ABSTRACT BOOK

Excellence in Diabetes and Endocrinology-2010: Cutting Edge Topics in Clinical Diabetes and Endocrinology

Thursday 25th to Saturday 27th November 2010, Khalidiya Palace Rayhaan Hotel and Resort, Corniche Street, Abu Dhabi. UAE.

Guest Editors: Salem A. Beshyah[1] and Asma Deeb[2]

1. Endocrine Division, Institute of Medicine, Sheikh Khalifa Medical City, Karamah Street, Abu Dhabi, UAE.
2. Department of Paediatrics, Mafraq Hospital, Abu Dhabi, UAE.

*Corresponding Editor: Salem A. Beshyah Email: beshyah@yahoo.com
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Abstract

These are the abstracts of a 2.5 days of continuous medical education meeting that was held in Abu Dhabi, UAE to mark the World Diabetes Day 2010. It brought together doctors taking care of children and adults with diabetes and other metabolic and endocrine disorders. The organizers thought it would be particularly relevant to bring pediatric and adult endocrinologists together to exchange experiences because the age gap between pediatric and adult is fairly small. The lectures covered a wide range of issues, such as growth, pituitary tumours, neonatal diabetes, old and new antidiabetic drugs, type 2 diabetes in the adolescence, and calcium disorders. Special emphasis was given to thalasaemia as an important medical problem with medical and endocrine ramifications in this region, management of hypoituitarism in adults, and interdisciplinary issues in endocrinology.

Abstracts of Presentations

Session 1. Current Perspectives in Paediatric Endocrinology

A. Regional Experience with Insulin Pump Therapy

1.1 A Rare Form of Neonatal Diabetes: Diagnostic and Management Challenges

Majedah Abdul-Rasoul, Department of Pediatric Endocrinology, Faculty of Medicine, University of Kuwait, Kuwait.

Neonatal diabetes is a very rare form of diabetes. Its diagnosis presents a major challenge both to the family and to the treating physician. The presenting case was born near term with severe low birth weight. Hyperglycemia was noted for the first time at the age of 17 days associated with ketonemia but no acidosis. She was also failing to gain

weight and extreme irritable. The diagnosis of diabetes was made, and after initial management with intravenous insulin, she was shifted to subcutaneous insulin using a combination of intermediate and short acting insulin. Blood sugar failed to be controlled, and at the age of 45 days, insulin pump (Minimed 712) was used as her mode for insulin delivery, using insulin APIDRA diluted with normal saline because of small doses required both for boluses and basal. Her insulin requirements dropped significantly from 2.1u/kg/D to 0.9u/kg/D on the pump. Glucose values continue to fluctuate, but the variability were significantly lower in amplitude. Currently at the age of 14 months, she has normal motor and cognitive development for her age, and her weight and height remains appropriate for her age. All antibodies, including thyroid, pancreatic and celiac were negative. Genetic testing failed to show any abnormalities in chromosome 6 or any mutation in Kir 6.2 and SUR1 genes.

1.2 Clinical Aspects of Using Pumps and Advanced Technology in Diabetic Children

Asma Deeb, Department of Paediatrics, Mafraq Hospital, Mafraq, Abu Dhabi, United Arab Emirates.

There has been a wide utilization of advanced technology in various branches of Medicine in the recent decades. Recent therapeutic and technological advances have made dramatic changes in management of diabetic patients. Continuous glucose monitoring system (CGMS) has proven to be an advantageous diagnostic and therapeutic tool in diabetes management. Various studies confirmed the role of CGMS in detecting significant diabetes problems like nocturnal hypoglycemia, postprandial hyperglycemia, Dawn and Somogyi phenomena and has given an insight to management of these challenging conditions. There have been advances in the use of CGMS either as a real time sensing (Minimed guardian, Dexcom system, Navigators) or as a blind tool for retrospective diagnoses (Minimed Gold and IPro). Use of continuous subcutaneous insulin infusion (CSII) via insulin pumps has made revolutionary changes in management of diabetes. CSII is the most physiological way of delivery of insulin currently available. It offers the possibility of more flexibility and precise insulin delivery. The feasibility of basal rate alteration offers the option of modifying the basal rates according to the individual requirements. Up to 48 different basal rates are offered by some insulin pumps. Various types of bolus delivery methods are available in most insulin pump technologies to match the glycemic index contained in food. And various patterns of pump settings can be programmed to match various requirements; exercise, weekends, fasting…etc. CSII use in children and adolescents may be associated with improved glycemic control and improved quality of life and poses no greater risks than other modalities of administering insulin. A summary of the use of technology in management of childhood diabetes will be presented and selection of case scenarios in relation to technology use will be discussed.

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1.3 Experience with Insulin Pump in Adults

Waleed Aldahi (Kuwait)

No Abstract.

B. Growth Update

1.4 Growth Charts for Saudi Children: Development and Clinical Uses.

Ibrahim A. Al-Alwan. College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

Introduction: Children's normal growth is monitored by charts, which are specific for sex and age. These measurements, which reflect normal growth, are indicative of overall health and nutritional status of the children. The growth charts are specific for different nations and should be taken into consideration with immediate family parameters and the child's ethnic background. Healthy children grow in a predictable fashion and normal growth is pulsatile with rapid periods of growth. The episodes of fastest growth occur during infancy and puberty. As recommended by WHO, Saudi Arabia and Gulf Region, use CDC growth charts for monitoring healthy children and patients. However, these charts are not race or ethnicity specific.

