.85	4.5±0.34	24.8±0.86	105.2±2.15
K ⁺ +D +Ins(10)	123.0± 7.07 ^{ac}	4.8 ± 0.36	26.2 ± 1.69	92.4 ± 2.79 ^{ac}
K ⁺ +D +Ins (20)	125.6± 1.57 ^{ac}	3.5 ± 0.15 ^{ac}	31.8 ± 0.58 ^{ac}	88.4 ± 1.29 ^{ac}
K ⁺ +D +Ins (40)	126.4± 2.16 ^{ac}	4.0 ± 0.21	29.0 ± 1.87	85.4 ± 2.79 ^{ac}

Values are mean ± SEM.

(n=5 per group). ^bP<0.05 significantly different from the control, ^{ab}P<0.05 significantly different from the diabetic group, ^{ac}P<0.0001 significantly different from the potassium adapted diabetic group and ^{ad}P<0.05 significantly different from the potassium adapted group.

N/S: Normal saline group

Ins : group treated with Insulin

K⁺ group adapted to potassium.

D: diabetic group

Table 4: Effect of potassium adaptation on urine electrolyte of streptozotocin- induced diabetic rats treated with insulin.

Treatment (i.u/kg)	Urine electrolyte (mmol/l)			
	Na ⁺	K ⁺	HCO ₃ ⁻	Cl ⁻
N/S (2ml/kg)	247.8±11.21	33.9±2.89	22.5±4.33	53.2±5.98
K ⁺	223.0±30.98	26.6±2.70	70.4±6.17 ^b	39.6±7.40
D	124.8±5.1 ^a	34.0±2.52	9.0±1.73 ^a	49.6±3.82
D + Ins (5)	239.4±0.58 ^{ab}	23.2±0.78 ^{ab}	56.2±0.66 ^{ab}	34.0±5.18 ^{ab}

Table 4 continues

D + Ins (10)	96.4 ± 1.86 ^{ab}	54.0 ± 7.97 ^{ab}	22.0 ± 4.66 ^{ab}	131.2 ± 4.84 ^{ab}
D + Ins (20)	92.5 ± 0.65 ^{ab}	36.3 ± 2.39	14.0 ± 1.83	126.0 ± 10.9 ^{ab}
K ⁺ + D	249.2 ± 12.50 ^{ab}	13.3 ± 0.80 ^{ab}	84.0 ± 4.65 ^{ab}	35.4 ± 4.58 ^{ab}
K ⁺ + D + Ins (10)	96.4 ± 3.54 ^{ac}	10.6 ± 5.09	15.0 ± 0.71 ^{ac}	136.0 ± 9.27 ^{ac}
K ⁺ + D + Ins (20)	100.8 ± 1.24 ^{ac}	9.2 ± 1.45 ^{ac}	13.4 ± 1.33 ^{ac}	146.8 ± 13.7 ^{ac}
K ⁺ + D + Ins (40)	94.6 ± 1.60 ^{ac}	15.0 ± 1.39	14.0 ± 2.03 ^{ac}	115.6 ± 8.66 ^{ac}

Values are mean ± SEM.

(n=5 per group).

^aP<0.0001, ^bP<0.05 significantly different from the control, ^{ab}P<0.05 significantly different from the diabetic group, ^{ac}P<0.0001 significantly different from the potassium adapted diabetic group and ^{ad}P<0.05 significantly different from the potassium adapted group.

N/S: Normal saline group

Ins : group treated with Insulin

K⁺: group adapted to potassium

D: diabetic group

Discussion

The effects of potassium adaptation on insulin reported to be useful in type 1 and unresponsive type 2 diabetes is being reported. On the blood glucose of normal diabetic rats, the lowering effect of insulin increased proportionately with the dose, such that the 20 i.u/kg dose gave the highest significant reduction of blood glucose in diabetic rats. However the normal rats did not survive the 20 i.u/kg dose of insulin. Apparently hypoglycaemia must have accounted for the mortality noted at that dose level. Insulin is known to induce hypoglycaemia (Katzung, 2001).

In the potassium adapted diabetic rats, resistance to lower doses of insulin (5, 10 i.u/kg) was observed, suggesting insulin resistance by potassium adaptation. The 5 and 10 i.u/kg doses were unable to reduce the blood glucose of potassium adapted diabetic rats which was noted to be significantly higher than the blood glucose of normal diabetic rats. However the higher doses (20 and 40 i.u/kg) significantly lowered the blood glucose. Resistance to insulin treatment could simply mean that the cells are unresponsive (insulin resistance) to lower doses of insulin, it will take a higher dose for the cells to respond to the presence of insulin. Insulin resistance means that body cells do not respond appropriately when insulin is present (DeFronzo and Ferrannini, 1988). For patients with type 1 diabetes mellitus, in which insulin is the mainstay for treatment and type 2 where control is poor (Jackson, 2001), it becomes a problem when the patient is unresponsive to insulin therapy as observed in cases of potassium adaptation. Hence potassium adaptation may not be

considered for type 1 diabetes mellitus patient with co-existing hypertension as the presence of potassium adaptation may hinder response or better still a higher dose of insulin may be needed (higher than 0.6 to 0.7 i.u/kg which is the average dose of insulin) (Davis and Granner, 2001).

