Ecos do "50th EASD Annual Meeting"

Realizou-se, entre 15 e 19 de Setembro de 2014, na Feira Internacional de Viena, Áustria, o "50th EASD Annual Meeting", maior congresso científico a nível mundial dedicado à diabetes, que reune profissionais de saúde e investigadores biomédicos.

Nesta Revista Internacional, dedicada ao "50th EASD Annual Meeting", publicamos os "abstracts" dos trabalhos científicos apresentados por portugueses, ou em que participaram portugueses, por ordem de numeração no respectivo livro de "abstracts".

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Hypothalamic nitric oxide regulates insulin signalling and hepatic lipid metabolism

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Background and Aims: Human studies demonstrated that NO is an important regulator of insulin clearance. Whether the control of insulin clearance is solely dependent on hepatic mechanisms or also involves hypothalamic regulation is currently uncertain. Since hypothalamus is a critical regulator of energy metabolism and endocrine functions, we previously hypothesized that NO production by central/hypothalamic axis regulates insulin clearance and therefore peripheral insulin bioavailability. We found a significant inverse correlation between NO production in the paraventricular nucleus (PVN) and systemic insulin clearance. However, the metabolic consequences of PVN NO-mediated regulation of insulin clearance remain unknown, so we hypothesized that in addition to insulin clearance, it also modulates hepatic glucose and lipid metabolism.

Materials and Methods: Male Wistar rats underwent brain surgery using a stereotaxic apparatus for implantation of the double cannulas, for nucleus specific infusion in the PVN region. After the bregma localization the following coordinates were used: AP: -1.8mm, Lat: +/- 0.4mm, DV: -8.0mm. Bolus infusion of 250ug/2uL of L-NAME (or 2uL of saline in the control animals) were performed in each side of the brain, once only in the day of the experiment. An oral glucose tolerance test (OGTT) (2g/kg) was subsequently performed. Liver was harvested and kept at -80º for protein extraction and analysis of glucose and lipid metabolism-related enzymes by immunoblotting.

Results: We observed that PVN NO depletion led to changes in insulin signaling as well as glucose and lipid metabolism. Regarding insulin signaling, IRS-1 and AKT expression as well as IRS-1 and AKT phosphorylation were decreased. In addition, expression of hepatic Glut 1, 2 and 4 were all significantly decreased suggesting a reduced capacity for glucose uptake by the liver. Interestingly, depletion of PVN NO levels suppressed the lipogenic enzymes (ACC, FAS, ATP citrate lyase and pATP citrate lyase), which is consistent with the observed diminished hepatic non-esterified fatty acids (NEFA) content. Meanwhile, hepatic DGAT expression was increased, possibly in response to decreased NEFA. Hepatic TG levels were not diminished by PVN-NO depletion possibly due to this compensatory DGAT upregulation.

Conclusion: These results support the hypothesis that increased PVN NO results in a decreased insulin clearance and a stimulation of de novo lipogenesis. This suggests that hypothalamic NO signaling has a role in regulating hepatic lipid metabolism.

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Selective expression of ROCK1 in the liver promotes insulin resistance and hepatic steatosis in diet-induced obese mice

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Background and Aims: In the European Union approximately 29 million people suffer from a chronic liver condition. The prevalence of non-alcoholic fatty liver disease (NAFLD) is 2-44% in the European population and 42.6-69.5% in people with type 2 diabetes. Furthermore, over 50% of adults in the European Union are overweight or obese. Obesity is a risk factor for NAFLD and is strongly associated with insulin resistance. Our previous data showed that liver-specific deletion of Rho-kinase 1 (ROCK1) caused a significant improvement in insulin sensitivity and hepatosteatosis in obese mice induced by a high-fat diet. The current study was designed to further determine the physiological role of hepatic ROCK1 in regulating whole-body glucose and lipid metabolism.

Materials and Methods: Mice expressing a constitutively active (CA) mutant of ROCK1 in liver were studied. These mice started a high-fat diet (HFD) at 6 weeks of age for a period of 12 weeks. Insulin sensitivity and glucose tolerance were assessed and body weight and glucose levels were also monitored. Hepatic and serum content in triglycerides and cholesterol was determined. Hematoxylin and eosin stain (H&E stain) of liver sections from control and CA-ROCK1 mice was performed. Gene expression of key molecules involved in lipid metabolism was also determined for control and CA-ROCK1 mice.