Aim: The aim of this study is to evaluate current growth

charts in Saudi Arabia. We evaluated any differences noted between Saudi and international growth charts.
Methods: Systematic review of all published literature about Saudi growth charts, including height, weight, BMI from 0–19 years; PubMed was the main search engine.
Results: Several large Saudi studies were conducted over the last 20 years. They differ on several points. These studies were either male only, in major cities only, cross-sectional and school based or clinical based. The largest recent study was a national study, cross-sectional, door-to-door and included children from birth to 19 years. A total of 42,000 healthy Saudi children were included. These growth charts, for height, weight and BMI were compared to CDC 2000 charts. A significant difference was noted on the final height for both boys and girls, with Saudis being shorter compared to their American counterparts. On the other hand, weight and BMI were higher in Saudi children, both boys and girls, compared to American children.
Conclusions: Based on our comparison, we found that healthy Saudi children showed a difference in final height, weight and BMI. A national growth chart-based study is more appropriate than using an international reference. A national growth chart will eliminate the need for unnecessary testing, since it will more accurately reflect national norms.

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1.5 Treatment of Growth Failure with rhIGF-I in the Context of the Continuum of GH-IGF-I Axis Defects.

Martin O. Savage. Department of Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine & Dentistry, London, UK

Defects in the GH-IGF-I axis extend from severe GH deficiency (GHD) to extreme GH insensitivity (GHI) and form a continuum, which can be plotted against a scale of GH sensitivity (1). GH deficient patients respond well to hGH therapy, however as the degree of GH sensitivity decreases, growth responsiveness to hGH is also reduced. Idiopathic short stature (ISS) can be situated between GHD and GHI. GH insensitivity was thought to be confined to the severe phenotype of homozygous GH receptor defects (Laron syndrome). In the past 15 years, the spectrum of GHI has broadened and now extends from extreme growth failure to mild short stature. New genetic disorders have been identified such as mutations in STAT5B, IGFALS and dominant negative and pseudo-exon GHR defects. All these disorders are resistant to therapy with hGH. Fortunately rhIGF-I, first used for clinical use in the late 1980s, is now available and licensed by the FDA and EMA for use in GHI patients. rhIGF-I administered sc in doses of 80-120 μg/kg twice daily increased height velocity (HV) from 3.8 to 8.2 cm/year in children with extreme GHI and long term benefit on height SDS was seen after >4 years of therapy. Hypoglycaemia was reported in some subjects and a low incidence of benign intracranial hypertension occurred during the first 6 months. Recently rhIGF-I (Increlex) has been used in more mildly affected patients and induced an increase in HV to 7.9 cm/yr vs 5.2 cm/yr ($p<0.0001$) in untreated patients. New preliminary data using a combination of hGH (0.043 mg/kg) + rhIGF-I (150 μg/kg) once daily gave excellent growth responses in ISS patients (Height <-2SD, IGF-I <-1SD) increasing HV to 12.1 cm/year. This new form of therapy has great potential for the future.

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Session 2. Current Issues in Diabetes Care I

2.1 Epidemiology of Diabetes in UAE and Gulf

Khaled Al-Jaberi, Department of Medicine, Mafraq Hospital, Mafraq, Abu Dhabi, United Arab Emirates.

No abstract

2.2 Update on Diagnosis and Screening for Diabetes 2010

Ahmed A.K. Hassoun, Consultant Endocrinologist, Dubai Diabetes Center, Dubai, UAE.

Diabetes is a disease characterized by abnormal metabolism, most notably hyperglycemia, and an associated heightened risk for relatively specific long-term complications affecting eyes, kidney, and nervous system. Diabetes also substantially increases the risk for the non-specific cardiovascular complications.

Historically, the measurement of glucose has been the means of diagnosing diabetes. Unlike the characteristic clinical onset of type 1 diabetes, type 2 diabetes has a more gradual onset, with slowly rising glucose levels over time, and its diagnosis has required specified glucose values to distinguish pathologic glucose concentrations from those in the non-diabetic population. For decades, either the FPG or the OGTT has been used in the diagnosis of diabetes.

In 1997, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus reexamined the basis for diagnosis of diabetes focusing on the relationship between glucose levels and the presence of diabetic complications. The diagnostic criteria were updated accordingly.

Several observations later suggested that a measure of chronic glycemic levels by HbA1C is related more intimately to the risk of complications, and may be considered a diagnostic tool. In 2008, an International Expert Committee (IEC) with members appointed by the ADA, the EASD, and the IDF was convened to consider the current and future means of diagnosing diabetes in non-pregnant individuals. After an extensive review of both established and emerging epidemiological evidence, the committee recommended the use of the A1C test to diagnose diabetes, with a threshold of ≥6.5%. The ADA affirmed this decision and updated its diagnostic criteria in 2010 to include A1c which should be performed using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized or traceable to the DCCT reference assay.

In 2009, a consultation working group which was appointed by the WHO reviewed the place of HbA1C in diagnosis and screening for diabetes. The recommendations have been submitted to the WHO awaiting its approval. The group's recommendations took in consideration the needs and capabilities of all health systems world-wide.

2.3 Lifestyle Modification for Diabetes: The Principles and Practicalities.

Jumaa M. Al–Kaabi, Department of Medicine, Faculty of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, UAE.

Diabetes mellitus in adults is a global health problem and the prevalence rate of diabetes in the UAE is rated as the second highest in the world according to the International Diabetes Federation (2010).

It is well established that physical activity and good dietary practices can improves metabolic control of diabetics and this may reduce disease complications. Local studies demonstrated low level of physical activities and inappropriate dietary practices among patients with Type 2 diabetes mellitus. The importance of dietitian and the diabetic educator in the management of diabetes mellitus should be revisited and patients should be encouraged to seek a proper dietary and health education consultations to optimize the diabetes management.

It is well known that lifestyle modifications are difficult to achieve and need continuous education, dedication and facing daily challenges by providing alternative practical solutions. The number of practicing dietitians and diabetic educators need to be increased in the UAE to meet the demand of educating and sustaining lifestyle changes in a growing number of patients with diabetes.

