

## Abstracts

# 11<sup>th</sup> Annual Workshop on Diabetes Mellitus and its Complications Al Ain, United Arab Emirates

### **Type 2 diabetes: is it only a sugar matter?**

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The rationale for the treatment of diabetes has hitherto been directed to the correction of hyperglycaemia because hyperglycaemia is known to be responsible for the symptoms of polyuria and polydipsia in the short term and microangiopathic complications in the long term. The correction of hyperglycaemia leads to immediate resolution of polyuria and polydipsia, while a decline in HbA1c below 7 has been shown to predict a fall in the rate of microangiopathic complications. Thus, glycaemic control is the cardinal measure required to prevent microangiopathic complications. However, the most important complications leading to mortality in type 2 diabetes is macroangiopathy or atherothrombosis. Heart attacks and stroke are 2-4 times more frequent in people with diabetes compared with controls, and account for 70% of the mortality in these patients. People with diabetes without prior myocardial infarction have a similar risk of fatal or nonfatal myocardial infarction as non diabetic patients with a previous history of a heart attack. Hyperglycaemia contributes to macrovascular disease but the evidence related to its prevention by the control of hyperglycaemia is limited. Whereas observational studies demonstrate a relationship between HbA1c and cardiovascular events, prospective interventional studies (UKPDS; Kumamoto) do not show an impressive reduction in these events with a fall in HbA1c. Indeed, type 2 diabetes is not an isolated disease but is rather part of the metabolic (X) syndrome in which atherogenic risk factors (obesity, impaired glucose tolerance or diabetes, dyslipidaemia, hypertension, hypercoagulability) combine with underlying insulin resistance. Moreover, inflammation plays a central role in the insulin resistance syndrome and contributes to atherogenicity because atherosclerosis is also an inflammatory condition. Type 2 diabetes should thus be considered first and foremost a macrovascular disorder needing to be managed not only by glucose lowering, but also by aggressively treating underlying inflammation and associated metabolic disorders.

The restoration of normoglycaemia by the conventional drugs ensures the control of diabetic symptoms and the reduction in microangiopathic complications. However, the prevention of macrovascular disease, the main cause of morbidity in diabetes, involves the use of those glucose-lowering drugs that have an additional anti-inflammatory effect and the control of morbid conditions associated with this disease. It is of great interest that insulin,

thiazolidinediones and metformin not only reduce blood glucose concentrations but also exert anti-inflammatory and potential antiatherogenic effects. It is also relevant that the common drugs used to treat dyslipidemia and hypertension, such as the statins, ACE inhibitors and ARBs, not only improve clinical outcomes in type 2 diabetes, but also have anti-inflammatory properties.

### References

1. Dandona P, Aljada A, Chaudhuri A, Bandyopadhyay A. The potential influence of inflammation and insulin resistance on the pathogenesis and treatment of atherosclerosis-related complications in type 2 diabetes. *J Clin Endocrinol Metab* 2003; 88:2422-2429.
2. American College of Endocrinology Insulin Resistance Syndrome Conference Presentations. *Endocrine Practice*. September/October 2003, Volume 9 Supplement 2.

### **Diabetic dyslipidaemia: rationale for new lipid targets**

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Atherosclerosis is the leading cause of death among Type 2 diabetic (DM-2) patients and there is evidence to show that this prothrombotic tendency is present even in the prediabetic phase. In DM-2, there is clustering of traditional coronary artery risk factors, such as obesity, insulin resistance, hypertension, and dyslipidemia. Atherogenic diabetic dyslipidaemia is characterised by elevated serum triglycerides, low HDL cholesterol and a rise in small dense LDL particles. A landmark Finnish study published in 1998, convincingly demonstrated that the risk of subsequent coronary attacks is the same in a DM-2 patient as in a patient with established ischemic heart disease (IHD). As DM-2 is now regarded as a coronary equivalent, ATP III recommends the same lipid targets for DM-2 patients as for an IHD patient that is LDL -C < 100 mg/dl, HDL > 45 mg/dl and triglycerides < 200 mg/dl. Lowering the serum lipid levels below these lipid targets, leads to ~ 30 % reduction of subsequent coronary episodes. Among diabetic patients, coronary benefits of further lowering of total cholesterol from a level >135 mg/dl is apparent in the recently published Heart Protection Study. This new evidence is reflected in the 2004 ADA recommendation that 'in diabetic patients above 40 yrs of age, with total cholesterol > 135 mg/dl, a statin therapy to achieve LDL reduction of ~ 30%, regardless of baseline LDL cholesterol level, may be appropriate'.

