ADA 72nd Scientific Sessions (2012) Conference Review

HONG KONG

Making Education Easy

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In this review:

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Welcome

to this review of the American Diabetes Association's 72nd Scientific Sessions, the largest diabetes meeting in the world. This year's meeting brought together the world's leading experts on diabetes for five days of scientific presentations, discussions, and analysis of cutting-edge research on type 1 and type 2 diabetes, gestational diabetes, pre-diabetes, and obesity and other risk factors. More than 14,000 clinicians and researchers (nearly 18,000 total participants) participated from all 50 states and 111 countries. This year's programme included 800 speakers addressing participants in the meeting's 94 symposia, 49 oral abstract sessions, 68 guided audio posters, and nine interest group discussions. In addition, more than 2,000 abstracts were given as oral or poster presentations.

This review has been created to allow those unable to attend, but with a keen professional interest, to access a summary of some of the presentations.

I hope you enjoy this review and I look forward to your feedback.

Kind regards,

Prof Ronald Ma

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Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD).

Authors: Inzucchi SE et al; American Diabetes Association (ADA); European Association for the Study of Diabetes (EASD).

Summary: The ADA and the EASD convened a joint task force to evaluate the evidence and develop recommendations for antihyperglycaemic treatment of nonpregnant adults with type 2 diabetes. Updated recommendations were considered necessary because of recent information on the benefits and risks of glycaemic control, recent evidence regarding the efficacy and safety of several new drug classes, the withdrawal/restriction of other drugs, and increasing calls for a move toward more patient-centered care. The position statement was based on the best available evidence. Glycaemic control needs to be pursued within a multifactorial risk reduction framework. Patients with type 2 diabetes are at increased risk for cardiovascular morbidity and mortality so the aggressive management of cardiovascular risk factors such as hypertension, hypercholesterolaemia and smoking is likely to have even greater benefits. The ADA and EASD recommendations should be considered within the context of the needs, preferences, and tolerances of each patient. Individualisation of treatment is the cornerstone of success.

Comment: The previous version of the ADA/EASD treatment algorithm was considered to be too rigid and restrictive by some healthcare professionals. This long-overdue updated position statement has adopted a patient-centred approach, and provides clinicians with more flexibility in the choice of treatment. Glycaemic targets and glucose-lowering therapies must be individualized based on patient characteristics including age, disease duration, presence of comorbidities and complications, as well as patient attitude towards the disease. Metformin remains the first line treatment, though there is more flexibility in choices for second-line agent if suboptimal control on metformin monotherapy. Newer agents including DPP-4 inhibitors, GLP-1 receptor agonists were included as second-line treatment choices after metformin. The statement recognizes that treatment with sulphonylurea, TZD, DPP-4 inhibitor, GLP-1 agonist or insulin are all suitable options to combine with metformin as second-tier treatment. In terms of insulin titration, it was suggested that after addition of basal insulin, possible options to intensify insulin treatment include basal insulin + 1 meal-time short-acting insulin, before increasing to more meal-time prandial insulin injections, or switch from basal insulin to premixed insulin twice daily. This welcomed shift towards a patient-centred treatment approach should help clinicians select the best treatment for patients, both to maximize benefit, and minimize harm.

Diabetes Care. 2012 Jun;35(6):1364-79. Epub 2012 Apr 19. No abstract available.

Insulin glargine versus sitagliptin in insulin-naive patients with type 2 diabetes mellitus uncontrolled on metformin (EASIE): a multicentre, randomised open-label trial.

