

IX Advanced Course of Endocrinology • IX Curso Avançado de Endocrinologia [2019;14 (Supl. 3)]

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5-6 APRIL 2019
CONGRESS CENTRE OF
PORTO PALÁCIO HOTEL

ORGANIZATION
Associação dos Amigos do Serviço de
Endocrinologia do Hospital de S. João

COLLABORATION
Serviço de Endocrinologia, Diabetes e
Metabolismo do Centro Hospitalar S. João /
Faculdade de Medicina da Universidade do Porto



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IX ADVANCED COURSE OF ENDOCRINOLOGY



Welcome Words

Davide Carvalho¹

¹ *Presidente da Sociedade Portuguesa de Endocrinologia, Diabetes e Metabolismo; Director do Serviço de Endocrinologia, Diabetes e Metabolismo do Centro Hospitalar Universitário S. João; Professor Associado com Agregação Faculdade de Medicina da UP; Investigador Principal do i3S da UP; Presidente da Associação dos Amigos do Serviço de Endocrinologia, Diabetes e Metabolismo Centro Hospitalar Universitário S. João.*

Dear Friends,

Welcome to the IX Advanced Course of Endocrinology. This course brings together interns, young specialists of Endocrinology, and well-known specialists, and is a melting pot of different perspective and diverse interests which has the sole focal challenge of improving the quality of care of patients.

For the second time we are going to hold an Insulin-Pump therapy course, which will be very practical and will accordingly enable all participants to have an opportunity to update their practical knowledge of this method of managing this disorder. Although insulin pump therapy is increasing in Portugal, we are far from treating the same average number of patients as Europe as a whole. We will also discuss the role of ultrafast insulins and that of the SGLT2-i in type 1 diabetes

Medullary thyroid cancer accounts for 2–5% of all thyroid cancers. A germline activating mutation in the RET (which is rearranged during transfection) proto-oncogene (RET) is reported in nearly all cases of hereditary medullary thyroid cancer, with somatic RET mutation in up to 50% of sporadic tumours. Recently, the National Institute for Health and Care Excellence (NICE) has recommended that cabozantinib be subsidised. In the light of the new therapeutic options, it is important to review and update our knowledge in this field.

Calcium-phosphorus metabolism will be also a topic for discussion when addressing kidney bone disease, hypoparathyroidism, and hypophosphatemic rickets.

Finally, in the warm-up to the European Neuroendocrine Association Meeting which will take place in Porto in September, 2020, we will count on the presence of the Chairman of ENEA to talk to us about pituitary disorders.

Sharing experiences from Portugal with colleagues from around the world is important for discovering a new clinical perspective.

I hope that you will all enjoy the IX Course and I look forward to receiving suggestions for the topics to be discussed at the next one!

Davide Carvalho

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5th April Friday

17h30 **WELCOME WORDS** – Davide Carvalho (Porto)

17h45 – 19h45 **FROM THE SCIENTIFIC EVIDENCE TO THE CLINICAL PRACTICE: CSII EFFICACY AND SAFETY**

Chairmen: José Luís Castedo (Porto), Helena Cardoso (Porto)

Moderators: Celestino Neves (Porto), Cíntia Castro Correia (Porto)

17h45 – 18h30 **The Spanish Perspective: The Experience of a National Reference Center** – Ignacio Conget (Barcelona)

18h30 – 18h45 **The Portuguese Perspective** – César Esteves (Porto)

18h45 – 19h45 **How to Use Specific Features of CSII Therapy. The Example of Bolus Calculator for Meals and Corrections. The Use of Computer's Downloading Supports and Softwares** – Ignacio Conget (Barcelona)

Sponsored by Eli-Lilly

20h00 – 21h00 **Dinner**

21h00 – 23h00 **WORKSHOP: Clinical Cases** – Ignacio Conget (Barcelona)

Moderators: Celestino Neves (Porto), Luísa Barros (Coimbra)

6th April Saturday

08h30 – 10h30 **MEDULLARY THYROID CARCINOMA**

Chairmen: Valeriano Leite (Lisboa), Elisabete Rodrigues (Porto)

08h30 – 09h00 **Natural History, Treatment, and Long-term Follow-up of Patients with Multiple Endocrine Neoplasia Type 2B** – Maria João Bugalho (Lisboa)

09h00 – 09h30 **Genotype-Phenotype Correlation in Medullary Thyroid Carcinoma** – Paula Soares (Porto)

09h30 – 10h00 **Medical Management** – David Viola (Pisa)

Sponsored by Ipsen

10h00 – 10h30 **Discussion Panel** – L. Matos Lima (Porto), Claudia Freitas (Porto), Isabel Torres (Porto)