Results: Liver-specific CA-ROCK1 mutant mice exhibited higher body weight 2 weeks after HFD feeding (21.6 ± 0.4 g N=10 vs. 23.6 ± 0.6 g N=10, p = 0.01) and this difference was increased by the period on HFD (33.8 ± 1.28 g N=10 vs. 39.4 ± 1.4 g N=10, p = 0.01). Blood glucose was also increased after 4 weeks of HFD (148.0 ± 3.7 mg/dL N=10 vs. 165.4 ± 7.1 mg/dL N=10, p = 0.05). These mice were insulin resistant, as revealed by the failure of blood glucose levels to decrease after in insulin injection (AUC 16058 ± 594.0 N=6 vs. 20581 ± 1102 N=10, p = 0.01), but normal glucose tolerant. These effects were accompanied by hyperinsulinemia, increased hepatic triglycerides (430.2 ± 40.7 mg/dL N=9 vs. 674.1 ± 108.0 mg/dL N=8, p = 0.05) and serum cholesterol (94.2 ± 8.4 mg/dL N=10 vs. 131.4 ± 12.6 mg/dL N=9, p = 0.05) in the CA-ROCK1 mice. Histological analysis showed that hepatic steatosis by high-fat feeding was greatly increased in liver-specific CA-ROCK1 mutant mice compared with control mice. Moreover, activation of ROCK1 in liver caused an increase in gene expressions of key lipogenic enzymes, including FAS (fatty acid synthase) and ACC (Acetyl-CoA carboxylase). However, overexpression of hepatic CA-ROCK1 had no effect on gene expression involved in fatty acid oxidation and fatty acid uptake.

Conclusion: Our data demonstrate that activation of hepatic ROCK1 is sufficient to cause insulin resistance and hepatic steatosis in diet-induced obese mice, suggesting an important role for hepatic ROCK1 in regulating fuel metabolism. Thus, hepatic ROCK1 could be a molecular target for the treatment of obesity and obesity-related metabolic disorders such as NAFLD.

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Activation of oestrogen receptor alpha in macrophages controls high-fat diet-induced inflammation of adipose tissue and prevents obesity and glucose intolerance

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Background and Aims: Estrogens have been recognized as key regulators of body composition and glucose homeostasis. However, although both clinical and experimental data clearly evidenced the crucial role of estrogen receptor alpha (ERa), the mechanisms involved in the protective actions of estrogens against obesity and diabetes remain obscure. For instance, although estrogens are known to modulate inflammatory responses through ERa dependent effects, it is still uncertain wether specific actions of these sex steroid hormones on the stroma-vascular fraction (SVF) of adipose tissue could contribute to their benefits on body composition and glucose metabolism. In the present study, we aimed to determine 1) the influence of estrogens on the adaptation of SVF cells in response to a nutritional stress; 2) the contribution of ERa-expressing myeloid cells to the prevention of obesity by estrogens.

Materials and Methods: In a first set of experiment, 3 groups of C57Bl/6 female mice were subjected to a chow or a high-fat (HFD) diet for 12 weeks: ovariectomized (estrogen deficiency), sham-operated (endogenous estrogens) and ovariectomized treated with 17b-estradiol (E2, 80µg/kg/d, sc). Weight gain, body composition and glucose tolerance were monitored and both isolated adipocytes and SVF from visceral adipose tissue (VAT) were analyzed by flow cytometry and RT-qPCR. Then, metabolic phenotype and SVF characteristics were studied in HFD-fed mice with specific invalidation of ERa in myeloid cells (ERa-LysM-Cre+ mice).

Results: Both endogenous estrogens and E2 administration prevented HFD-induced obesity and glucose intolerance, as well as adipocyte hypertrophy. HFD increased the number of CD45- cells in VAT SVF, irrespective of estrogen status, but VAT infiltration by immune cells (CD45+) was strongly reduced by endogenous estrogens and E2, with a significant decrease in macrophage content (-65% CD45+/F4/80+ cells) and a predominance of M2 macrophages, as confirmed by mRNA analysis (+13-fold Ym1; -4.5-fold iNOS in E2-treated as compared to ovariectomized mice). VAT infiltration by B and TCD4+ and TCD8+ lymphocytes was also reduced by estrogens, but the pool of regulatory T cells was preserved. Demonstrating the role of ERa-LysM-Cre+ mice were characterized by a significant increase of HFD-induced inflammation of VAT and developed exacerbated adiposity and glucose intolerance.