Authors: Aschner P et al, on behalf of the EASIE investigators

Summary: This 24-week open-label trial compared the efficacy, tolerability and safety of SC insulin glargine titrated from 0.2 U/kg (target fasting plasma glucose level 4.0–5.5 mmol/L) and oral sitagliptin 100mg daily in patients with type 2 diabetes mellitus for ≥6 months (HbA1c 7–11%; body mass index 25–45 kg/m2) uncontrolled with metformin. Compared with participants randomised to sitagliptin (n=265), those randomised to insulin glargine (n=250) had a significantly greater adjusted mean reduction in baseline HbA1c at the end of the study (primary endpoint; –1.72% vs. –1.13%; p<0.0001) and a significantly greater estimated symptomatic hypoglycaemic episode rate (4.21 vs. 0.50 events per patient-year; p<0.0001). Severe hypoglycaemia was reported in three insulin glargine recipients and one sitagliptin recipient, and the respective rates of ≥1 serious adverse event were 6% and 3%.

Comment: The latest position statement from the American Diabetes Association and European Association for the Study of Diabetes advocates the use of sulphonylurea, DPP-4 inhibitors, TZD, injectable GLP-1 agoinst or insulin as possible second line agents in the case of inadequate glycaemic control on metformin. However, there is limited data on head-to-head comparison between these treatments to guide clinicians. This study compared the addition of insulin glargine with the oral agent sitagliptin in patients with inadequate glucose control on metformin alone. The main findings were greater reduction in HbA1c in the glargine arm, with a greater proportion of patients achieving HbA1c <7%. There were significantly more hypoglycaemic episodes in the glargine arm compared to sitagliptin (approximately 8-fold), though the frequency of severe hypoglycaemic episodes were relatively low. Results of the study, although not surprising, provides some useful data on the medium term effectiveness of both treatments. The authors proposed that better glycaemic control early in the course of disease in the glargine arm may lead to long-term benefits.

Reference: Lancet 2012;379(9833):2262–9

http://tinyurl.com/Lancet-379-2262

Exenatide twice daily versus glimepiride for prevention of glycaemic deterioration in patients with type 2 diabetes with metformin failure (EUREXA): an open-label, randomised controlled trial

Authors: Gallwitz B et al

Summary: Patients with type 2 diabetes mellitus inadequately controlled by metformin were stratified by HbA1c level and randomly assigned to receive add-on exenatide twice daily (evaluable n=490) or glimepiride once daily (n=487) in this open-label RCT. Compared with glimepiride, exenatide was associated with: i) a significantly lower treatment failure rate (41% vs. 54%; hazard ratio 0.748 [95% CI 0.623–0.899; p=0.002]); ii) significantly greater proportions of participants achieving HbA1c levels of <7% (44% vs. 31%; p<0.0001) and <6.5% (29% vs. 18%; p=0.0001); iii) a significantly greater reduction in bodyweight (p<0.0001); iv) significantly lower symptomatic, nocturnal and non-nocturnal hypoglycaemic event rates; and v) significantly greater adverse event-related discontinuations during the first 6 months of treatment (p=0.0005), but not after 6 months.

Comment: This study from Europe compared the long-term effects of two treatments advocated as 2nd line treatment in the revised ADA/EASD Position Statement. It aims to address whether the two treatment have differences in the durability of glycaemic control. Similar to earlier studies using GLP-1 agonists, addition of exenatide was associated with more sustained glycaemic control, with 44% of patients in the exenatide arm able to maintain a HbA1c <7% at 48 months. Treatment choices in future should go beyond glycaemic control, but take into account long-term cardiovascular safety, complications risk and sustainability of glucose control. Adverse events were mainly related to gastrointestinal intolerance. There was 1 case of pancreatitis in each arm of the study. Costs and patient acceptability may be some of the limiting factors in clinical practice.

Reference: Lancet 2012;379(9833):2270–8

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2812%2960479-6/fulltext

Article selection and Independent commentary by Prof Ronald Ching Wan Ma, Professor, Department of Medicine and Therapeutics, Chinese University of Hong Kong. Prof Ronald Ma has served on the advisory boards and as a consultant to various pharmaceutical companies, proceeds of which have been donated to support diabetes research.