- 10h30 – 11h00 **Poster Discussion** – Duarte Pignatelli (Porto), Ana Varela (Porto), Ana Isabel Oliveira (Porto), Eva Lau (Porto), Sandra Belo (Porto)
- Screen 1: EP1 to EP3**
- EP01 FOLLICULAR THYROID CARCINOMA: A DIFFERENT PRESENTATION**
Sara Pinheiro; Tiago Silva
- EP02 LIVER METASTASIS FROM DIFFERENTIATED THYROID CANCER: IS IT ALWAYS RELATED TO A POOR PROGNOSIS?**
Ana Figueiredo; Joana Simões Pereira; Valeriano Leite
- EP03 68GA-DOTANOC AND 18F-FDG PET/CT IN METASTATIC MEDULLARY THYROID CARCINOMA: NOVEL CORRELATIONS WITH TUMORAL BIOMARKERS**
Pedro Souteiro; Patricia Gouveia; Gonçalo Ferreira; Sandra Belo; Claudia Costa; Davide Carvalho; Hugo Duarte; Ines Lucena Sampaio
- Screen 2: EP4 to EP6**
- EP04 METASTATIC MEDULLARY THYROID CARCINOMA: 20 YEARS OF FOLLOW-UP**
Marta Borges-Canha; Cláudia Nogueira; Ana Oliveira; Eduardo Vinha; Elisabete Rodrigues; Paula Soares; Catarina Fernandes; Davide Carvalho
- EP05 HYPERTHYROIDISM SECONDARY TO COMPLETE HYDATIFORM MOLE, A CASE REPORT**
Catarina Chaves; Mariana Martinho; Susana Garrido; Filipe Cunha; Margarida Vieira; Ana Rita Pinto; Margarida Almeida
- EP06 GRAVES' DISEASE: EXPERIENCE OF A CENTRE**
Sara Esteves Ferreira; Isabel Inácio; Patrícia Rosinha; Márcia Alves; Rosa Dantas; Teresa Azevedo; Joana Guimarães
- Screen 3: EP7 to EP10**
- EP07 BARIATRIC SURGERY CARDIOMETABOLIC OUTCOMES: IS PATIENT AGE A FACTOR TO CONSIDER?**
Fernando Mendonça; Maria Manuel Silva; Maria João Ferreira; Daniela Salazar; Jorge Pedro; João Sérgio Neves; Vanessa Guerreiro; Sara Viana; Ana Varela; Sandra Belo; Paula Freitas; Davide Carvalho
- EP08 PATIENT'S EDUCATION LEVEL AS A PREPONDERANT FACTOR IN THE SUCCESS OF SURGICAL TREATMENT OF OBESITY**
Daniela Salazar; João Sérgio Neves; Maria João Ferreira; Jorge Pedro; Vanessa Guerreiro; Sara Viana; Mendonça Fernando; Maria Manuel Silva; Sandra Belo; Ana Varela; Paula Freitas; Davide Carvalho
- EP09 MAGNESIUM SUPPLEMENTATION IS ASSOCIATED WITH A LOWER RISK OF CARDIO-METABOLIC RISK FACTORS IN PATIENTS SUBMITTED TO BARIATRIC SURGERY**
Maria Manuel Silva; Maria João Fonseca; Fernando Mendonça; Maria João Ferreira; Daniela Salazar; Jorge Pedro; Vanessa Guerreiro; João Sérgio Neves; Sara Viana; Eva Lau; Sandra Belo; Ana Varela; Paula Freitas; Davide Carvalho
- EP10 ASSOCIATION BETWEEN THE USE OF INSTAGRAM AND DISORDERED EATING IN COLLEGE STUDENTS**
Francisco Antunes; Miguel Pereira; Ana Rita Vaz; Eva Conceição; Celestino Neves; Davide Carvalho
- Coffee break*
- 11h00 – 13h00 **CALCIUM PHOSPHORUS METABOLISM**
Chairmen: Paula Bogalho (Lisboa), Ana Paula Barbosa (Lisboa)
- 11h00 – 11h30 **Secondary Hyperparathyroidism: Clinical Consequences and New Therapies** – João M. Frazão (Porto)
- 11h30 – 12h00 **Hypoparathyroidism: From Diagnosis to Clinical Management** – Davide Carvalho (Porto)
Sponsored by Takeda
- 12h00 – 12h30 **Hypophosphatemic Rickets: From Diagnosis to Clinical Management** – Agnès Linglart (Paris)
Sponsored by Kyowa Kirin Farmacêutica
- 12h30 – 13h00 **Discussion Panel** – Paula Freitas (Porto), Conceição Pereira (Lisboa)
- 13h00 – 14h30 **Lunch**

- 14h30 – 16h00 **WHAT IS NEW IN TYPE 1 DIABETES MANAGEMENT?**
Chairmen: José Luis Medina (Porto), João Raposo (Lisboa)
Moderators: Silvestre Abreu (Funchal), João Jácome de Castro (Lisboa)
- 14h30 – 15h00 **Latest Mealtime Insulins: Improving Postprandial Glucose Control** – Francisco Carrilho (Coimbra)
Sponsored by Novo-Nordisk
- 15h00 – 15h30 **SGLT2i: A Paradigm Shift in Type 1 Management** – Chantal Mathieu (Leuven)
Sponsored by Astrazeneca
- 15h30 – 16h00 **Discussion Panel** – Olinda Marques (Braga), Ana Maia Silva (Viana do Castelo)
- 16h00 – 16h30 **Poster Discussion** – Duarte Pignatelli (Porto), Ana Varela (Porto), Ana Isabel Oliveira (Porto), Sandra Belo (Porto)

Screen 1: EP11 to EP13

- EP11 ADRENOCORTICAL CARCINOMAS: TREATMENT AND SURVIVAL ANALYSIS OF A REFERENCE CENTRE**
Pedro Souteiro; Claudia Costa; Ana Paula Santos; Joana Oliveira; Isabel Torres
- EP12 SILENT AND METASTATIC PHEOCHROMOCITOMA IN A SDHB-MUTATED PATIENT: CHALLENGES IN FOLLOW-UP**
Inês Damásio; Rita Santos; Valeriano Leite
- EP13 PITUITARY INCIDENTALOMAS IN PAEDIATRIC AGE: EXPERIENCE OF A TERTIARY CENTRE**
Pedro Souteiro; Rúben Maia; Rita Santos-Silva; Rita Figueiredo; Carla Costa; Sandra Belo; Cíntia Castro-Correia; Davide Carvalho; Manuel Fontoura