Conclusion: These data demonstrate that estrogens limit HFD-induced inflammation of VAT and suggest that macrophages of the SVF largely contribute to their protective action against obesity and though the activation of ERa.

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SP regulates macrophage function in diabetic wound healing

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Background and Aims: Chronic diabetic foot ulcerations develop in areas affected by diabetic neuropathy. As consequence, neuropeptides, such as substance P (SP), known to modulate inflammation, showed to be important in wound healing. However, little it is known about the effect of SP on macrophages activation. We aimed to study the effect of SP on macrophage function in diabetic wound healing progression.

Materials and Methods: We used wild type (WT) mice and two types of genetically modified mice: one deficient of the NK1 receptor of SP (NK1RKO) and one deficient of the TAC1 gene that encodes for SP and other takinins (TAC1KO). Also, we treated the wound with SP or CJ012,255 (CJ), an inhibitor of SP receptor. Diabetes was induced by sreptozotocin intraperitoneal injection, 50 mg/Kg, 5 days. The animals were kept 8 weeks diabetic prior wound healing experiment. M1 and M2 macrophages were identified by using immunohistochemistry at several phases of wound healing: baseline (Day-0), Day-3 and Day-10 post-wounding. MCP-1, IL-a and KC was quantified by q-RT-PCR.

Results: The M1/M2 ratio was increased at Day-0 in WT-diabetic mice and nondiabetic and diabetic NK1R and TAC1 mice when compared to

WT-nondiabetic mice. In WT-nondiabetic mice, the ratio increased at Day-3 but returned to normal levels by Day-10. In contrast, in WT-diabetic and nondiabetic and diabetic NK1R and TAC1 mice at Day-0, Day-3 and Day-10, the M1/M2 ratio remains high, suggesting a persistent inflammation. At Day-10, the M1/M2 ratio was increased in CJ-treated WT-nondiabetic and WT-diabetic mice. In contrast, SP treatment reduced the diabetes-induced increase in M1/M2 ratio. Similar results were observed in the skin gene expression of the monocyte chemoattractant 1 (MCP-1) that recruits monocytes in areas of inflammation where they are converted to macrophages. At Day-0, MCP-1 was increased in the TAC1KO mice. MCP-1 expression increased at Day-3 in all non-diabetic and diabetic mice. At day-10, all mice groups had a decreased MCP-1 expression but, nonetheless, it was increased in WT-diabetic. SP treatment increased MCP-1 expression at Day-3 in both WT-nondiabetic and diabetic wounds. At Day-10, SP treatment reduced MCP-1 expression in both WT-nondiabetic and diabetic mice while CJ-treated mice had higher expression when compared to SP-treated mice. Moreover, diabetic mice showed an increase in IL-6 expression at baseline while SP induced a further increase in IL-6 gene expression in WT-nondiabetic mice at Day-3. NK1RKO and TAC1KO mice showed an increase in IL-6 expression at baseline. KC gene expression was also increased in WT diabetic mice at baseline and this increase persisted at Day-10. SP induced an acute increase at Day-3 that was followed by a reduction to normal levels at Day-10. NK1RKO and TAC1KO mice had also higher KC gene expression at baseline and NK1RKO mice showed a higher KC expression at Day-3.

Conclusion: In conclusion, the reduction in SP availability results in a proinflammatory activation of skin macrophages before wounding. SP also plays a major role in shifting macrophages to the M2 activation promoting wound healing. Furthermore, SP induced an increase in the acute inflammatory phase of wound healing during the early stages of wound healing but considerably reduces it in later stages, which is essential for a good skin repair.