Session 3. Current Issues in Diabetes Care II

3.1 The Role of DDP-IV Inhibition In the Management of Diabetes: An Overview of the Short and Long Term Effects.

Salem Beshyah, Endocrinology Division, Institute of Medicine, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Incretins are hormones from the gut that are released in response to ingestion of food. They have effects of central biological importance in regulation of glucose homeostasis. They stimulate release of insulin, inhibit release of Glucagon, maintain beta-cell mass, delay gastric emptying and inhibit feeding. Incretin receptors are also present in other parts of the body including the brain, where their effects may induce satiety and suppress appetite.

Incretin metabolism is abnormal in T2DM, evidenced by a decreased incretin effect, reduction in nutrient-mediated secretion of GIP and GLP-1 in T2DM, and resistance to GIP. The use of incretins as therapeutic agents offers a new approach to the treatment of type2 diabetes (T2DM). Intravenously administered GLP-1 in T2DM increases

insulin secretion and improves glucose homeostasis. However, GLP-1 has a very short half-life, due to rapid degradation by the enzyme dipeptidyl peptidase IV (DPP-IV). Two strategies were explored to normalize the incretin effect. DPP-IV enhance the activity of incretins by Incretin mimetics are analogues of GIP and GLP-1 that are resistant to the action of DPPIV have been developed and clinical trials have shown their effectiveness.

A couple of DPP-IV inhibitors that has been licensed for the treatment of T2D in the USA, and several other agents are undergoing clinical trials. Strategies to augment the biological actions of GIP and/or GLP-1 in T2D are expected to minimise weight gain, reduce hypoglycemic episodes and prevent progressive beta-cell failure by increasing beta-cell mass. The advantage of DPP 4 inhibitors is their availability in oral form. Their efficacy is commendable. Sitagliptin monotherapy led to HbA_{1c} reduction of 0.6–0.7% after 54 wk. Vildagliptin monotherapy lowered HbA_{1c} by 0.9–1.4% after 24 wk. Long-term data on sitagliptin and vildagliptin are needed to evaluate their glucose-lowering effects. DPP 4 inhibitors are weight neutral, and their effects on other DPP-IV substrates need further research. Best HbA1c reduction is observed by combination therapy. They may be used as part of triple oral therapy regimen and they may also be used in insulin treated type 2 patients. The latter may reflect their action on glucagons. Incretins have gained a role in management of T2DM in all the professional guidelines. Some experts argue for these to be used fairly early as monotherapy or with metformin (1) although some still express a very reserved views (2)

A few unresolved Issues regarding DPP-IV inhibitors have been raised by some experts. These questions include: 1. Do DPP-IV inhibitors have favorable effects on β-cell mass in humans? 2. Is the modest increase in aGLP-1 levels the sole modulator of glyaemia using DPP-IV inhibitors? 3. How might DPP-IV 4 inhibition lead to a decline in plasma glucose levels without an increase in insulin secretion? 4. Was the development of DPP-IV inhibitors, which are not specific for GLP-1 and actually resulted in decreased tGLP-1 secretion, really needed to increase plasma aGLP-1 levels?. How much cautious should the medical profession be more careful in embracing newer has been argued nicely in a recent counterpoint in Diabetes care (3).

Future work should help understanding of the effects of this group of drugs on β-cell mass in humans, elucidating their long-term vascular outcome data and enhanced safety profile.

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3.2 Multifactorial Intervention in the Course of Type 2 Diabetes

Jens Sandahl Christiansen, Department of Endocrinology and Diabetes, M, Aarhus University Hospital, Aarhus Denmark.

Multifactorial intervention in type 2 diabetes includes mean simultaneously targeting control of glycemic, lipid and hypertension in addition to antiplatelet therapy.

Glycemic control: The UKPDS trial proved that intervention in terms of more intensive metabolic control is of importance in the prevention or postponement of micro- as well as macro vascular complications in type 2 diabetes. More recent follow-up studies on as well UKPDS as Steno 2 have shown that intervention should be implemented as early as possible. During the years guidelines for HbA1c levels to be aimed for have become more and more strict – and levels below 6.5% (even 6.3%) have been recommended. However, more recent studies suggest call for caution I elderly patients with long standing disease. In addition the potential importance of managing postprandial glycaemia has been discussed intensely. Type 2 diabetes is a disease characterised not only by insulin resistance but also by a steady decline in beta cell function. Thus, more than 50% of the patients will need insulin treatment within 6 years of duration of disease. Insulin therapy should preferably be combined with metformin treatment.

Antihypertensive treatment: Effective antihypertensive therapy is mandatory in the care of patients with type 2 diabetes. All patients with raised urinary albumen excretion rate should be offered blockage of the Renin-Angiotensin-Aldosterone system with ACE inhibitors or AII receptor antagonists. In addition all patients with BP levels exceeding 140/90 should be offered antihypertensive therapy – aiming at BP levels below 130/80. Multipharmacological intervention with 3 – 4 different antihypertensive agents will most often be needed. Diuretics should always be introduced as first or second choice.

Lipid lowering treatment: Recent prospective studies suggest, that statin treatment should be offered to all patients

with type 2 diabetes irrespective of cholesterol levels –and certainly to all patients with LDL cholesterol in excess of 3.5 mmol/L.
Anti-platelet therapy: There is good evidence, that all type 2 diabetics with manifest cardiovascular disease should be treated with aspirin (secondary prevention). In addition, many recommend, that this should be offered to all patients suffering of type 2 diabetes (primary prevention).