Screen 2: EP14 to EP16

- EP14 EUGLYCEMIC DIABETIC KETOACIDOSIS IN A PATIENT WITH VERY HIGH CARDIOVASCULAR RISK**
Diana Silva; Luísa Ruas; Nelson Cunha; Diana Catarino; Lúcia Fadiga; Joana Guiomar; Luís Cardoso; Isabel Paiva; Margarida Bastos
- EP15 MALIGNANT INSULINOMAS: CLINICOPATHOLOGICAL CHARACTERISTICS**
Vanessa Guerreiro; João Neves; Ana Isabel Oliveira; Eva Lau; Luís Graça; José Manuel Lopes; Luís Teles; Paula Freitas; Davide Carvalho
- EP16 DIABETIC PATIENTS ADMITTED FOR HYPOGLYCEMIA IN HOSPITALS IN THE NORTH OF PORTUGAL: HIPOS-WARD STUDY RESULTS**
Silvia Alão; Lélita Santos; Jorge Soares; Francisco Araújo; João Pelicano Romano; João Conceição; Paula M De Jesus

Screen 3: EP17 to EP19

- EP17 OSTEOPOROTIC BONE FRACTURE HIDING A RARE SEX CHROMOSOME DISORDER: CASE REPORT**
Indira Fortes; Mário Rui Mascarenhas; Francisco Sampaio; Jacinto Monteiro; Ana Paula Barbosa
- EP18 A MENOPAUSAL WOMEN WITH DWARFISM AND OSTEOPOROSIS: CONSEQUENCES OF A CONGENITAL HYPERGONADOTROPHIC HYPOGONADISM LATE DIAGNOSIS**
Catarina Chaves; Mariana Martinho; Susana Garrido; Filipe Cunha; Margarida Vieira; Margarida Almeida
- EP19 HYPOPHOSPHATEMIA AND PITUITARY TUMOR: A CASE REPORT**
M.J Ferreira; J.L Castedo; E Vinha; J Pereira; D Carvalho

Coffee break

16h30 – 17h30 **PITUITARY DISORDERS**

Chairmen: João Sequeira Duarte (Lisboa), Isabel Paiva (Coimbra)

Moderators: Maria João Oliveira (V.N. Gaia), Leonor Gomes (Coimbra)

16h30 – 17h00 **Acromegaly: From Genetics to Management** – Thierry Brue (Marseille)

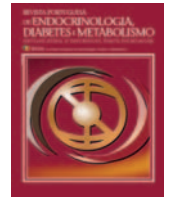
Sponsored by Novartis

17h00 – 17h30 **Discussion Panel** – Claudia Amaral (Porto), Mariana Martinho (Penafiel), Patrícia Polónia (Porto)

17h30 **Closure and Award Ceremony** – Davide Carvalho (Porto)



IX ADVANCED COURSE OF ENDOCRINOLOGY



Conference Abstracts

L01. FROM THE SCIENTIFIC EVIDENCE TO THE CLINICAL PRACTICE: CSII EFFICACY AND SAFETY

Ignacio Conget¹

¹*Hospital Clínic de Barcelona · Diabetes Unit. Endocrinology and Nutrition Department, Barcelona*

Type 1 diabetes (T1D) requires life-long insulin replacement therapy with continuous health care support to achieve optimal blood glucose control and reduce the risk of long-term diabetes-related complications. Despite remarkable advances in diabetes treatment, highly motivated and everyday life dedicated patients continue to struggle in achieving glucose targets avoiding a high frequency of severe and non-severe hypoglycemia. Having been used for nearly 40 years, there is no doubt that continuous subcutaneous insulin infusion (CSII) therapy is an efficient, safe and flexible treatment for improving both glucose control and quality of life of patients with T1D. In order to obtain success, this modality of treatment should be provided under a specific and structured self-management education and care program addressed to patients starting and using CSII by an expert group of professionals in the field. Information regarding the use of CSII and related devices can be precisely obtained after downloading it from specific software. This gave to us the opportunity to analyze which features and parameters of insulin pump use are routinely more used by T1D patients and which are associated with better glucose control. Amongst other parameters (usage and adherence) the number of SMBG, temporary basal rates and the use of bolus wizard have been found to be independently associated with a better metabolic control. This relationship has been found in several studies and could be considered a crucial adherence factor in order to predict CSII success in terms of effectiveness.

L02. FROM THE SCIENTIFIC EVIDENCE TO THE CLINICAL PRACTICE: CSII EFFICACY AND SAFETY THE PORTUGUESE PERSPECTIVE

César Esteves¹

¹*Department of Endocrinology, Diabetes and Metabolism, Centro Hospitalar e Universitário de S. João*

Continuous subcutaneous insulin infusion (CSII) therapy, once relevant only in a small subset of type 1 diabetic patients, is currently viewed as preferential treatment in motivated patients with active lifestyles, with increased need of a flexible insulin

regimen. In some countries, the prevalence of insulin pump use exceeds 40% in type 1 diabetic patients. In Portugal, the SNS (Portuguese National Health Service) initiated the distribution of insulin pumps, free of charge, to type 1 diabetics according to recognized indications, in 2008. Those cases included the failure of multiple daily injections to achieve good glucose control, the occurrence of severe hypoglycemia or hypoglycemia unawareness, the need of a flexible lifestyle, the use of low total daily insulin dose or current/planned pregnancy. Since then, more than 1000 patients (adult and pediatric) were initiated in insulin pump therapy, distributed by several treatment centers. As of 2019, the SNS will deliver insulin pumps to all diabetics up to the age of 18 years and in limited numbers to adult patients. As many young patients using insulin pumps transition to adult care, there will be an increasing need for appropriately timed appointments as well as well-trained staff and well-equipped ambulatory departments for the care of these patients. In insulin pump treatment centers across Portugal the benefits of CSII therapy in treatment targets, HbA1c as well as hypoglycemia risk, are clear.