The creatinine (plasma and urine) for potassium adapted diabetic rats, treatment with insulin significantly lowered the plasma creatinine at all doses (5, 10, 20 and 40 i.u/kg), and significantly increased the urine creatinine at the highest dose (40 i.u/kg). Creatinine is filtered out of the blood by the kidney and is a direct measure of renal excretory function. If the filtering by the kidney is deficient, plasma levels rises above normal, the urine levels reduces. Therefore creatinine in both blood and urine may be used to calculate the creatinine clearance which is a reflection of the glomerular filtration rate (Delanghe *et al.*, 1983). The result thus points to the fact that treatment with insulin may actually facilitate the glomerular filtration rate. This is further seen in the results showing the creatinine clearance.

All the doses of insulin administered significantly increased the creatinine clearance of both potassium adapted normal and potassium adapted diabetic rats, in comparison with those not treated with insulin. Creatinine clearance is also used to estimate the glomerular function (Bazari *et al.*, 2007).

A lowering of the volume of urine was also observed on treatment with all the doses of insulin used for both the normal and diabetic rats (potassium adapted and those non adapted to potassium) in comparison with the untreated groups. Polyuria and polydipsia are known symptoms of diabetes (Katzung, 2001).

Insulin significantly decreased the LDL and increased the triglycerides of the diabetic animals in comparison with the untreated diabetic rats. However for the potassium adapted diabetic rats, treatment with insulin seems to have significantly increased the total cholesterol, LDL, and lowered the triglycerides levels in comparison with the adapted diabetic rats untreated.

A high level of LDL can be suggestive of medical problems such as diseases of cardiovascular system (Segrest *et al.*, 2000), also the higher the level, the higher the risk for coronary artery disease (El-Hilaly *et al.*, 2006).

Insulin administration to diabetic animals that are adapted and non-adapted will thus afford protection and probably reduced the risk of developing coronary artery disease and disease of the cardiovascular system, whose incidence rate is high in diabetic individuals (Katzung, 2001). This is seen from the reduction in LDL levels of diabetic rats treated with the different doses of insulin.

It seems that potassium adaptation increases the risk towards cardiovascular disease and coronary heart disease, as seen by the raised triglyceride value; however treatment with insulin significantly lowered the triglyceride value to acceptable levels. Here again confirming the protective effect of insulin. Lowering of the triglyceride value on treatment with insulin may indicate an increase in the LDL value. As shown in the results, though a higher LDL value was noted for those treated in comparison with the untreated potassium adapted diabetic group, the values are still within the normal range.

The significant increase in total cholesterol obtained on treatment with the different doses of insulin is disadvantageous. Elevated total cholesterol above 180 mg/dl in plasma is a risk factor for coronary heart disease. The build-up of plaque in the artery may lead to narrowing (high blood pressure) or complete blockade (heart attack) of the vessel (Olson *et al.*, 1998). Though the total cholesterol of the potassium adapted diabetic rats were significantly increased on treatment with insulin, which probably indicates a risk for coronary heart disease via atherosclerosis, the raised values obtained however fall below 180 mg/dl.

A decrease in concentration of plasma sodium here on treatment with insulin (hyponatremia) could be suggestive of diseases of the liver, kidney or congestive heart failure (Markel and David, 1987). Persistent low levels of sodium in plasma in diabetic rats here is unacceptable because of the increased risk of developing congestive heart failure. However though

the plasma sodium levels were lowered on treatment, the values still fall within the normal acceptable range. The plasma chloride values were reduced on treatment. This is an indication of an underlying disease of the kidney or adrenal gland. The results on the plasma chloride for the potassium adapted diabetic and non-adapted diabetic rats treated with insulin, shows a reduction of the chloride value below the normal range, probably this loss could be as a result of heavy sweating, adrenal gland or kidney disease (Feldman and Bierbrier 1993).

Conclusion

Potassium adaptation may worsen the hyperglycaemia in diabetic rats, such that insulin resistance occurs with lower doses of insulin and response is seen only with higher doses of insulin. Insulin administration to potassium adapted and non-adapted diabetics may increase the creatinine clearance of diabetic individuals.

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