Session 4. State of the Art Lecture

4.1 Growth Hormone Therapy for Non Growth Hormone Deficiency Disorders.

Martin O. Savage, Department of Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine & Dentistry, London, UK

Since the availability of recombinant hGH in 1985, therapeutic trials have been performed to test the efficacy of hGH therapy in children with non GH deficient (GHD) short stature. Efficacy and safety have been demonstrated leading to FDA and EMA approval of hGH treatment in the following disorders; Turner syndrome (TS), small for gestational age (SGA), Chronic renal insufficiency (CRI), idiopathic short stature (ISS) [FDA only] and Noonan syndrome [FDA only]. In TS, the recommended dose of hGH is 50μg/kg/day, which in a Canadian controlled trial led to mean adult height gain of 7.2 cm compared to untreated patients (p=0.001). Higher doses were used in Dutch studies and starting treatment at age 6 years achieved mean height gain of 11.9 cm. hGH therapy was licensed for SGA patients in 2003 with the recommended dose of 33 μg/kg/day. Some groups advocate a higher dose of 67μg/kg/day, although final height was not influenced by dose. hGH is licensed for ISS in the USA but not in Europe. A recommended starting dose is 50μg/kg/day[1], however results are highly variable and also dose-dependent, with ISS patients with genetic short stature showing less response. At least 50% of ISS patients did not show catch-up growth (Δ Height SDS <0.5 in 12 months and HV <-1.0 SD)[2]. In such cases hGH therapy should be stopped. Noonan syndrome patients show responses similar to TS when treated with hGH 50μg/kg/day. Limited therapeutic trials of hGH in growth failure due to chronic inflammatory diseases such as Crohn's disease and juvenile arthritis have shown efficacy compared with untreated controls. In conclusion, responses to hGH therapy in non GHD short stature are dependent on diagnosis, dose of hGH and duration of therapy. Not all patients will respond and the clinician must have the courage to discontinue therapy in cases of non-response.

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Session 5. Pediatric Endocrinology 2010

5.1 Hereditary Vitamin D resistant Rickets

Jamal Al Jubeh, Division of Endocrinology, Institute of Pediatrics, Sheik Khalifa Medical City. Abu Dhabi.

Vitamin D is a prohorormone. Vitamin D2 is obtained from yeast and plants and Vitamin D3 is synthesized in the skin of humans and animals upon adequate exposure to UV-B light rays. Vitamin D is hydroxylated in the liver to 25 OH Vitamin D which can be stored for many weeks. This is the substrate for the most potent form of Vitamin D which is 1, 25 (OH)2 Vitamin D which is made in the kidneys. Vitamin D is important for Calcium and phosphate absorption.

Vitamin D deficiency is the most common case of Rickets. Mutations in the vitamin D receptor lead to severe form of rickets that is resistant to Vit D therapy. We present our experience with 2 children with R274H mutation in the ligand-binding domain of the Vit D receptor. Both patients presented with severe demineralization, multiple fractures in the extremities, recurrent chest infection and difficulty breathing. They were failing to thrive with delayed gross motor development but no alopecia. They did not respond to high dose Calcitriol up to 15 mcg daily. They both had excellent response to high dose continuous IV calcium infusion in a dose of 150 – 200 mg/kg/day. This therapy resulted in normalization of Calcium, PTH and alkaline phosphatase and remarkable improvement in bones with resolution of rickets and healing of fractures. Hypercalciuria

occurred in both children but no hypercalcemia and no nephrocalcinosis.

5.2 Adrenal Disorders in Childhood and Adolescence: A Clinical Review

Ian G. Jefferson, Division of Endocrinology, Institute of Pediatrics, Sheik Khalifa Medical City. Abu Dhabi.

An overview of Adrenal Disorders in childhood is presented with emphasis on those presenting as Congenital Adrenal Hyperplasia. The current SKMC experience is presented with emphasis on the pitfalls of ensuring an accurate diagnosis; the importance of accurate diagnosis; the difficulties presented in attaining safe replacement treatment with adequate adrenal androgen control and the social implications of the diagnosis. The practicalities of the various treatment options will be discussed.

5.3 Genital Surgery in Congenital Adrenal Hyperplasia: An Overview of Approaches and Outcomes.

Sleiman Gebran MD, Consultant Pediatric Surgeon, Department of Surgery, Mafraq Hospital, Abu Dhabi, UAE.

The past several decades have seen multiple advances in the surgical reconstruction for girls born with Disorders of Sexual Differentiation. This surgery can be technically very demanding, and must be individualized for each patient, as the degree of virilization and level of confluence of the vagina and urogenital sinus will dictate the surgical approach.

In this lecture we present our approach and experience in the surgical options for girls born with Congenital Adrenal Hyperplasia, with special attention regarding clitoroplasty, labioplasty, and vaginoplasty. Few areas in pediatric surgery are more challenging and controversial than genital reconstruction for girls with virilization. This situation is most commonly seen as a result of congenital adrenal hyperplasia (CAH). Debate exists mainly regarding the optimal timing and extent of genital reconstruction for these children. Additionally, the surgical reconstruction itself can be difficult, requiring meticulous attention to detail and tissue handling. The degree of virilization and level of the confluence of the vagina with the urogenital sinus is variable and unique to each girl. There are several options for surgical repair of these anomalies, which must be matched to the anatomy of the child to achieve a functional and cosmetic outcome. Knowledge of each of these techniques and their applicability is critical. The main focus of this article is to address the surgical aspects of feminizing genitoplasty for CAH, focusing on the different types of repairs in use today and when each should be employed, and outcomes of clitoroplasty and vaginoplasty. A multi-disciplinary approach to these children is imperative, employing input from an endocrinologist, psychologist or psychiatrist, pediatric surgeon and most importantly, the family. We advocate a multi-disciplinary conference with each specialist and the family present, to discuss these issues together. Parents should be encouraged to read and discuss the views held by national and international advocacy groups such as Congenital Adrenal Hyperplasia Research and Education Support (CARES) and the Intersex Society of North America (ISNA).