L03. MULTIPLE ENDOCRINE NEOPLASIA TYPE 2B

Maria João Bugalho¹

¹*Centro Hospitalar e Universitário Lisboa Norte (Serviço de Endocrinologia) e Faculdade de Medicina de Lisboa*

Multiple endocrine neoplasia type 2B (MEN 2B) is characterized by the association of medullary thyroid carcinoma (MTC) in 100% cases, pheochromocytoma (FEO) and multiple extra-endocrine features.

MEN 2B is due to autosomal dominant activating germline mutations of the *RET* proto oncogene. The most frequent mutation is a methionine to threonine substitution at codon 918 in the tyrosine-kinase domain of *RET*. Less frequently (< 5%), mutations involving codon 883 (A883F) or rare double mutations involving codon 804 in combination with other *RET* mutations have been reported. The majority of cases correspond to *de novo* mutations.

Recently, a rare M918V *RET* mutation was reported in 50 Brazilian patients. None of the patients presented with extra-endocrine features characteristics of MEN 2B; the age at diagnosis of MTC varied from 24 to 59 years and none of the patients presented with FEO. It is, therefore, questionable whether this variant is responsible for a true form of MEN 2B. Extra-endocrine features include Marfanoid habitus and other skeletal features; mucosal neuromas; alacrimia, eversion of upper eyelids, conjunctival neuromas and prominent corneal nerves; diffuse intestinal ganglioneuromatosis leading to impaired colonic motility and ultimately to megacolon being constipation, usually, the first non-

specific complaint in this setting. Coarse facies, tooth malposition and abnormal feet may also be present. The penetrance of the extra-endocrine features may be incomplete for a particular patient but all MEN 2B patients will present one or more of them.

MTC is the major endocrine component and the one determining prognosis, it is more aggressive and appear much earlier than other forms of hereditary MTC, generally within the first years of life, however the mean age at diagnosis is around 14 years.

The penetrance of FEO is 50% and in 50% of cases it is bilateral by 28 years of age, in ~3% of patients it is the cause of death. The youngest age reported for FEO was 12 years, thus it is suggested to start routine pheochromocytoma screening at age 11 years.

FEO is not present in MEN 2B patients without a mutation in RET codon 883 or 918. The phenotypic variability and aggressiveness of MTC among MEN 2B patients suggest the involvement of genetic modifiers such as somatic mutations.

The aggressiveness of the M918T mutation is higher than the A883F mutation justifying different approaches. 2015 American Thyroid Association guidelines on MTC management have reclassified the A883F mutation as a high risk variant recommending early thyroidectomy by 5 years of age while patients with the M918T mutation considered as a highest risk variant should have a thyroidectomy in the first year of life. However, in clinical practice this is difficult to achieve, since the majority of patients harbor *de novo* mutations leading to a delayed diagnosis until after MTC has become clinically evident and most of the times regionally advanced or metastatic and ultimately to early death.

Improved education of all health providers, particularly paediatricians, about the extra-endocrine signs will contribute for greater awareness of the phenotype and for an earlier diagnosis and better outcome.

Appropriate management of pheochromocytoma via adrenal sparing surgery is likely to reduce adrenal insufficiency and the need to take life-long replacement treatment thus improving quality of life.

L05. MEDULLARY THYROID CANCER MEDICAL MANAGEMENT

Viola David¹, Rossella Elisei¹

¹ *Department of Clinical and Experimental Medicine, University of Pisa*

Medullary thyroid cancer (MTC) is a rare thyroid tumor that originates from parafollicular C cells. The incidence of MTC is unknown but its prevalence is about 3% of all thyroid malignancies with a prevalence in subjects with thyroid nodules of about 0.4% - 1.4%. MTC can be sporadic or hereditary in about 75% and 25% of cases, respectively. The hereditary forms present with MTC (100%) but can involve multiple endocrine and non-endocrine organs and are classified in: a) Multiple endocrine neoplasia type 2A (MEN 2A), in which pheochromocytoma (50%) and hyperparathyroidism (25%) are present; b) Multiple endocrine neoplasia type 2B (MEN 2B), in which MTC is associated to pheochromocytoma (50%); c) Familial medullary thyroid carcinoma (FMTC), which is the most frequent and characterized by the presence of isolated MTC. A distinctive feature of some MEN 2A is lichen cutaneous amyloidosis (CLA) (15%) and in some cases also Hirschsprung disease can be present. Cutaneous/mucosal neuromas (100%),

bumpy lips (100%), megacolon (100%), and marfanoid habitus (100%) are peculiar of MEN 2B.

However, the most frequent forms are sporadic cases in which early diagnosis should be made. Parafollicular C cells and MTC produce and secrete calcitonin (Ct) that is a sensitive and specific marker of MTC. The patients with thyroid nodules that are not subjected to Ct screening and develop MTC have a very high prevalence of metastases at diagnosis and a very poor prognosis.

Up to know early diagnosis and radical surgical treatment is the only possibility to cure MTC patients. In fact, those diagnosed by serum Ct screening were demonstrated to have significantly better prognosis than those diagnosed by cytology or at histology. In case of serum basal detectable Ct a calcium stimulation test could help in the differential diagnosis with other causes of detectable serum Ct.

More recently, RET genetic screening allowed the identification of apparently sporadic cases that is present in a non-negligible percentage of cases (about 8%). The presence of the mutation in apparently sporadic cases or in a family member of hereditary forms is of paramount importance to guide future diagnostic and therapeutic strategies in the subject and his/her first-degree family members.