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Disclosing acute caffeine action on insulin sensitivity: effects on skeletal muscle

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Background and Aims: Caffeine, a non-selective adenosine antagonist, is the behaviorally active substance most widely consumed in the world. When consumed regularly, this xanthine presents beneficial effects on type 2 diabetes and metabolic syndrome. However, the sensitizer effect of chronic caffeine intake contrasts with acute caffeine administration that has been associated with an increase in insulin resistance (IR). The aim of this work was to investigate the effect of acute caffeine administration on insulin sensitivity and the involvement of adenosine receptors. Additionally, the mechanism behind caffeine-mediated effects in skeletal muscle was assessed.

Materials and Methods: In vivo experiments were performed in Wistar rats of both sexes, aged 3 months (200-350g) anaesthetized with pentobarbitone (60mg/Kg). The effect of the acute administration of caffeine (0.001-5μM), DPCPX (A1 antagonist, 0.0005-5μM), SCH58261 (A2A antagonist, 0.0005-5μM) and MRS1754 (A2B antagonist, 0.001-

5μM) on insulin sensitivity was evaluated by means of an insulin tolerance test. Skeletal muscle Glut4 and AMPKα1 expression were quantified by Western-blot. The effect of A1 and A2B adenosine agonists on glucose uptake was evaluated. Sodium nitroprussiate (SNP, 10nM), a nitric oxide (NO) donor was used to evaluate the effect of NO on adenosine antagonism induced-IR.

Results: Acute caffeine decreased insulin sensitivity in a concentration dependent manner (Emax=55.54 ± 5.37%, IC50=11.61nM), an effect that is mediated by A1 and A2B adenosine receptors. Additionally, in skeletal muscle, acute caffeine administration did not modify AMPK expression, however it significantly decreased Glut4 by 23.23% and 31.81% (0.05 and 0.5μM of caffeine, respectively). We found that A1, but not A2B agonists significantly increased glucose uptake to 2.11±0.04 nmol.mg-1 tissue in skeletal muscle when compared to control (1.69±0.04nmol.mg-1tissue). SNP partially reversed DPCPX and MRS1754 induced-IR by 77.4 and 51.1%, respectively, when compared with the application of adenosine antagonists alone (KITT DPCPX=2.12± 0.44%glucose.min-1; KITT MRS1754=2.16±0.08%glucose.min-1).

Conclusion: Acute caffeine administration decreases insulin sensitivity in a concentration dependent manner being this effect mediated by A1 and A2B adenosine receptors. In skeletal muscle, the effect of caffeine on insulin sensitivity involves a decrease in Glut4 expression and in insulin-dependent glucose uptake that is mediated mainly by A1 adenosine receptors. Additionally, adenosine-mediated insulin sensitivity seems to involve NO production and its sensitizer actions.

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Glucose uptake independent of insulin action: role of S-nitrosilated insulin chains

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Background and Aims: Portal insulin is removed (50-70%) during first pass transit in the liver by a process called insulin clearance. Protein disulfide isomerase (PDI) mediates insulin clearance by reduction of insulin disulfide bonds, breaking it into A and B chains by a mechanism that requires glutathione (GSH). Previously, we reported that A/B chains of insulin could be S-nitrosated (A-SNO and B-SNO) in vitro, forming nitrosothiols. After a meal, the increase of GSH levels together with the activation of parasympathetic nervous system which leads to nitric oxide (NO) release results in an increase in peripheral insulin sensitivity. A concurrent increase in hepatic PDI activity cleaves and nitrosilates A and B chain of insulin (A-SNO e B-SNO). Our hypothesis is that S-nitrosilated modified derivatives of insulin, A-SNO and B-SNO, produced during the insulin clearance process stimulates glucose uptake in skeletal muscle by a mechanism independent of the insulin signalling pathway.

Materials and Methods: The presence of BSNO in the liver of Wistar rats was analyzed by immunoprecipitation of S-nitrosilation proteins following by western blot for B-chain. Physiological effects of S-nitrosilated modified derivatives of insulin were evaluated in differentiated skeletal muscle cells (L6-mycGLUT4 cells) and adipocytes (3T3-L1 cells). The cells were stimulated with 100nM insulin, A-chain, B-chain, A-SNO and B-SNO to evaluate glucose uptake using 3H-Glucose method. To analyse detailed signalling pathways activated by these insulin derivatives we performed cellular extracts and by western blotting technique we investigate the enrolled proteins.