Session 6. Hot Topics in Clinical Endocrinology

6.1 Polycystic Ovary Syndrome: Reproductive and Metabolic Aspects

Huda Ezzeddin Mustafa, Division of Endocrinology, Institute of Medicine, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality in women in their reproductive age. Based upon the diagnostic criteria used, and the population studied, its prevalence ranges from 4% up to 28%. PCOS is a heterogeneous condition that encompasses a wide spectrum of hyperandrogenism and ovarian dysfunction. Both insulin resistance and hyperandrogenemia contribute to its complex pathophysiology. Each accounts for 50-80% of PCOS cases. Biochemical, clinical, and ultrasonographic features of the syndrome are variable amongst patients. The commonest clinical sign is menstrual irregularities (70-80%), followed by hirsutism (60%). Obesity is reported to be evident in about 50% of cases. Recent evidence suggests that women with PCOS are at an increased risk of dyslipidemia, abnormal glucose metabolism, and cardiovascular disease. Treatment of PCOS is tailored to the clinical presentation. For the large majority, lifestyle measures, aiming for a modest weight loss of 5-10%, are optimal for both the reproductive and the metabolic effects. The role of oral contraceptive pills, Metformin, and antiandrogens for the management of hyperandrogenism and fertility concerns are elucidated.

With the increasing prevalence of type 2 Diabetes and obesity in the population, targeting women with PCOS with multidisciplinary approaches is a commendable public health strategy. The main objective of this presentation is to increase the awareness of physicians investigating or

treating women with PCOS to its diagnostic and prognostic challenges.

6.2 Evidence Based Management of Osteoporosis

Pierre Najm, Imperial College London Diabetes Center, Abu Dhabi, UAE.

No abstract

6.3 Acromegaly Update 2010: A Clinical Review.

Ali B Khalil, Endocrinology Division, Institute of Medicine, Sheilk Khalifa Medical City, Karama Street, P.O. 51900, Abu Dhabi, UAE.

Acromegaly is a condition due to the production of too much growth hormone by the pituitary gland after the end of adolescence or insulin like growth factor. Although the pituitary tumors associated with acromegaly are nearly always benign, the elevated GH and IGF-I levels lead to a wide range of cardiovascular, respiratory, endocrine, and metabolic morbidities as well as a 32%increased risk for all-cause mortality. The diagnosis of acromegaly is usually based on clinical, biochemical (concordant Growth hormone(GH) and insulin growth factor, (IGF) elevated levels) and radiological changes (mass effect). In cases where GH and IGF-I results are divergent, it is important to consider the degree of the biochemical abnormality and the clinical context before initiating further therapy. Therapies for acromegaly have the aim of reducing or controlling tumor growth, inhibiting GH hypersecretion, and normalizing IGF-I levels. The three approaches to therapy are surgery, medical management, and radiotherapy. Each treatment modality has specific advantages and disadvantages, but the optimal use of these treatments should result in a reduction in mortality in the acromegaly patient population compared to that of the general population. Transsphenoidal surgery is the treatment of choice for intrasellar microadenomas, noninvasive macroadenomas (*i.e*. those without cavernous sinus or bone invasion), and when the tumor is causing compression symptoms (with normalization of IGF-I in 75–95% of patients). Complications of transsphenoidal surgery in acromegaly are rare and include transient oculomotor palsies, deterioration of vision, carotid artery injury, and epistaxis.(occurring in less than 1% of patients). Approximately 40–60% of macroadenomas are unlikely to be controlled with surgery alone . Their hormonal control might require the inclusion of either primary medical therapy or primary surgical debulking followed by medical therapy for hormonal control and/or radiation therapy for treatment of residual tumor.

Somatostatin receptor ligands (SRLs) are effective in controlling GH/IGF-I hypersecretion and in reducing tumor size.(≈ 70% of patients receiving SRLs have GH levels below 2.5 ng/ml and normalized IGF-I), and maximal benefit may be achieved after 10 yr of therapy. Pegvisomant (GH receptor antagonist) has an indication for its use either as a single monotherapy or in association with a SRL in patients that have persistently elevated IGF-I levels despite maximal therapy with other treatment modalities .

Radiation therapy should generally be reserved for third-line treatment, occasionally as second-line treatment, but rarely as first-line treatment for patients who do not have tumor growth control or normalization of hormone levels receiving GHRA and are at risk of tumor expansion, to allow for potential termination of such therapy, which would otherwise be lifelong.

As with most medical management decisions, treatment needs to be individualized and an experienced team should evaluate risks and benefits for each patient

Session 7. Symposium II.

7.1 The Efficacy and Safety of Incretin Mimetics in Trials and Clinical Practice.

Tarek M. Fiad. Consultant Diabetologist. Shaikh Khalifa Medical City, PO Box 51900, Abu Dhabi, UAE.

Type 2 diabetes (T2DM) pauses a major health and economic burden to affluent and deprived societies alike. Traditional therapies used by the medical community included metformin, sulphonylureas and insulin. The last 2 decades witnessed the emergence of newer therapies including alpha-glucosidase inhibitors, insulin secretagogues, thiazolidinediones and insulin analogues. Use of such therapies was met with a limited success owing to minor impact on glycaemic control, weight gain and neutral or deleterious cardiovascular sequelae. For long time scientists recognized that incretin activity plays an integral part in the metabolic derangement underlying T2DM and the work of many years reached fruition with the introduction of two Glucagon- like peptide–1 (GLP-1) receptor agonists to the clinical field, Exenatide and Liraglutide. Both agents lead to improved β-cell insulin secretion and decreased glucagon levels with a meaningful fall in HBA1c of 1.0 – 1.5 %. The glucose lowering properties of GLP-1R agonists is expressed in a glucose dependent manner and therefore, the use of these therapies is not associated with hypoglycaemia. Among currently

available glucose lowering therapies, GLP-1R agonists are the only agents associated with weight reduction of approximately 2 -4 kg. Clinical studies demonstrated a favourable impact on blood pressure and lipid parameters and small clinical studies suggested a possible cardio- and neuroprotective effects. Nausea is the commonest side effect of GLP-1 R agonists but tend to dissipate overtime in most patients and the safety data related to the possible link with pancreatitis and thyroid neoplasm is very reassuring. In conclusion, GLP-1R agonists represent a novel approach to control hyperglycaemia in T2DM through subcutaneous injections. The role of GLP-1R agonists in cardiovascular protection and β-cell preservation requires further elucidation.