In case of persistent disease after thyroidectomy and central compartment lymph node dissection asymptomatic patients without immediately threatening disease not expected to have significant morbidity and mortality within the following 6 months should be followed with serum Ct measurement until disease progression. In fact, Ct is a specific serum marker of MTC and its doubling time is one of the most important prognostic factors able to distinguish patients that should be subjected to computerized tomography scan to establish possible disease progression.

Until recently no therapeutic options were available for these patients. New targeted therapies, namely tyrosine kinase inhibitors (TKIs), are nowadays available and able to block or reduce tumoral growth, increasing progression free survival and at least in some cases also overall survival and relieve symptoms. The approved multikinase TKIs available are vandetanib and cabozantinib and hopefully in the near future at least two new effective, potent and selective and more tolerated drugs (Loxo-292 and Blu-667) will be available.

L06. SECONDARY HYPERPARATHYROIDISM: CLINICAL CONSEQUENCES AND NEW THERAPIES

João M. Frazão¹

¹ *Centro Hospitalar e Universitário de S. João – Departamento de Nefrologia*

In dialysis patients secondary hyperparathyroidism (SHPT) is associated with increased bone turnover, risk of fractures, vascular calcifications, cardiovascular and all-cause mortality.

The classical treatment for SHPT includes active vitamin D compounds and phosphate binders. However, achieving the optimal laboratory targets is often difficult because vitamin D sterols suppress PTH secretion, but also promote calcium and phosphate intestinal absorption.

Calcimimetics increase the sensitivity of calcium sensing receptor leading to the decrease of the set-point for systemic calcium homeostasis. This enables a decrease in plasma PTH levels, and consequently of calcium levels.

Cinacalcet was the first calcimimetic approved for clinical

use. After more than 10 years from its approval, cinacalcet demonstrated that effectively reduces PTH levels and improves biochemical control of mineral and bone disorders in chronic kidney patients. Three randomized controlled trials analyzed cinacalcet treatment effects on hard clinical outcomes such as vascular calcification, bone histology and cardiovascular mortality and morbidity. However, a final conclusion on the effect of cinacalcet on hard outcomes remains open.

Etelcalcetide is a new second generation intra-venously administered calcimimetic agent with a pharmacokinetic profile that allows thrice-weekly dosing at the time of hemodialysis. It was recently approved and is regarded as a second opportunity to improve outcomes optimizing the treatment for SHPT.

Cinacalcet treatment effect on biochemical and relevant clinical outcomes, the improved efficacy and adherence of etelcalcetide and possible effect in improving outcomes will be reviewed.

Parathyroidectomy still indicated for dialysis patients with severe SHPT who fail to respond to medical or pharmacological therapy. Parathyroidectomy continues to be the last therapeutic option to control SHPT. In recent years the number and efficacy of compounds available to control SHPT increased and the need for parathyroidectomy should progressively decrease.

L07. HYPOPARATHYROIDISM: FROM DIAGNOSIS TO CLINICAL MANAGEMENT

Davide Carvalho¹

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Hypoparathyroidism results from the destruction of the parathyroid glands (PG) by surgery or as a result of autoimmune disease, developmental abnormalities of the PG, or alteration of the regulation of PTH production or secretion. The most common cause is surgery. Post-surgery hypoparathyroidism can occur after thyroid, parathyroid, or radical surgery for head and/or neck cancer. Post-surgical hypoparathyroidism may be transient, with recovery after a matter of days, weeks, or months, and may be permanent or intermittent. Transient hypoparathyroidism occurs in up to 20% of cases after surgery for thyroid cancer, being permanent in 0.8% to 3% of patients undergoing total thyroidectomy, particularly in the case of a large goiter and when the anatomical marks are shifted or are unclear. Hypoparathyroidism causes bone hypermineralisation, hypocalcemia, hypercalciuria, hypomagnesaemia, and hyperphosphatemia. A therapeutic challenge is how to maintain normal levels of calcium with calcium and vitamin D supplementation. For in cases of low or excessive calcium and vitamin D supplementation, patients with hypoparathyroidism are at risk of serious complications over time. For example, hypocalcemia can cause neuromuscular symptoms, while hyperphosphatemia contributes to the ectopic mineralisation of soft tissues (e.g., vascular, brain, kidney, and other organs). To minimise such risks, the objectives of the treatment are defined, examples being: patients are considered to be well controlled if albumin-adjusted serum calcium levels or calcium ionised are at the lower limit, or are slightly below the reference values in the case of patients without signs or symptoms of hypocalcemia; a 24-hour urine calcium level of <300 mg/24 hours for men and 250 mg/24 hours

for women; phosphorus and magnesium at the normal level; calcium phosphorus product of <55 mg/dL; vitamin D at adequate levels, avoiding hypercalcemia, and; renal or soft tissue calcifications which are considered normal. In a Danish cohort study, renal comorbidities for hypoparathyroidism were higher than those of the general population and the risk of renal disease was at least three times higher in the case of both postoperative and non-postoperative hypoparathyroidism when compared with the general population. With regards to renal failure, the risk is approximately 3 times higher in the case of postoperative disease and 6 times greater during the non-postoperative period. Patients with post-surgical hypoparathyroidism have a 4-fold increased risk of being hospitalised for renal lithiasis. The risk of the afore-mentioned complications was investigated for a case-control study (case - patients with hypoparathyroidism who developed complications; control - patients who did not develop complications). A level of phospho-calcium product greater than the median was associated with an increased risk of kidney disease. One or more episodes of hypercalcemia were experienced by 41% of patients who suffered an increased risk of kidney disease. Two retrospective cohort studies of adults and children studied the effects of hypoparathyroidism on renal function, whereby renal imaging showed that 31% of a sample of 54 adults had either lithiasis or nephrocalcinosis. Nephrocalcinosis was observed in 38% of paediatric patients with hypoparathyroidism, the main predictors being the degree of hypercalcemia and relative hyperphosphatemia. The glomerular filtration rate was calculated for patients over 18 years of age, with 41% having a rate equal to or lower than 60 mL/min/1.73 m² and a compatible renal insufficiency of less than 3, or higher. In the case of children, this value was 45%.