Results: We detected the existence of BSNO in liver homogenates of rats and that BSNO levels were decreased (23% comparing with sham

rats) in animals that were subjected to an hepatic denervation of parasympathetic nerves - NO pathway. We observed that A-SNO and B-SNO significantly stimulates glucose uptake in L6 muscle cells (159.8 ± 19.2% and 204.8 ± 30.2% to control, respectively), similar to insulin stimulus (203.1 ± 15.0). The stimulation of glucose uptake was mediated by the activation of AMPK pathway, detected by the increase in phosphorylation of Thr172 AMPK. We also observed that these insulin derivatives did not activate the canonical insulin pathway. In adipocytes we observed that A-chain and B-chain insulin derivatives increase glucose uptake (309.2 ± 83.2% and 319.0 ± 23.6% to control, respectively). In a lesser extent B-SNO also stimulates glucose uptake (193.6 ± 13.8% to control). In adipocytes these derivatives does not activate either the canonical insulin pathway or AMPK signaling pathway.

Conclusion: As a conclusion insulin clearance process can lead to the formation of A/B chain and/or the respective S-nitrosilated derivatives. In adipocytes, mainly A-chain and B-chain stimulates glucose uptake. On the other hand when insulin derivatives are S-nitrosilated (A-SNO and B-SNO) they act on skeletal muscle promoting glucose uptake, through activation of AMPK signaling pathway.

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FKBP5 gene polymorphisms and expression in human adipose tissue are associated with insulin resistance and type 2 diabetes

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Background and Aims: Central obesity is associated with a cluster of metabolic alterations, which include insulin resistance (IR), dyslipidemia and cardiovascular disease. Glucocorticoid excess is associated with redistribution of fat from peripheral to central depots and with IR and development of diabetes. To identify potential novel mechanisms for IR we investigated dexamethasone-induced changes of gene expression in human adipose tissue.

Materials and Methods: Subcutaneous and omental adipose tissue, obtained from 25 non-diabetic subjects (28-60 yrs; 20.7-30.6 kg/m^2), was incubated without or with dexamethasone (0.003-3 μM) for 24 h. Gene expression was assessed by microarray and real time-PCR. Protein levels were assessed by immunoblotting.

Results: FKBP5 (FK506 binding protein 5) was one of the genes responding most to dexamethasone. Gene expression increased up to 7-fold in a dose-dependent manner in both subcutaneous and omental fat depots (p<0.001). The protein coded by this gene, the FKBP51, is an immunophilin, which means that it plays a role in the immune system. FKBP5 mRNA is widely expressed in metabolically active tissues with the highest gene expression in muscle and adipose tissue. However, FKBP51 protein was about 10-fold higher in the omental than in the subcutaneous fat depot (p<0.05), whereas the mRNA levels were similar. 80-90% of the FKBP5 protein in adipose tissue could be attributed to the adipocytes, while the stromal vascular cells contribute to 10-20% (p<0.05). FKBP5 gene expression in the subcutaneous fat depot was positively correlated with markers of IR including, HOMA-IR and subcutaneous adipocyte diameter (r=0.59, p<0.001; r=0.48, p<0.05, respectively). In addition, FKBP5 gene expression in omental adipose tissue was associated with reduced insulin effects on glucose uptake in subcutaneous and omental adipocytes (p<0.05). Interestingly, FKBP5 SNPs (e.g. rs2817056, rs2395635, rs1334894) were found to be significantly associated with type 2 diabetes and with 2-h OGTT glucose, HDL-cholesterol and triglycerides in publicly available datasets from large, population-based cohorts.

Conclusion: The FKBP5 gene is regulated by glucocorticoids in both subcutaneous and omental adipose tissue, and its expression in human adipose tissue is correlated to markers of IR. In addition, SNPs in the FKBP5 region are associated with type 2 diabetes and diabetes-related traits. We hypothesize that FKBP5 is a mechanism linking alterations in nutrient metabolism with immune function, both following glucocorticoid excess and in other conditions with IR. Further studies will address whether FKBP5 is causally linked to IR and whether the related mechanisms can provide novel pharmacological targets for the treatment of IR.