Session 8. Current Perspectives in Endocrinology

8.1 Subclinical Thyroid disease: Treating the Patients or the Blood Results?

MM Benbarka, Sheikh Khalifa Medical City, Abu Dhabi, UAE

No Abstract

8.2 Contemporary Management of Hyperprolactinaemia and Prolactinomas

Iyad Ksseiry, The City Hospital, Dubai, UAE.

Hyperprolactinemia can be due to multiple physiological and pathological etiologies. Medications commonly cause hyperprolactinemia and their use must be differentiated from pathologic causes. Prolactinomas are the most common cause of persistent hyperprolactinemia and account for 50% of the functioning pituitary tumors. The majority of prolactinomas are microprolactinomas. The primary goal of treatment in patients with microprolactinoma is the recovery of gonadal and sexual functions by normalizing prolactin levels, while tumour size reduction is also of importance in patients with macroadenoma. Pharmacological treatment with dopamine agonists is currently the treatment of choice for prolactinoma. These drugs normalize prolactin levels and significantly reduce tumour volume in the majority of patients. Drug resistance, and Drug intolerance were reported in some of patients receiving bromocriptine or cabergoline. Surgical treatment and Radiation treatment are used in certain situations for those prolactinoma patients who are resistant to pharmacological therapy and intolerant of dopamine agonists.

Prolactinomas are common in females during reproductive age. Treatment of prolactinomas usually restores fertility and results in pregnancies. In microadenomas, due to the low risk of tumor growth, follow-up without treatment according to clinical symptoms can be considered. In macroadenomas, pregnancy should be planned after the control of tumor growth. Close follow-up or dopamine agonist treatment throughout pregnancy may be preferred depending on the patient. Prolactin measurement is of little help during pregnancy. Breastfeeding may be allowed since the data are not enough to be against it.).

8.3 Cushing's Disease in Young People

Martin O. Savage, Department of Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine & Dentistry, London, UK

Cushing's disease (CD) is caused by an ACTH-secreting adenoma of corticotroph cells of the anterior pituitary. CD is very rare in children and accounts for 75%-80% pediatric-onset endogenous Cushing's syndrome. Early diagnosis and treatment is essential for optimal therapeutic outcome. We report data on 41 cases aged 5.7-17.8 yrs (26 male, 15 female) managed in our centre over the past 25 years. Some features differentiated paediatric from adult CD; male preponderance, subtle clinical presentation with weight gain, change in facial appearance, growth failure, minimal Cushingoid signs and pseudo-precocious puberty. Biochemical changes were similar to adults with detectable ACTH, elevated urinary free cortisol and midnight serum cortisol (100%), lack of suppression in low dose Dex test (89%) and increased cortisol response to IV CRH. Pituitary MRI scan was a poor indicator of the microadenoma, showing concordance with findings at transsphenoidal surgery (TSS) in only 34%. Inferior petrosal sinus sampling for ACTH (BIPSS), introduced in 1986, identified the location of the microadenoma with more accuracy showing a concordance with surgical findings of 82%. Selective microadenomectomy by TSS is accepted first-line therapy for CD. This is a highly specialized technique with few neurosurgeons having experience in children. Our overall cure rate (post-op cortisol <50 nmol/l) by TSS alone was 24/35 cases (69%). In subjects treated since introduction of BIPSS, the cure rate was 74%. In subjects not cured by TSS (n=11), second-line therapy was direct external pituitary radiotherapy (RT) in a dose of 45 cGy, which was successful in 88%. Post-RT, GH deficiency was common but anterior pituitary function was otherwise preserved. Catch-up growth was induced with hGH ± GnRH analog therapy in the majority of patients. Successful management

of paediatric CD requires a multidisciplinary approach with adult endocrinologists playing a key advisory role.

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Session 9. Occasional Lecture

9.1 Hypopituitarism Replacement Therapy: We Can Do Better!

Ibrahim H. Sherif, The Libyan Board of Medical Specializations, P O box 81308, Tripoli, Libya

Hypopituitarism replacement therapy saves life and has tremendous impact on its quality resulting in so many grateful patients. However, there has been little progress in optimization of therapy and in making the replacement physiological rather than pharmacological. The treatment is still replacing the target organ hormone with crude attempts to mimic the physiological pattern of the trophic hormone action, pulsatile nature and diurnal variation in secretion and the variable effect at the receptor level depending on hormone concentration and time of day it is given.

Hypopituitarism is associated with reduced life expectancy (1) and poor quality of life childless broken marriages. However, newer replacement protocols will improve a situation that remained unchanged for many years (2). Although our current protocols of replacement therapy are adequate (3), we should endeavor to achieve: 1. Thyroid hormone replacement without compromising cardiac or bone health and find a marker for optimal thyroxine replacement 2. Cortisol replacement mimicking the normal physiological pattern and avoiding intermittent supraphysiological doses 3. Androgen replacement for both sexes to achieve a satisfactory libido and maintain the sanctity of marriage 4. Oestrogen therapy for women below the age of 50 to maintain as near normal female function as possible 5. Gonadotrophin replacement to achieve spermatogenesis in the male and ovulation in the female 6. Growth hormone replacement therapy for the under 50s at least 7. Prevention of osteoporosis and 8. A meaningful increase in life expectancy

A hypopituitary patient should feel and look like the peers in their gender with near normal life expectancy, a job, a normal sexual function and a happy married life with children if they choose.

