Scientific Events

Highlights of the Annual meetings of Diabetes UK, Liverpool Arena & Convention Centre 4-7th of March 2014

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The annual meeting of Diabetes UK (formerly British Diabetic Association) took place in Liverpool in the first week of March. As it is the annual meeting of the association it is considered one of the largest gathering of diabetes health care professionals in United Kingdom and Europe. It attracts diabetes physicians from around the globe. The meeting had plenary sessions which focused new agents, basic science and clinical aspects of diabetes. There was strong focus on the use of technologies in the management of diabetes specially insulin pumps and closed loops systems. The named Lectures was delivered by leading names in the field.

The session on new insulin was delivered by Dr Russell-Jones from Guildford, Surry. Dr Russell-Jones elaborated on long acting insulin. Of these, the recently launched insulin Degludec (by Novo-Nordisk) which has a half life (t1/2) of 25 hours (insulin glargine t1/2 is 12 hours), has a more flat pharmacokinetics it proves to be convenient for patients which could be given any time of the day with no rigid adherence to the same time of use as with glargine, more safe (compared with glargine) having less incidence of nocturnal hypos and less no excess hypos and having an HbA1c reduction similar to glargine. The second long acting insulin which is currently in phase 3 trials is U300 glargine by Sanofi. It has the same molecular weight of the conventional glargine, but it has more flat pharmacokinetic profile that lasts longer, with less overall hypos and less nocturnal hypos. It is expected to be launched early in 2015. Two published studies edition I in type-2 diabetes patients and edition II in type-1 diabetes has so far been published. The major breakthrough in insulin therapy highlighted by Dr Russell-Jones is the insulin Bill (by Eli Lilly) which is a pegylated insulin where ethylene glycol is attached to insulin and the whole molecules behaves like a protein which has a very long duration of action of 168 hours. This insulin is hepato-selective with a hepato-preferential effect compared to human insulin. The drug is currently in phase 2 trials with a couple of published papers; the first by Rosenstock et al in Diabetes Care 2013 and the second by Bergenstal also published in Diabetes Care (2012). The two papers suggested less overall hypoglycaemia and less nocturnal hypoglycaemia plus weight reduction. However, the catch as pointed by Dr Russell-Jones is the observed abnormalities of hepatic function with rise of AST and ALT and the abnormalities of lipoprotein subfractions with rise in LDL, TG and reduction in HDL. Whether these effects were toxic or mere reflections of the hepato-preferential effects will only be revealed by the ongoing phase 3 trials. These will be published late in 2014 or early 2015.

Dr Russell-Jones also covered the forthcoming ‘Bio-similar insulin’ which will be launched very shortly. The first of these is the bio-similar glargine. Other insulin are expected to follow suit. Further, Dr Russel-Jones pointed out that rapid acting insulins also currently undergoing development. Of these is insulin FIASpNN1218 (Novo-Nordisk). This insulin is same like insulin Aspart, but it is in different formulation with a different and quicker action. There are no published data about this insulin yet. The
other fast acting insulin is Humalog U200 by Eli Lilly which has similar properties to FIASpNN1214. Another major development is the success of combining insulin Humalog U200 Degludec with the GLP analogue liraglutide (I-DegLira) which is currently in clinical trials spearheaded by Prof Stephen Gough from Oxford. Dr Russell-Jones concluded his presentation by pointing out to the fact that 3 oral insulin are currently in development, they seem to be hepatoselective and has very long duration of action and that the results look very promising. Finally, inhaled and buccal insulin are also in development.

On Thursday 6th of March one of the named Lectures; the Arnold Bloom Lecture 2014 was delivered by Prof Stephen Greene, Professor of Paediatric Endocrinology and President of International Society for Pediatric and Adolescent Diabetes (ISPAD). Prof Greene lecture was entitled ‘Diabetes in the young, technologies, engagements and context’. His lecture focused on the milestones achieved in the care of young people with diabetes, including children, adolescents and young adults. Dr Greene is considered one of the icons of care in this area as is exemplified by his own career since he was training in the late 1970’s and early 1980’s. Dr Greene’s lecture took the audience into a journey showing how care for children has developed through amalgamation of clinical research with cutting edge basic science research as well as use of advances in technology from the introduction of simple glucose meters to the latest insulin pump and closed loop systems. One of the following sessions on that day was a symposium on renal and pancreas transplantation. In that symposium Prof Rayaz Malik, from Manchester University Medical school, delivered a review on the impact of islet and pancreas transplantation on diabetic complications. Prof Malik showed data compiled over the last two decades which suggest that despite achievement of euglycaemia and remission of diabetes in most patients there was little benefit on the established microvascular complications, especially neuropathy and nephropathy. However, Prof Rayaz presented very interesting early data from his owned pioneered neuropathy surrogate the corneal confocal microscopy which indeed suggested some improvement in this particular surrogate in those who had islet and pancreas transplantation. Prof Malik pointed out that despite the limitations of his own observation as the numbers were small, but he felt that the observed lack of benefit in the microvascular complication could well be related to the endpoints which were used. On going further evaluation may provide more insight into this area.