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Novel paracetamol glucuronide derivative for quantifying gluconeogenesis using the deuterated water method

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Background and Aims: In fasted humans, the analysis of plasma glucose ^{2}H-enrichment in position 5 relative to position 2 (H5/H2) following ingestion of deuterated water (^{2}H$_2$O) is widely used to measure the fractional contribution of gluconeogenesis to endogenous glucose production (EGP). This information can be noninvasively obtained via urinary Paracetamol glucuronide (PG): a product that is more stable and abundant compared to blood glucose. However, current methods for derivatizing urinary PG to a form that can be analyzed for positional ^{2}H-enrichment by NMR or MS are laborious and ill-suited for high-throughput studies. We developed a novel procedure where urinary PG is derivatized to 5-O-acetyl monoacetone glucuronic lactone (MAGLA). The chemical transformation and purification steps are robust and amenable to automation and parallel processing and yield resolved signals for H5/H2 analysis by ^{2}H NMR (see Figure). We applied this procedure to a study where ^{2}H$_2$O and Paracetamol were given to overnight fasted healthy subjects and compared H5/H2 of plasma glucose with that of urinary glucuronide.

Materials and Methods: Eleven subjects were admitted to the clinical research unit on the evening before the study and provided a standard supper at 17.30. Each ingested 0.5 g ^{2}H$_2$O/kg body water in three equally divided doses at 20:00, 22:00, and 24:00. At 05:00 the following day, Paracetamol (0.5g) was given and a primed infusion of [6,6-^{2}H$_2$]glucose was initiated. Urine was sampled from 06:00-08:00 and blood was sampled at 07:40. Plasma glucose and urinary PG enrichments of positions 5 and 2 were measured by ^{2}H NMR following their derivatization to monoacetone glucose and MAGLA, respectively. The fractional gluconeogenic contributions to EGP were calculated from plasma glucose H5/H2. These were compared with estimates obtained from urinary glucuronide H5/H2.

Results: The overall yield of MAGLA from urinary glucuronide was 20-40% and the preparations gave well-resolved ^{2}H NMR signals for quantifying H5/H2. Analysis of MAGLA yielded identical estimates of fractional gluconeogenic contributions to EGP to that of plasma glucose (54 ± 2% versus 55 ± 3%, respectively). Furthermore, a Bland-Altman analysis indicated agreement at the 95% confidence level between the sets of plasma glucose and urinary MAGLA measurements.

Conclusion: The conversion of urinary Paracetamol glucuronide to MAGLA is a relatively simple and robust procedure for obtaining estimates of gluco-

neogenesis using ^2H_2O, or indeed any gluconeogenic tracer. For overnight-fasted healthy subjects, ^2H NMR analysis of MAGLA provides identical estimates of fractional gluconeogenesis to that of plasma glucose.
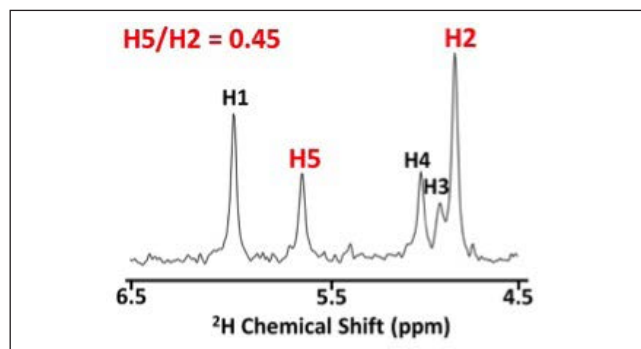
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Cost-effectiveness of metformin plus vildagliptin versus metformin plus sulphonylurea for the treatment of type 2 diabetes patients in Portugal