### **Update on pancreatic islet cell transplantation**

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The success realized by pancreas transplantation in patients with type 1 diabetes and autonomic insufficiency has paved the way to a less demanding method of beta cell replacement, "islet cell transplantation". The dream that begun in 1972 of transplanting islets in patients with diabetes to restore normoglycaemia and to eliminate the need for insulin injections remains a work in continuous progress. Islet transplantation does not involve major surgery, permits a lesser degree of immunosuppression, and is potentially less expensive for the recipient. The rates of successful islet transplantation are increasing and the information about the long-term benefits of transplantation with respect to the secondary complications of diabetes has only recently begun to surface.

However, it is not without complications associated with percutaneous liver puncture, anticoagulation, and immunosuppressive regimens. Practical issues, such as the huge loss of islets during isolation and purification, the clinical complications associated with the use of hepatic site, adverse reactions to immunosuppression, and insufficient supply from donors, should be resolved before islet transplantation can take its place as a conventional therapeutic procedure.

### **Erectile dysfunction in diabetics-international experience with vardenafil**

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Prevalence and incidence of erectile dysfunction (ED) in diabetic men are markedly increased by the numerous comorbidities and complications of diabetes, but still only a small percentage of men with ED are diagnosed and subsequently appropriately treated. The increased prevalence of undiagnosed diabetes in men presenting with ED is now increasingly recognized and ED may now be considered as the "tip of the ice berg". Multiple risk factors often coexists with type 2 diabetes and associated ED warranting multifactorial risk management and therapy. The treatment of these patients with ED is often very challenging and refractory with the available oral drugs and other modalities. Vardenafil Phosphodiesterase 5 inhibitor has recently been introduced in the UAE for the first line oral pharmacotherapy for ED. Overall 72% of males with ED and diabetes report significant improvements in their erections with 20 mg Vardenafil. The improvement occurs early and is sustained over 12-24 months of continuous therapy. The improvement in initializing and maintaining satisfactory erections has been reported in 64% and 54% patients, respectively. Dose related, transitory adverse effects are reported in 25% of patients and no major cardiac side effects have been documented.

### **Pathophysiology of diabetic neuropathy**

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The prevalence of diabetic neuropathy in the Rochester study was estimated at 66% in patients with type I diabetes

and at 59% in patients with type II diabetes. Diabetic neuropathy develops as a result of hyperglycaemia-induced local metabolic and microvascular changes in both type I and type II diabetes mellitus. Direct correlations between hyperglycemia and diabetic neuropathy have been well established in the 'diabetes control and complications trial', the 'UK prospective diabetes study' and the 'Steno-2 study'. Several therapeutic interventions have been investigated for the prevention of and/or reversal of the underlying diabetic neuropathy. These include aldose reductase inhibitors, Myo-inositol, antioxidants, essential fatty acids, AGE formation inhibitors, neurotrophic factors, PKC inhibitors and pancreatic (islet cell) transplantation. Unfortunately, the success of the majority of these interventions has been very limited. Ongoing research into the pathophysiology of diabetic neuropathy continues to provide valuable insight as well as new targets for intervention.

### **Diabetes & macrovascular complications**

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Cardiovascular complications (coronary, cerebral and peripheral) are by far the most prevalent in patients with type 2 diabetes (T2D) and the leading cause of mortality. Renal complications of type 1 diabetes (T1D) were the principal cause of death. However, with the advent of dialysis and renal transplantation and because of further increases caused by such management techniques on the already accelerated atherosclerosis of T1D, so cardiovascular complications have now become the principal causes of morbidity and mortality and account up to 80% of deaths in diabetics. Most of the impact of diabetes on the macrovasculature is the result of an accelerated atherogenesis with heightened thrombotic activity. Many factors, some of which may exist in the prediabetic state particularly in T2D, are involved in the etiology of macrovascular disease. An atherogenic pattern of risk factors (dyslipidemia, hypertension, hyperinsulinaemia and impaired insulin sensitivity) related to insulin resistance syndrome has been proposed to induce atherogenesis, long before the clinical diagnosis of T2D. Diabetes is also associated with hypercoagulable state, plasma concentration of (PAF-1) is increased and this contributes to impaired fibrinolysis.

Endothelial dysfunction has been described in both insulin resistant states and T2D (components of metabolic syndrome) which may reduce the antithrombotic (increased platelets adhesion, increased procoagulant activity, increased molecule adhesions, and decreased fibrinolytic activity), vasodilating (decreased .NO activity, increased endothelin-1, dec. prostocyclyne) & protective (against oxidative stress) properties of the endothelium.