There were two sessions on ‘Hot Topics in Diabetes’. The first one had a presentation on ‘new Biomarkers in Nephropathy’ delivered by Dr Christian Delles from Glasgow. He pointed out that there are currently several new biomarkers which were thought to be able to detect early development of nephropathy well ahead of development of microalbuminuria which is the currently used biomarker. Dr Delles showed that the most promising biomarkers under evaluation are TNF Receptor 1 & 2. Other in development are ‘Micro-RNA’ and ‘Urinary proteomics’. The topic of ‘new Drugs in Diabetes’ was delivered by Prof Clifford Bailey, from Aston University. Dr Bailey who is a well renowned authority in the field pointed out that the new and more promising agent among the gliptin group of drugs is Omapiigliptin (MK3102), which can be used once weekly. Other related drugs are the GLP receptor analogue, Albiglutin (GSK) and Dulaglutide (Eli Lilly), both are once weekly. The most exciting agent among this group is the novel MKC-253 which is administered as an inhaled drug. Dr Bailey pointed out the totally new class of drugs for type-2 diabetes include adipokine-based agents, bromocriptine and the lipid
lowering drug colesevelam.
Another interesting presentation in that session was the presentation delivered by Prof Andrew Hattersley from Exeter on ‘Mastermind Study’ which is a project utilizing the scientific concept of ‘stratified medicine’, where the use of several parameters including clinical, genetic and molecular research is aimed to shed the light on what patient will benefit from which class of anti-diabetic drug. Furthermore, the exercise is aimed at further assessing the ideal medicine which will exert the appropriate pharmacological effect with no risk of secondary failure ensuring longevity and durability of the used agent. Obviously this is a very clever and ambitious project which, if successful will prove to be a major breakthrough in cutting edge diabetes research. This project is a collaborative one with other leading researchers in the field including Dr Ewan Pearson from Dundee. The session on ‘Bariatric surgery: any downside’ was given by Dr Jennifer Logue from Glasgow. The types of bariatric surgery used for patients with type-2 diabetes include gastric banding, sleeve gastrectomy and bypass surgery has been shown in various studies to result in remission of diabetes after greater of one year follow-up with normalization of HbA1c <6.5%, fasting BG ≤5.6 mmol/l (= 101 mg/dl). Dr Logue, however, pointed out that the study by Romeo et al (2012) looking into the effect of the surgery on the chronic diabetic complications suggested some uncertainty on the positive impact on nephropathy, variable effect on retinopathy, and no effect on neuropathy but positive impact on macrovascular disease. The other positive impact was on lesser number of various medications. Dr Logue concluded that the long term sequelae remains uncertain and the cost of treatment has to be borne in mind. One of the most interesting and clinically important was the subject of hypertension in patients with diabetes. Prof Tony Heagerty from Manchester pointed out that the latest consensus driven from meta-analysis and outcome trials surprisingly in contrast to the well held dogma that prevailed over the last decades that the target for blood pressure control should be less stringent as was previously adopted. The quest for very tight blood pressure control has been shown not to be well founded by scientific evidence and the consensus is now for more conventional approach for BP control. This will put those with diabetes in line with those without diabetes having a target of BP of ≈140/90 mmHg. This has been recently advocated by the European Society of Hypertension. Dr Heagerty further pointed out in those with isolated systolic hypertension (ISH) the quest for lowering the systolic BP below 140/130 mmHg has been observed to be very detrimental resulting in triggering of malignant tachyarrhythmia, renal hypoperfusion with acute kidney injury, coronary events and symptomatic hypotension with resultant morbidity and mortality. The current advise is also for more conventional approach. Further, Dr Heagerty stressed that dual blockade of the RAS system by using the combination of ACE inhibitors and ARB agents has not been shown to be beneficial, and even it may be detrimental. Finally, he stated that 24 hour BP and home BP monitoring appears to be cost effective. He concluded his interesting talk by pointing out that data in the above in those with proteinuria is scanty.
In the ‘Hot topics 2’, Prof Peter Grants from Leeds University discussed the thrombotic effect of diabetes. He started by describing the pathophysiology of ‘diabetes associated thrombophilia’ which involves inhibition of fibrinolysis due to increased levels of plasminogen activator inhibitor 1, complement C3 associated inhibition of clot lysis, alteration in fibrin due to glycation, and increased platelet reactivation. He also described the pro-inflammatory role of insulin
resistance in enhancing the thrombotic effect of diabetes. Prof Grants explained the additional protective role of insulin sensitizers, ACE inhibitors and lipid lowering agents in reducing the thrombotic effect of diabetes by decreasing plasminogen activator inhibitor-1, fibrinogen, and triglyceride. In regard to plate reactivation Prof Grants discussed the role of current anti-platelet therapy, he emphasize that the risk of bleeding out weight the benefit when they are used as a primary prevention in patients with low cardiovascular risk (less than 10%), actually this is in line with current guidelines, but this would change when used as secondary prevention as there is significant absolute reduction in vascular events, non fatal MI, and stroke. Prof Grants went through explaining the current antiplatelet, what was interesting is the once daily dose of Aspirin doesn't achieve complete platelet inhibition, hence trials of BD aspirin currently underway, in regard to P2Y12 blockers he emphasis that Clopidogrel should be used with caution in the presence of renal impairment, Ticagrelor would be better option. Prasugrel on the other hand is more effective when used in secondary prevention post ACS compared to Clopidogrel in diabetic patients.