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Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis

Authors: Tricco AC et al

Summary: This systematic review and meta-analysis of 48 cluster RCTs (2538 clusters; n=84,865) and 94 patient RCTs (n=38,664) explored the effects of quality improvement strategies on HbA1c, vascular risk management, microvascular complication screening and smoking cessation in patients with diabetes. A random effects meta-analysis revealed that compared with usual care, quality improvement strategies were associated with mean difference reductions in: i) HbA1c of 0.37% (120 RCTs); ii) LDL cholesterol level of 0.10 mmol/L (47); and iii) systolic and diastolic blood pressures of 3.13mm Hg (65) and 1.55mm Hg (61), respectively. The effects appeared greater in participants with HbA1c values of >8.0%, an LDL cholesterol level of >2.59 mmol/L and systolic and diastolic blood pressures of >80mm Hg and >140mm Hg, respectively, at baseline. Baseline HbA1c control also affected the efficacy of quality improvement strategies. Quality improvement strategies were also positively associated with aspirin therapy (relative risk 1.33 [95% CI 1.21, 1.45]), antihypertensive therapy (1.17 [1.01, 1.37]), retinopathy screening (1.22 [1.13, 1.32]), renal function screening (1.28 [1.13, 1.44]) and foot abnormality screening (1.27 [1.16, 1.39]), but not statin therapy (1.12 [0.99, 1.28]), hypertension control (1.01 [0.96, 1.07]) or smoking cessation (1.13 [0.99, 1.29]).

Comment: The need for structured management of patients with diabetes in order to address the multiple risk factors is increasingly recognized. This systematic review highlights the utility of such quality improvement strategies, which can improve glycaemic control as well as cardiovascular risk factors. Patient-centred approaches and interventions that target chronic disease management appear to be most helpful. The challenge is to develop a suitable programme in a socially and culturally- appropriate context in order to influence the bebaviour of both patients and healthcare professionals.

Reference: Lancet 2012;379(9833):2252–61

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2812%2960480-2/fulltext

Basal Insulin and Cardiovascular and Other Outcomes in Dysglycemia

The ORIGIN Trial Investigators

Summary: Patients with impaired fasting glucose, impaired glucose tolerance or type 2 diabetes mellitus and CV risk factors (n=12,537) were randomised using a 2×2 factorial design to receive insulin glargine (target fasting blood glucose level ≤95 mg/dL [5.3 mmol/L]) or standard care and omega-3 fatty acids or placebo in the ORIGIN trial; data on insulin glargine versus standard care were reported in this paper. At median follow-up of 6.2 years, no significant differences were seen between the insulin glargine and usual-care groups for the coprimary endpoints of nonfatal myocardial infarction, nonfatal stroke or CV-related mortality (hazard ratio 1.02 [95% CI 0.94, 1.11; p=0.63]) or these endpoints plus revascularisation or hospitalisation for heart failure (1.04 [0.97, 1.11; p=0.27]). Among those without diabetes at baseline (n=1456), the new diabetes diagnosis rate at ~3 months after end of treatment was lower among insulin glargine recipients than usual care recipients (30% vs. 35%; odds ratio 0.80 [95% CI 0.64, 1.00; p=0.05]). Compared with usual care, insulin glargine was also associated with a greater severe hypoglycaemia rate (1.00 vs. 0.31 per 100 person-years), an increase in bodyweight (+1.6 vs. –0.5kg) and a similar cancer risk (hazard ratio 1.00 [95% CI 0.88, 1.13; p=0.97]).

Comment: The much-anticipated results of the ORIGIN Study were presented at the ADA Scientific Sessions in a dedicated session. Although the routine addition of insulin glargine in newly diagnosed patients with type 2 diabetes or impaired glucose tolerance did not reduce the co-primary endpoints for cardiovascular events, it reduced the incidence of new diabetes diagnosis among those free of diabetes at baseline. This is consistent with other studies of early insulinization which suggests beneficial effects on the decline in beta-cell function. The incidence of hypoglycaemia was increased in the Glargine arm, with 11 more suspected or confirmed episodes per 100 person-years, and 0.7 more severe episodes per 100 person-years. These rates were surprisingly low overall, perhaps due to the selection of subjects with mild glucose intolerance, and the concomitant use of metformin. Importantly, there was no difference in incidence of any cancer, death from cancer, or cancer at specific sites. Along with other studies presented at the ADA meeting (see below), these provide much reassurance and should settle previous controversies regarding insulin analogues and cancer risk.