Risk factors modification and intervention have been shown to minimize the occurrence of CV events in diabetics. For successful prevention of CV complications, clinicians should therefore pay particular attention to the means of attaining the goals for the management of established traditional as well as non-traditional CV risk factors.

## **Continuous glucose monitoring system (CGMS) in diabetic subjects before and during Ramadan fasting**

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CGMS is a relatively new technique well suited to studying pattern of blood glucose values in diabetes including those during the Muslim fasting period of Ramadan.

Seventeen subjects were studied (13 with diabetes) using CGMS (Metronics TM). Repeated analysis during Ramadan fasting was made in six subjects. There was no significant difference in the mean blood glucose value by CGMS sensor compared to the mean from patient's own glucose meter value (160.2 v 158 mg/dl). The pattern of glycaemic control changed during Ramadan fasting compared to non-fasting period (max 302 ± 107 v 347 ± 16 mg/dl, min 115 ± 55 v 93 ± 34 mg/dl), although mean blood glucose was not significantly different.

The changes to this pattern in diabetic subjects during Ramadan fasting may have major implications on treatment during this period and merit further evaluation in a larger study.

### **Diabetes-alcohol interactions: skeletal malformations in the offspring of diabetic mice**

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**Background:** Pregestational diabetes is associated with a two to eightfold increase in the incidence of congenital malformations in the offspring. Diabetes is largely multifactorial in origin. It is not known if exposure to environmental teratogens can accentuate maternal diabetes-related fetal malformations. **Methods:** Mice were made diabetic by a single injection (IP) of 200 mg/kg of streptozotocin in citrate buffer (pH 4.6) on gestation day (GD) 2. Controls received buffer. On GD 7 one half of diabetic and control mice were treated (IP) with a single dose of 0.03 ml/g body weight of absolute ethanol solution in saline (25% v/v). Insulin controls received similar treatments in addition to a daily injection of 2-4 IU (SC) of insulin from GD 6 to term. Fetuses were collected on GD 18. **Results:** Maternal and other fetal effects have been reported elsewhere. Ethanol-fixed fetuses were stained with alizarin red-S and alcian blue and observed with a stereomicroscope. Buffer controls had a well-formed cranial and facial skeleton. Alcohol alone induced maxillary-mandibular hypoplasia in about 20% of fetuses and a 2% incidence of basicranial hypoplasia. In the diabetes plus ethanol group, the basicranium and vault of the cranium were poorly ossified leaving behind wide fontanelles in about 80% of fetuses. About 45% of this group had supraoccipital bone at stage 2-3 instead of stage 4. Meckel's cartilage around which the mandible ossifies was persistent in 20% of fetuses of this group and in none of the control and ethanol groups. Alcohol did not accentuate diabetes-induced accessory ribs but caused a 20% incidence

of rib fusion and hemivertebrae as well as scoliosis in 2% of the diabetic group. The frequencies of caudal vertebral agenesis/-and hypoplasia, poor ossification of the bones of the forepaw and hind paw and variations in sternal ossification were increased significantly in the diabetes plus alcohol group fetuses. **Conclusion:** These data imply a strong interaction of ethanol with maternal diabetes in the causation of skeletal malformations in this animal model (Supported by generous grants from FMHS and UAE University).

### **Streptozotocin-induced diabetic rat kidneys: changes in atrial natriuretic peptide and its receptors**

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In this study the effect of diabetes mellitus on ANP receptors (ANP-R) in streptozotocin (STZ)-induced diabetic rat kidneys was studied. Moreover, plasma ANP concentration was evaluated in diabetic and control rats using radioimmunoassay. Localization of ANP cells was performed by immunohistochemistry. Bodyweight loss was used as an index of diabetes mellitus in the STZ rats. There was a significant loss in the bodyweight of the diabetic rats compared to controls (P<0.001). Diabetes mellitus was confirmed by rising blood glucose levels which were significantly higher (P<0.001) in diabetic rats compared with controls. The distribution and levels of ANP-R in diabetic rat kidneys and age-matched controls was investigated using quantitative receptor autoradiography. Our results demonstrated significant decrease in ANP-R in diabetic rat kidneys compared to controls. This significant decrease was found in the juxtaglomerular medulla, inner medulla and the papillae. Plasma ANP concentration was significantly greater in the diabetic rats in comparison with controls. In addition, the number of ANP immuno-reactive cells was higher in the kidneys of diabetic rats compared with controls. ANP-positive cells were observed mainly in the cells lining the proximal convoluted tubules. The increase in plasma ANP concentration could be as a result of plasma volume expansion present in STZ diabetic rats. The decrease in ANP receptors observed in the diabetic kidneys might have pathological consequences resulting in renal resistance to ANP in diabetes.