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Background and Aims: The objective of the study is to evaluate the cost-effectiveness of vildagliptin plus metformin compared with generic sulphonylurea plus metformin in patients with type 2 diabetes mellitus, not controlled with metformin, from a Portuguese healthcare system perspective.
Materials and Methods: A cost-effectiveness model was constructed using risk equations from the United Kingdom Prospective Diabetes Study Outcomes Model with a 10,000-patient cohort and a lifetime horizon. The model predicted microvascular and macrovascular complications and mortality in yearly cycles. Patients, who entered the model as metformin monotherapy failures, were modelled as switching to alternative treatments (metformin plus basal-bolus insulin and subsequently metformin plus intensive insulin) using a threshold of glycated haemoglobin A1c >7.5% for inadequate glycaemic control. Baseline patient characteristics and clinical variables were derived from a Portuguese epidemiological study. Costs estimates were based on direct medical costs only. One-way and probabilistic sensitivity analyses were conducted to test the robustness of the model assumptions.
Results: Over a lifetime horizon, there were fewer non-fatal diabetes-related adverse events (AEs) in patients treated with metformin plus vildagliptin compared with patients treated with metformin plus sulphonylurea (6752 versus 6815). Addition of vildagliptin compared with sulphonylurea led to increased drug acquisition costs counterbalanced with reduced costs of AEs, managing morbidities, and monitoring patients. Treatment with metformin plus vildagliptin yielded a mean per-patient gain of 0.1279 quality-adjusted life years (QALYs) and a mean per-patient increase in total cost of €1161, giving an incremental cost-effectiveness ratio (ICER) of €9072 per QALY. Univariate analyses showed that ICER values were robust and ranged from €4195 to €16,052 per QALY when different parameters were varied. The Probabilistic Sensitivity Analysis suggested that, for a willingness-to-pay threshold of €30,000 per QALY, treatment with metformin plus vildagliptin had a 79% probability of being cost-effective compared with metformin plus sulphonylurea.

Conclusion: Treatment with metformin plus vildagliptin compared with metformin plus sulphonylurea is expected to result in a lower incidence of diabetes-related AEs and to be a cost-effective treatment strategy.

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A patient centered approach on newly-arrived persons to a diabetes clinic

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Background and Aims: It's recognized that person-centred therapeutic education and group education with active methodologies promote experiences sharing, conviviality and stimulates learning among participants. The clinic introduced two structured programs for self-management education (DSME) addressed to newly-arrived patients covering a wide range of Diabetes Care in an integrated way. It's a comprehensive program of patient-centred care designed to increase autonomy, promote better adherence to treatment, and thus better metabolic control. We aim to perceive the programme's practical feasibility and people's adherence.
Materials and Methods: Programme 1: lasts for 04:30h;-During this period the person performs several tests: blood samples, EKG and retinography. A nurse performs a foot screening with risk assessment and foot care education. Then the person participates in two group sessions: a session with nurse guidance addressing pathophysiology of diabetes, relating the various important aspects in treatment and self-control, as well as doubts clarification and a final session about healthy eating, its importance for the metabolic control and lipid profile, and role of exercise in controlling diabetes (guided by a dietician/nutritionist). The average time between the program and the 1st medical consultation at the clinic is 4 weeks. Programme 2: lasts for 3 months, divided in three group education sessions before the diabetes individual medical consultation (med). Sessions are guided by a facilitator using an IDF approved education tool, which provides an interactive verbal and visual learning experience, allowing groups engagement in an open and meaningful debate about diabetes. Sessions are divided by themes: the 1st (S1) leads to a reflection on their role in disease's self-management, the 2nd (S2)covers general concepts for healthy eating, and the 3rd (S3) is a physical activity session with a gym teacher. Patients are selected based on their age (50-80 y) and HbA1c(< 10%), they are invited to attend programme 1 or 2 according to their convenience.
Results: Programme 1: A sample of 300 people (February to September 2013) with 60.4±10.3 years of age, an initial mean HbA1c of 8.7±1.5% and BMI mean of 28,2±4,6kg/m² were analysed. No consistent changes were observed in terms of BMI or HbA1c in this group between the session and the medical consultation. Programme 2: We analysed a sample of 231 people (same period of time), with 68.3±8.8 years of age and an initial mean HbA1c of 9.1±0.7% and BMI mean of 35,3 ± 3,2 kg/m². The drop-out rate was 10,8% at session 2 and 82% at session 3. No consistent changes were observed in BMI between the various groups. In terms of HbA1c it was observed a tendency of decrease between S1 and medical consultation directly related to the number of sessions attended ([[unable to display character: ∆]] A1c - Session 1: -0,27%; Session 2: -0,59 %; Session3: -0,85 %)
Conclusion: It's well known that active methods are a fundamental tool in group training. Here, the consistent decrease in HbA1c (programme 2) achieved independently of weight loss, hints to the impact of sharing solutions among peers by boosting diabetes acceptance, well-being and development of autonomy with DSME. The longer duration of this program also enables a slower integration of knowledge and skills in the daily life. However, the high drop-out before the exer-

cise session advises us to consider alterations on program implementation, further encouraging patients participation.