Reference: N Engl J Med [Published online June 11, 2012]

http://tinyurl.com/7h44toc

n–3 Fatty Acids and Cardiovascular Outcomes in Patients with Dysglycemia

The ORIGIN Trial Investigators

Summary: This study evaluated the effects of omega-3 fatty acids on cardiovascular risk in patients with or at risk for type 2 diabetes mellitus. 12,536 high-risk patients with impaired fasting glucose, impaired glucose tolerance, or diabetes were randomised to receive 1g of omega-3 fatty acids or placebo daily; patients also received either insulin glargine or standard care. During a median follow- up of 6.2 years, the incidence of death from cardiovascular causes did not differ significantly between groups (9.1% of patients taking omega-3 fatty acids and 9.3% of patients taking placebo). Omega-3 fatty acids also had no significant effect on the rates of major vascular events, death from any cause, or death from arrhythmia. Supplementation with omega-3 fatty acids significantly reduced triglyceride levels but had no significant effects on other lipids. In conclusion, supplementation with omega-3 fatty acids did not reduce the incidence of cardiovascular events in high-risk patients with or at risk for type 2 diabetes.

Comment: Although previous epidemiological studies have suggested an association between increased intake of fish or supplements containing omega-3 fatty acids, this study conclusively showed that daily supplements with 1g of omega-3 fatty acids do not reduce the incidence of cardiovascular events in subjects with cardiovascular risk factors and impaired glycaemia or type 2 diabetes. Previous trials in subjects post-MI or with heart failure had revealed some benefit from omega-3 fatty acids. Perhaps subjects with higher CV risk are more likely to derive benefits such as possible anti-arrhythmic effects. Several large multi-centre trials on omega-3 fatty acid supplementation in low or high risk subjects are still ongoing, and should help settle the debate on the use of the supplement.

N Engl J Med 2012; 367:309-318July 26, 2012

http://www.nejm.org/doi/full/10.1056/NEJMoa1203859

Cancer Link with Insulin- Data from the US and Northern Europe (11 June, 2012)

- What we know about insulin and cancer - John Buse, MD, PhD
- Northern Europe Database Study of Insulin and Cancer Risk - Peter Boyle, MD
- Results from the Kaiser-Permanente Collaboration and a Focus on Prevalent User Analysis - Laura A. Habel, PhD
- Results from Claims Data and a Focus on Incident User Analysis - Tim Sturmer, MD, PhD
- Implications for Practice and Future Research - James Meigs, MD

Summary: In a special session dedicated to the presentation of recent studies regarding insulin and cancer, several large multi-centre epidemiological surveys were presented. This included a meta-analyses of several Northern European Registries with a total of 447, 821 users of insulin, and a study from a health-claims database in the US with a total of 6548 new users of glargine and 39708 new users of NPH insulin. These studies compared the risk of different site-specific cancers in glargine users versus users of NPH insulin. Overall, all the studies were consistent in showing no evidence of increase in cancer risk, including the risk of breast, colorectal and prostate cancer.

Comment: Diabetes is associated with increased risk of cancer. The presenters highlighted some of the pitfalls of pharmaco-surveillance studies, and the flaws of earlier small studies regarding insulin analogs and cancer. The collection of recent studies reported here, with more careful study design, often using a new-user cohort design with active comparator, with much larger patient numbers and more detailed information of site-specific cancer endpoints, found no evidence of increased cancer risk with insulin analogs. Together with data from the ORIGIN Trial, these data are reassuring.