### **The prevalence of complications among diabetic patients in Al Ain Medical District**

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Diabetes Mellitus (DM) is a major health problem in the UAE. A WHO population survey in 1999 reported a prevalence of 24% in local citizens and 17.4% in expatriates. The aim of this study was to determine the prevalence of complications among diabetic patients in Al Ain district. A sample of 513 DM patients was recruited to

determine complications. The analysis showed the following rates: 19% had retinopathy and 39% neuropathy. Microalbuminuria was found in 58%, proteinuria in 12.5% and chronic renal failure in 1.4%. 12% had peripheral vascular disease, 14% had coronary artery disease and 4% had cerebrovascular disease.

### **Impact of structured diabetes clinic on the outcome of diabetes management in a tertiary care center in Abu Dhabi**

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**Introduction:** The Diabetes Clinic at SKMC is staffed by two consultant endocrinologists, senior registrar, diabetes educator, and a part-time dietician. They form the diabetes management team. Every effort has been made to have new patients referred to the clinic seen by all members of the team. Current diabetes management protocols have been employed to achieve improved glycaemic control. **Results:** We report on our experience with 124 patients who have been followed up in the Diabetes Clinic of SKMC for 9 – 15 months. Hemoglobin A1c dropped from a mean of 9.3% at the time of initial referral to the Diabetes Clinic to a mean of 7.4% one year later ( $p < 0.001$ ). Improvement in lipid profile was also noted. **Conclusion:** Structured diabetes clinic employing team management in diabetes care leads to improved glycemic control in a tertiary care center in Abu Dhabi.

### **Knowledge of diabetes-related issues and self-care in Abu-Dhabi patients: General perspectives**

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**Aim:** To evaluate the level of diabetes knowledge and self-care in educated and uneducated adults with diabetes mellitus and to identify the factors influencing them. **Setting:** The general medical and endocrinology clinics at a general referral hospital in Abu Dhabi. **Method:** Over a 10-week period, we randomly selected a number of adult diabetics who attended these two clinics and divided them on the basis of their level of education. Illiterates and others with only primary school education were considered as uneducated. Others with secondary schooling or higher were categorized as educated individuals. The patients were invited to answer a questionnaire containing eight items of diabetes-related knowledge and diabetes self-care. It included knowledge of self-monitoring blood glucose (SMBG), knowledge of urine testing, hypoglycaemic symptoms awareness, chronic complications awareness, self-injection of insulin among insulin users, compliance with medications, whether honey is useful for diabetics and whether herbal medicine is superior to conventional hypoglycaemic agents. Demographic and disease characteristics were also documented. The results of the two groups were subsequently compared and analyzed. **Results:** Out of 219 diabetics, 127 (58%) were uneducated and 92 (42%) were educated. The mean disease duration (10.3 years  $\pm$  6.1 vs. 8.2  $\pm$  5.7 SD,  $p = 0.007$ ) and the FBS

(175.6 mg%  $\pm$  67.9 vs. 185.2  $\pm$  76.2 SD) were not different in these two groups respectively. Nearly 71% of the educated diabetics expressed knowledge of SMBG vs. 30% of the uneducated individuals ( $p = 0.001$ ). They also scored marginal difference over the others in self-injection of insulin (89.5% vs. 79.5%,  $p = 0.04$ ). Yet, interestingly, a quarter of the educated patients appeared to believe in the superiority of herbal medicine over conventional therapeutics in comparison to the uneducated group (25.5 vs. 9.8%,  $p = 0.01$ ). Although the two groups did not differ in the remaining items of the questionnaire, one third of the patients in each group turned out to be in favor of using honey as a remedy for diabetes. **Conclusion:** The amount of knowledge on diabetes-related issues appeared modest in these representative groups. Educational efforts in any form are certainly needed for both groups. They should not be directed towards the evaluated items only, but should be extended to dismiss existing misconceptions too.