The objective of a survey of patients with hypoparathyroidism was to evaluate the 38 symptoms associated with hypoparathyroidism for a period of 12 months for patients treated with standard calcium and active vitamin D therapy. The symptoms were organised into 3 domains: physical (25 symptoms), cognitive (7), and emotional (6). On average, 370 patients reported 16 ± 8 symptoms, with 72% experiencing more than 10. By order of magnitude, more than 50% of the symptoms reported by patients were fatigue (82%), cramps and muscle pain 78%, paraesthesia (76%), tetany (70%), and bone or joint pain, pain, weight, or weakness in the extremities (53%). The cognitive symptoms reported by more than 50% of the patients included mental lethargy (72%), inability to concentrate (65%), forgetfulness and memory loss (61.5%), and sleep disturbances (57%). The emotional symptoms which were reported by more than 50% of the patients were anxiety and depression (53%).

Until recently, hypoparathyroidism was the only endocrine deficiency for which there was no substitution therapy. Recently, studies using human recombinant PTH have been carried out to evaluate its efficacy and safety for the treatment of hypoparathyroidism. These tests were granted approval by the European Medicines Agency (EMA) in April 2017. In the REPLACE study, which was a randomised, placebo-controlled study, the results show that there is a significant variation in the proportion of patients who received an active vitamin D dose, with doses less than, or equal to 500 mg/day of oral calcium at week 24. The effects of PTHrh were the following: 54.8% of patients in the PTHrh group reached the primary endpoint, compared to 2.5% in the placebo group. This study also demonstrated a significant reduction of the oral dose of calcium administered at week 24, when compared with the initial evaluation. Serum and urinary phosphate levels were assessed over the 24-week period and phosphate levels de-

creased by 0.2 (0.02) mmol/L in the PTHrh treated group, contrary to the placebo group (which had a baseline variation of 0.0 (0.03) mmol/L, $p < 0.001$). This decrease in phosphate levels was maintained from weeks 1 to 24, with phosphate levels being significantly lower when compared to the placebo group. When compared with the baseline, the phospho-calcium product was significantly improved with PTHrh at 36 months: with a base of 42.1 (6.3) mg^2/dL^2 and 35.9 (6.2) mg^2/dL^2 at 36 months. In a 3 year analysis, both the safety and efficacy of PTHrh (1-84) were evaluated. Urinary calcium decreased significantly to normal values after 3 years (260 mg / 24 hours) when compared with the baseline values (356 mg / 24 hours), $P = 0.05$. The filtration rate remained stable over the 3 years of treatment with PTHrh (1-84) and the calcium-phosphorus product was significantly reduced ($p < 0.0001$) after 3 years of treatment with PTHrh (1-84).

In conclusion, in addition to specific management measures, the guidelines describe an over-arching focus on treatment personalisation and on the overall well-being and quality of life of the patient. While many patients with hypoparathyroidism can be managed by treatment with calcium and vitamin D, a small but significant group remains who continue to experience clinical complications. rhPTH(1-84) is indicated as a supplementary treatment for those adult patients with chronic hypoparathyroidism who cannot be adequately controlled by standard therapy alone.

L08. HYPOPHOSPHATEMIC RICKETS: FROM DIAGNOSIS TO CLINICAL MANAGEMENT

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X-linked hypophosphatemia (XLH), due to *PHEX* mutations, is the most frequent form of hypophosphatemic rickets/osteomalacia. The molecular defect in *PHEX* leads to an increase production of circulating FGF23. FGF23 is critical in controlling serum phosphate level through the reabsorption of phosphate in the renal proximal tubule. In situations where FGF23 is produced in excess, phosphate leaks through the kidney in the urine, hence serum phosphate is below the normal range. In addition, FGF23 has a strong inhibitory effect on 1,25(OH)₂D synthesis, hence reduces calcium absorption through the gut. Therefore patients with *PHEX* mutation usually present with low serum phosphate, mildly decreased serum calcium, phosphate wasting and reduced 1,25(OH)₂D levels. The abnormal phosphate level, the defect in 1,25(OH)₂D synthesis, and the accumulation of ASARM peptides lead to an impaired mineralization of the skeleton and ultimately, rickets, osteomalacia and insufficient growth. Children with XLH present with rickets, waddling gait, bone pain, bone deformities, growth retardation, tooth abscesses and/or craniosynostosis. Adults with XLH present with persistent bone pain, fractures, pseudofractures, osteoarthritis, enthesopathies and/or periodontitis. As explained above, the biochemical picture includes phosphate wasting, elevated FGF23, low urinary calcium and elevated alkaline phosphatase (bone ALP in adults).

Therapies include the association of vitamin D analogs and phosphate supplements that counteract the renal phosphate wasting and 1,25(OH)₂ vitamin D deficiency. This treatment improves,

yet inconstantly, bone mineralization, growth velocity, and dental mineralization. However, the burden of disease remains significant, even in treated patients.

The alternative to this conventional therapy is the antibody against FGF23, burosumab, which aims at restoring the reabsorption of phosphate through the proximal renal tubule and the endogenous synthesis of calcitriol; in Europe, burosumab is authorized in children above the age of one year. The talk will provide an overview of the diagnosis of XLH from birth to menopause, and of the management of treatment.

L09. LATEST MEALTIME INSULINS: IMPROVING POSTPRANDIAL GLUCOSE CONTROL

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Since the discovery of insulin that the main objective is to develop one that presents a profile as similar as possible to the one verified in healthy subjects. Regarding prandial insulins, and since 1996 with the discovery of insulin analogues, it has been possible to improve post-prandial glycemic control when compared to human insulin.