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Session 10. Symposium III.

Recent Advances in Insulin Therapy: Improving Efficacy and Enhancing Safety !

Waleed Aldahi, Department of Diabetes and Endocrinology, Mubarak Al Kabeer Hospital, Kuwait.

No Abstract

Session 11. State of the Science Lecture

11.1 How to Approach Monogenic Diabetes of Unknown Etiology?

Sian Ellard, Institute of Biomedical and Clinical Science, Peninsula Medical School, Exeter, UK.

In recent years there has been significant progress in defining the genetic aetiology of neonatal diabetes (NDM). It is likely that all cases result from single gene disorders since markers of autoimmunity associated with polygenic type 1 diabetes are rare in patients diagnosed before 6

months.

Activating mutations in the KCNJ11 and ABCC8 genes encoding the Kir6.2 and SUR1 subunits of the beta-cell ATP sensitive potassium (KATP) channel are the most common cause of neonatal diabetes, accounting for around 40% of case. The majority (~90%) of patients can achieve improved glycaemic control on high dose sulphonylureas. INS (insulin) gene mutations are the next most common cause of NDM; either recessive loss of function mutations or dominantly acting mutations that affect folding of the proinsulin molecule with consequent endoplasmic reticulum stress.
Animal models can inform the search for new genetic aetiologies and the development of next generation sequencing technologies provides exciting possibilities for large scale sequencing studies.
The identification of specific genetic subtypes of neonatal diabetes not only provides accurate information regarding inheritance and prognosis, but can inform treatment decisions and improve clinical outcome.

Session 12. Perspectives in Pediatric and Adolescent Endocrinology

12.1 Regional Lecture: Growth and Endocrine Complications of Beta Thalassemia Major
Abdel Hadi M Habeb, Paediatric Endocrine Unit, Maternity & Children Hospital, Al-Madinah, KSA

Beta thalassemia major (β thal) is a severe autosomal recessive anaemia that is common in the Middle East. Although intensive transfusion regimen increased the life expectancy of affected individuals, it can lead to iron deposition in various body tissues of which endocrine system is no exception.
The prevalence of endocrine dysfunction in β thal various between different centres with hypogonadism and short stature are the commonest. Patients are also at risk of hypothyroidism, hypoparathyroidism, diabetes, osteopenia and osteoporosis. Most endocrinopathies in β thal are related to the toxic effects of iron on endocrine glands, however short stature is multifactorial and rarely caused by growth hormone deficiency.
In Al-Madinah region, we found that around 50% of our transfusion dependent β thal patients have at least one endocrine dysfunction. The commonest of which was hypogonadism (23%) followed by short stature (20%). The main risk factors for developing endocrinopathies were older age and longer duration of transfusion. Interestingly, serum ferritin was not significantly related to the presence of endocrine dysfunction in our cohort.
While prevention of endocrine complications of β thal remains a challenge, regular screening for early detection is essential.
The lecture will provide an overview of endocrine complications of β thal and highlight our experience of the management of endocrinopathies in children and young adults with β thal via joint endocrine- haematology clinic.

12.2 Pitfalls in Diagnosis and Management of Diabetic Ketoacidosis in Young People.
Walid Kaplan, Houston, USA.

Diabetic ketoacidosis (DKA) is a severe metabolic disorder that is seen mainly in patients with type 1 diabetes, but it can also develop, albeit to a less extent, in type 2 diabetes patients. It is usually encountered in newly diagnosed diabetic patients. However, it can happen anytime throughout the course of the disease due to poor compliance or acute illnesses.
Due to the higher risk of complications in pediatric patients, it is crucial that diagnosis and treatment are concise and well planned. While there are limited evidence-based data pertaining to the best treatment modalities of DKA in children, the International Society for Pediatric and Adolescent Diabetes (ISPAD), along with other international pediatric endocrinology groups have developed clinical practice consensus guidelines compendium in 2009 based on the available body of evidence and the expert consensus or clinical experience.
The following points regarding DKA in children are worth special attention, definition, pathophysiology and prevalence, clinical and biochemical findings, recommended approach and monitoring, common treatment mistakes and finally, risk factor and presentation cerebral edema.

12.3 Type 2 Diabetes in Young People.
Asma Deeb, Department of Paediatrics, Mafraq Hospital, Mafraq, Abu Dhabi, United Arab Emirates.

Type 2 Diabetes Mellitus (Type 2 DM) in children is a growing epidemiological problem. While type 2 DM was unheard of to Paediatric Endocrinologists in the past, the incidence of the disease has now increased considerably and children with type 2 are nowadays commonly seen in Paediatric clinics. In contrary to the old teaching concepts, there is a major overlap of features of type 2 DM in

children and differentiation of the actual type of diabetes in a given child can be challenging. There are evidence that autoimmunity per se is no longer a sole differentiating factor between type 1 and type 2 in children. The positive evidence of autoimmunity in children with type 2 clinical phenotype results in misdiagnosing genuinely insulin-resistant children as type 1. On the other hand, the increased incidence in obesity can lead to misdiagnosis of obese children with type 1 DM as type 2. Although the underlying pathophysiology for type 2 DM in children might be similar to that in adults, there are key features peculiar to the paediatric age group. These include the clinical presentation, response to treatment, co-morbidities and the disease natural history. There is a wealth of information in the literature about Obesity and type 2 DM prevalence globally. However, there are no data on clinical trials or clear guidelines about management of type 2 DM in children. In particular, there is no international consensus in relation to the use of varying anti diabetes medication in children and adolescents. An overview of the disease prevalence, clinical presentations and special features will be discussed.