### **Infections due to gas forming organisms in type 2 diabetic patients – Al Ain hospital experience**

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We present our experience in managing diabetic patients with life threatening infections with gas forming organisms. Emphysematous pyelonephritis (EP) is a necrotising infection of renal parenchyma, usually caused by facultative anaerobes like *E. Coli*. The probable mechanism of gas formation in EP is fermentation of glucose in necrotic tissues with production of nitrogen, hydrogen and carbon dioxide. Though earlier reports recommend either surgical drainage or nephrectomy to prevent further systemic spread of infection, we observed successful outcome with early aggressive antibiotic therapy alone. Unlike EP, we advocate early surgical intervention in necrotising fasciitis (NF). Mostly our diabetic patients had NF involving lower limbs, but infections of other rare sites like abdominal wall, neck were also noted. The clinical suspicion arose due to presence of crepitus in the affected region and an urgent plain X-ray or CT scan was confirmatory. The infection was mainly caused by facultative anaerobes, but was often polymicrobial in origin. Repeated extensive debridements and prolonged antibiotic therapy were curative in some of our patients. We stress the need of early diagnosis of this potentially fatal infection in all diabetic patients. We also report an unusual presentation of spontaneous rupture of liver abscess due to Klebsiella infection in a type 2 diabetic patient who was saved by early surgical intervention.

### **Reducing coronary risk in type 2 diabetes- an intergrated, risk-focuses approach**

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**Aim:** To asses if a dedicated specialist nurse intervention in addition to conventional diabetes care will reduce the cardiovascular risk profile in patients with type 2 diabetes mellitus attending a hospital clinic. **Setting:** Diabetes Clinic at Clatterbridge Hospital in the North West of England, with

2004 patients on the clinic database, 89.7% with type 2 diabetes and 10.3% with type 1 diabetes. **Methods and material:** This is a prospective structured pilot study, based on a three-month close follow-up of 209 type 2 diabetic patients; with or without coronary heart disease (CHD). The patients were randomised either to standard diabetes care or risk-focused intervention facilitated by a dedicated research nurse. Both groups were followed up over a period of 12 months. Systolic blood pressure (SBP), diastolic blood pressure (DBP), glycaemic control (HbA1c), smoking status and total cholesterol were measured at baseline and 12 months later. 89% of patients returned at 12 months. Blood pressure (BP), HbA1c, total cholesterol and smoking status were assessed at 0 and 12 months. **Results:** In the intervention group, (n=57) with CHD, there was reduction in systolic (158-153,  $p < 0.05$ ) and diastolic (86-82,  $p < 0.001$ ) BP, HbA1c (7.5-7.2%,  $p < 0.01$ ), and smoking (25-14%,  $p < 0.01$ ), but not cholesterol. In contrast the CHD control group (n=52) reduced systolic (162-148,  $p < 0.001$ ) and diastolic (89-84,  $p < 0.01$ ) BP, cholesterol (5.3-4.8,  $p < 0.001$ ), and smoking (37-24%,  $p < 0.01$ ), but not HbA1c. The non-CHD control patients (n=48) reduced systolic (165-154,  $p < 0.01$ ) but not diastolic BP, cholesterol (5.5-4.9,  $p < 0.001$ ), HbA1c (7.9-7.4%,  $p < 0.01$ ), but not smoking. We conclude that relatively brief nurse-led risk factors counseling followed by targeted clinic interventions leads to greatly reduced risk factors profiles in type 2 diabetic patients.

#### **Factors associated with obesity in Arabian women**

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**Objectives:** An increasing prevalence of obesity over a short period of time has been reported in the rapidly developing Arabian Gulf countries especially among women. We investigated the association between measures of obesity and factors related to it in a population-based sample of Arabian women. **Subjects and Methods:** All subjects completed a questionnaire on demographic and reproductive factors, dietary calcium intake, and physical activity. Body mass index (BMI) was calculated from measured height and weight, and body fat percent (BFP) was estimated by bioelectric impedance. **Results:** Four-hundred and eighty-nine non-pregnant women (age range, 20-75 years) participated in this study. The rate of obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) was 33.7%. The peak prevalence of obesity (61%) was reached in the 5<sup>th</sup> decade and 21% of women in the third decade were obese. BMI correlated significantly with BFP ( $r = 0.67$ ,  $P < 0.001$ ), although the correlation declined after the fifth decade. BMI ( $\geq 30$  kg/m<sup>2</sup>) and BFP ( $> 35\%$ ) were inversely associated with education and physical activity, and positively associated with age, parity, chronic illnesses, and perceived good health status ( $P < 0.05$  for all variables). There were no significant associations between age at menarche, menstrual irregularity, menopausal status (after adjustment for age), and dietary calcium intake, and measures of obesity. Women in the highest tertile of physical activity were less likely to be obese (odds ratio 0.59, 95% confidence interval 0.36-0.96) compared to the lowest tertile. **Conclusions:** The prevalence of obesity in this population is among the highest reported in the literature, especially in younger age groups. The associated factor that may be most amenable to intervention is low physical activity.