In Portugal we expect to be available for the treatment of diabetes a fast-acting insulin analogue that will enable the possibility of mimic endogenous insulin secretion profile, referred above, in people with diabetes.

FIASP, fast-acting insulin aspart, active molecule is the well know aspartic insulin, in which the addition of vitamin B3 (niacinamide) and an amino acid (L-arginine), enable a faster absorption of the insulin monomers and stabilizes the formulation.

This new formulation of IAsp demonstrated, when comparing to IAsp, increases in 74%, in the first 30 minutes after sub-cutaneous administration, onset of appearance in the bloodstream, translating into clinical relevant benefits as been shown in the ONSET Program, the FIASP clinical development program.

In the studies published until know have clearly demonstrated an improvement in terms of glycemic control, mainly concerning PPG control, it's safe profile regarding hypoglycaemia reduction and pump compatibility, and also, as verified in several studies the possibility of a more flexible administration profile (pre or post-meal initiation) without compromising efficacy and safety.

L11. ACROMEGALY, FROM GENETICS TO MANAGEMENT

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Acromegaly patients exhibit characteristic acral and soft tissue overgrowth, joint pains, jaw overbite, respiratory obstruction and

hypertension, as well as headache, visual disturbances and cranial nerve palsy from tumor mass effects. Metabolic dysfunction increases the risk of diabetes mellitus and cardiovascular-related morbidity and mortality. Treatment of patients with acromegaly is aimed at normalizing GH and/or IGF1 levels to alleviate signs and symptoms of the disease and reduce excess mortality. Long-term biochemical control is achieved in fewer than 60% of patients after surgical resection of the tumor, which makes it necessary to use additional medical therapy to achieve control of IGF1 levels. Radiation therapy - nowadays more and more using stereotactic radiosurgery instead of conventional fractionated radiotherapy - remains an option in patients with persistently active disease, however with a favorable risk/benefit ratio only in selected patients. Management of acromegaly and its comorbidities is complex and requires a comprehensive approach coordinated by a multidisciplinary team of expert physicians.

In the vast majority of cases, acromegaly is caused by a benign pituitary GH-secreting tumor (somatotropinoma), a monoclonal tumor that can occur sporadically or more rarely in a familial setting. In the last few years, novel familial syndromes have been described and several studies explored both somatic and germline mutations found in these tumors. Activating *GNAS* mutations (gsp mutations) have been shown several decades ago to be responsible for 30% - 40% of sporadic somatotropinomas. Acromegaly can be part of a syndromic disease occurring concomitantly with other endocrine tumors, such as in MEN1, MEN4, Carney complex, McCune-Albright and SDHx-related pituitary adenomas or

presents as part of familial isolated pituitary adenoma (FIPA) in aryl hydrocarbon receptor interacting protein (AIP) or *GPR101* (G-protein coupled receptor 101) mutation positive and negative cases. Moreover, almost 50% of childhood-onset cases leading to gigantism now have an identifiable genetic background.

Definition of biochemical control currently includes GH nadir $< 0.4 \mu\text{g/L}$ after OGTT using ultrasensitive assays and normal age/sex-adjusted IGF1 levels at least 12 weeks after surgery. Most recent guidelines recommend surgical resection of the pituitary adenoma by an experienced neurosurgeon whenever possible and follow-up in a multidisciplinary team dedicated to pituitary diseases. Medical therapy is necessary in case of persistent disease: a first-generation long-acting somatostatin receptor ligand (SRL) - i.e. octreotide or lanreotide - is recommended as first-line therapy. Cabergoline may be considered if IGF1 is below 2.5 times the upper limit of normal. In case of residual tumor and inadequate control on first-generation SRLs, a switch to long-acting release pasireotide can be considered, while patients with significant pre-existing impaired glucose metabolism can be switched to the GH-antagonist pegvisomant. In case of poor response, with tumor concern and impaired glucose metabolism pegvisomant may be added to first-generation SRL. Temozolomide is proposed in unusually aggressive or proven malignant tumors in cooperation with a neuro-oncologist).

In conclusion, acromegaly requires an individually-tailored management in an expert center.



IX ADVANCED COURSE OF ENDOCRINOLOGIA



E-Posters

PRÉMIO PROFESSOR MANUEL PINHEIRO HARGREAVES / ENDOCRINOLOGIA

EP01. FOLLICULAR THYROID CARCINOMA: A DIFFERENT PRESENTATION

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Follicular thyroid carcinoma (FTC) is much less common than papillary carcinoma and has a different clinical presentation due to its predisposition to metastasize via vascular invasion. In a recent retrospective study, 60% of the patients with FTC were diagnosed with metastatic disease at presentation, with the bones being the most common site (75%). Here, we describe a 66-year-old woman with a 10 year history of left hip pain with a recent inability to walk. A bone scan and PET-FDG revealed a 14 cm lesion in the left iliac bone and occipital bone. The iliac computed tomography-guided biopsy was compatible with bone metastasis from FTC. The lesions were treated with 20 Gy (iliac) and 12 Gy (occipital) of palliative local radiation (RT). After RT, the patient referred significant improvement of the leg pain, presently walking with a crutch. The imaging exams performed after RT document stability of both bone lesions. Few papers have been published on the management and outcomes of patients with FTC with distant metastases at presentation. RT can be considered as local treatment modality for patients with symptomatic bone metastases. The primary goal is to provide pain relief, preserving patient's quality of life.

Keywords: Carcinoma, Papillary, Follicular

EP02. LIVER METASTASIS FROM DIFFERENTIATED THYROID CANCER: IS IT ALWAYS RELATED TO A POOR PROGNOSIS?