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Annual deterioration of renal function in hypertensive patients with diabetes vs without diabetes

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Background and Aims: Chronic renal disease (CKD) complicates hypertension and diabetes. Knowledge of the deterioration rate of CKD may anticipate adjustment of therapies with predominant renal elimination. We aim to evaluate the rate of annual deterioration of renal function in a large cohort of hypertensive patients either with diabetes (DM) and without it (non-DM) followed for 5 years in a reference outpatient hospital clinic of hypertension, and to relate it with BP and glycemic control.

Materials and Methods: Out of a total of 1924 patients, 1023 patients (594 non-DM and 429 DM, 53% female, ageing 62.1±10.2 years) were evaluated during the last 5 years for the annual evolution of renal function (MDRD) ambulatory 24-h blood pressure (ABP, SpaceLabs 90207) and metabolic parameters, corresponding to the analysis of 2378 patients-years.

Results: DM and non-DM did not differ for age (60.9 ± 10.1 v 62.8 ± 10.5 years), mean 24h BP levels (134/86 ± 12/10 v 136/87 ± 11/11, nighttime 123/74 ± 16/10 v 122/73 ± 15/10 mm Hg), albuminuria (145 ± 430 vs 130 ± 370 mg/24h) and body mass index (28 ± 6 v 29 ± 8 Kg/m^2). DM v non-DM showed a higher (qui square p &gt 0.01) prevalence of stage 3 CKD (24.2% v 18.1%, GFR 30-59 mL/min/1.73m2), stage 4 (5.4% v 2.7%, GFR 15- 29) and stage 5 (0.8% v 0.5%, GFR 8.0 %). Each year net GFR was reduced by 3.3 ± 8.2 in DM vs 2.4 ± 7.7 mL/min/1.73m^2 in non-DM (p=0.12, ns). In multivariate analysis, age, nighttime BP, the use of double inhibition of renin angiotensin system and HbA1C &lt 8.0 % in DM were independent factors associated with the deterioration of GFR. Also in average 16.2% of DM and 13.1% on non-DM moved each year towards the next and more severe stage of CKD (p=0.051). For initial GFR &gt90 mL/min/1.73m2, 24% of DM and 18% of non-DM showed a reduction per year &lt 10% of the previous GFR value (qui square, p=0.049).

Conclusion: A progressive deterioration of renal function for each next year is frequent in diabetics and non-diabetics with hypertension. Beyond ageing, renal deterioration may be particularly dependent on BP control particularly at nighttime, on certain therapies and on highly abnormal glucose control.

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> AGENDA DE CONGRESSOS

2014

8º Fórum Nacional da Diabetes
2 de Novembro
Local: Centro de Congressos do Estoril
Informações: www.forum-diabetes.org

Congresso Internacional "Presente e Futuro: Realidade Clínica, Social e Económica na Diabetes"
14 e 15 de Novembro
Local: Salão Nobre do Instituto de Ciências Biomédicas Abel Salazar (Universidade do Porto)
Informações: http://totusalus.org/EVENTOS%202014/EVENTOS%202014/CONGRESSO

2015

ATTD 2015 - Advanced Technologies & Treatments for Diabetes
18 a 21 de Fevereiro
Local: Paris, França
Informações: http://cts.vresp.com/c/?KenesInternationalAT/f3bf4dd189/9ba20ffc6a/b75aa7f121

8º Simpósio Internacional DIP 2015: Diabetes, Hypertension, Metabolic Syndrome & Pregnancy
15 a 18 de Abril
Local: Berlim, Alemanha
Informações: http://em-sender4.com/fb/fb/D9F89CD257914C3591E9A9B6CE623F3068A79695B9384CB7705E6A5124C769D6/show.aspx

World Diabetes Congress 2015
30 de Novembro a 4 de Dezembro
Local: Vancouver, Canadá
Informações: http://www.wdc2015.org