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Session 13. Inter-disciplinary Endocrinology

13.1 Management of Diabetes and Endocrine Disorders During Pregnancy: An Obstetric Physician's Perspective

Bashir Taha Salih, Obstetric Medicine Services, Corniche Hospital, Salam Street, Abu Dhabi, United Arab Emirates.

Corniche Hospital is the major Maternity Hospital in the UAE with more than 8000 deliveries per annum. Diabetes in pregnancy is a major cause of morbidity and mortality for mother and the newborn. 16% of patients delivered in Corniche Hospital are diabetic (pre-gestational or gestational) and 35% of them are UAE nationals. Pre-conceptional counseling by Health Care Providers and screening before or early in pregnancy and tight control throughout pregnancy is mandatory for successful outcome. Management of this group of patient should be in a multidisciplinary team where the patient and her family are actively involved.

Multiple Insulin injections (rapid and long acting) may be required to achieve good control, but recent studies have shown that oral hypoglycaemic agents can be used – i.e. Metformin (Mig Trial).

Other endocrinopathies are of great influence on conception and pregnancy outcome. Thyroid gland dysfunctions are associated with recurrent miscarriage, premature delivery and other morbidities for mother and her newborn. Tumors of the adrenal gland and the pituitary are relatively rare in pregnancy and need close monitoring and a multidisciplinary approach. Pituitary macroadenoma can be treated with Dopamine receptor agonists throughout pregnancy with regular visual fields testing. Pheochromocytoma, is a rare neuroendocrine tumor, caused by the overproduction of catecholamines in the adrenal medulla. The incidence in pregnancy is reported 1 in 50,000 but if not diagnosed the maternal and fetal mortality rate is extremely high.

13.2 Diabetes in Adolescents: When to Transition Care?

Eiman Awad Abdelrahman, Department of Medicine, Al Ain Military Medical Center, Al Ain, United Arab Emirates.

The number of newly diagnosed diabetics is constantly on the rise including type1 diabetes in children and adolescents. On the other hand, there are many new cases of type 2 diabetes being reported in the young, hence came the need to tailor care based on the specific needs and challenges of this special age group. Transition of care from Pediatric providers to adult care givers have to be prepared for and organized to maintain the integrity of care.

Adolescents are defined as those young people between the ages of 14 and 18 years. Each health care facility has its own cutoff age in terms of when such young people need to be transitioned to adult care. However the decision as for the exact time for transition depends on the physical and the emotional maturity of the individual. Adolescents with chronic illness require special attention due to the peculiarity of their situation considering the role of puberty hormones, which make them vulnerable to emotional turmoil. This is aggravated in the presence of chronic illness.

Diabetes is considered among the most devastating and emotionally disturbing illnesses due to limitations and restrictions required for diabetes care, which affects daily life activities. The aim of diabetes care in adolescents is to offer support and guidance and promote physical and psychological well-being. Achieve optimal glycemic control, provide adequate. Screening for early detection of complications. Ensure proper integration in school, social

and working life of their peers. All of diabetes subgroups are seen in adolescents including type1, type2, MODY, secondary diabetes and gestational diabetes. The latter is not as common as seen in western communities.

Special emphasis should be considered regarding acute complications such as DKA and hypoglycemia. Looking for early signs of chronic complications such as retinopathy, nephropathy is mandatory. Screening for depression especially for type 1 patients should be done on annual bases. Screening for associated autoimmune diseases such as thyroid diseases and celiac disease should be on diagnosis.

Special challenges include the pubertal hormonal changes, which creates more insulin resistance and increased insulin requirements. Adolescents' rebellion and experimentation lead to decreased adherence to treatment regimens. Special counseling should be given for patients with eating disorders and distorted body image. At the end, transition of diabetic patients should be planned for and negotiated between the patient, parents, pediatrician and adult care team to ensure a smooth and successful transition.

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13.3 The Adult Turner: Reproductive, Cardiovascular and Metabolic Perspectives

Abdulrazzaq Ali Al Madani, Department of Medicine, Dubai Hospital, Dubai, UAE.

Turner syndrome is a genetic disorder in which an X chromosome is missing or structurally abnormal. Girls with Turner syndrome, are usually diagnosed at early age, especially if they present with characteristic clinical features, few of them are diagnosed late in adolescent age when they present with short stature or primary amenorrhea. Short stature is the most common feature of Turner syndrome, this is usually treated with growth hormone by the pediatric endocrinologist, but there are many other recognizable characteristics which may also exist in adults with Turner syndrome and need care and attention. Girls and women with Turner syndrome are at increased risk for cardiovascular problems, these include congenital heart anomalies, premature ischaemic heart disease and aortic dissection. Autoimmune hypothyroidism (Hashimoto thyroiditis) occurs in up to 35% of patients, they have twice the risk of the general population for developing type 2 diabetes and the risk of developing osteoporosis in women with Turner syndrome is 10-fold greater than that of the general population, estrogen deficiency in adulthood is an important factor that contributes to osteopenia and osteoporosis. Ovarian failure and infertility is another concern for women with Turner syndrome. Ovarian dysgenesis affects about 95% of girls with Turner syndrome, these results in delayed or absent sexual development; they fail to enter puberty and, therefore, are infertile.

Cardiovascular anomalies are a common feature of Turner syndrome; they are a major cause of morbidity and the highest cause of death in these patients. The most frequent defects include co-arctation of the aorta, bicuspid aortic valve, and aortic atresia. The prevalence of aortic dissection in Turner syndrome is increased as well.