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Introduction: Liver metastases (LM1) from differentiated thyroid cancer (DTC) are rare (0.5% of DTC) and generally occur in the later stages of disseminated disease. The median reported survival after DTC-LM1 diagnosis is 1-60 months.

Case Report: We present a case of an 80-year-old female patient submitted to total thyroidectomy for a follicular variant of papillary thyroid cancer (FVPTC) at the age of 64. She was referred to our department at age 73, after left humerus fracture due to FVPTC metastasis. Radiotherapy (30Gy) was then delivered to

this site. A re-staging computed tomography scan showed a hepatic mass (83x67 mm) and a biopsy confirmed FVPTC metastasis. She was submitted to four radioiodine (RAI) therapies (total activity=600 mCi), all demonstrating high focal hepatic avidity. After RAI, a decrease in serum thyroglobulin (Tg) levels and in size of LM1 was observed. FDG-PET scans were negative. In the past 4 years, LM1 and Tg levels have remained stable.

Discussion: In our case survival was higher than previously reported, probably related to the maintenance of differentiation, as proved by high RAI uptake/response, and negative FDG-PET scans.

Keywords: Liver Neoplasms/secondary; Thyroid Neoplasms

EP05. HYPERTHYROIDISM SECONDARY TO COMPLETE HYDATIFORM MOLE, A CASE REPORT

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Introduction: Hydatidiform mole (MH) is the most common form of gestational trophoblastic disease. Hyperthyroidism occurs as a complication of complete HM in 7% of cases, due to the structural similarity between the alpha subunit of human chorionic gonadotropin and thyroid stimulating hormone.

Case Report: A 55-year-old woman with regular menstrual cycles and no thyroid pathology or chronic medication went to the emergency department due to a three-week history of metrorrhagia. The study revealed: Hg 10.8 g/dL (12-16), hCG 268400 mU/mL (5-50), TSH <0.01 mIU/mL (0.38-5.33), FT4 3.81 ng/dL (0.54-1.24) and FT3 8.74 ng/dL (2.5-3.9); Transvaginal echography: enlarged uterus with multiple cystic images suggestive of HM. Total hysterectomy with urgent bilateral anexectomy was proposed, conditioned by anesthetic risk due to hyperthyroidism. After assessment by Endocrinology, she started therapy with corticosteroid, methimazole, iodide and beta-adrenergic blocker, which led to the normalization of free fractions in 4 days, allowing surgical treatment, which was performed without complications.

Conclusion: Hyperthyroidism secondary to HM resolves with HM treatment, however it represents some risks in the preoperative period, conditioning the surgical treatment, which should be performed as early as possible regarding the risk of progression to choriocarcinoma.

Keywords: Hydatidiform Mole; Hyperthyroidism

EP06. GRAVES' DISEASE: EXPERIENCE OF A CENTRE

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Introduction: Appropriate treatment of Graves' disease (GD) is crucial, since it is associated with worst quality of life and morbimortality.

Objective: Characterize patients with GD followed in CHBV and their treatment.

Methods: Retrospective study of the adult population with GD followed in Endocrinology CHBV between October/2016 and September/2018; excluding pregnant.

Results: Included 77 patients: 50 (68%) referenced for first episode, with symptoms setting predominantly in December (24%; n=9); remaining for recurrence, with symptoms setting mainly in March (50%; n=5). All were treated with anti-thyroid drugs (ATD), 44% had remission; of these, 28% (n=9) recurred. Maximum daily ATD dose was significantly lower in patients with remission (15.00 vs 19.64 mg, $p<0.05$) and with durable remission, beyond 12 months (11.25 vs 17.14 mg, $p<0.05$); with no significant difference regarding duration of treatment. Eleven patients (14%) went through radioactive iodine therapy, 73% (n=8) responded. Active smoking occurred in 10 patients (25%); these had higher rates of ophthalmopathy (80% vs 36%, $p=0.028$), surgical treatment (70% vs 27%, $p=0.025$).

Discussion: This study suggests seasonality in incidence of GD and reinforces the reproducibility of what is reported in literature in our population. It intends to deepen the knowledge of our population and help with therapeutic orientation of such patients.

Keywords: Graves Disease

EP10. ASSOCIATION BETWEEN THE USE OF INSTAGRAM AND DISORDERED EATING IN COLLEGE STUDENTS

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Introduction: The social networks are a new form of communication and the way it influences eating disorders lacks understanding.

Objective: To explore the use of social networks and the occurrence of disordered eating behaviours.

Methods: For this correlational study we evaluated 182 college students, 85.1% female, that were using Instagram, with a mean age of 23.3±5.3 years. Data was gathered using online questionnaires, namely the Body Shape Questionnaire (QFC), Three-Factor Eating Questionnaire (TFEQ-21) and Eating Disorders(ED-15).

Results: We compared the genders between themselves according to the time spent on Instagram and we did not find any sig-

nificant differences between women who spent the most time on Instagram and women who spent the least time (QFC - 78.5 vs 81.7; $p=NS$, TFEQ-21 - 46.01 vs 44.02; $p=NS$ and ED-15 - 13.56 vs 13.15; $p=NS$). Men who spent most time scored consistently higher than those who spent less time, although no significantly differences were found (QFC - 60.4 vs 52.46; $p=NS$, TFEQ-21 - 47.3 vs 39.77; $p=NS$ and ED-15 - 9.5 vs 5.1; $p=NS$).

Conclusion: Longer time spent on Instagram is related to increased body shape concerns and disordered eating behaviours in men. Women scores did not differ based on the time spent on this social network.

Keywords: Feeding and Eating Disorders; Internet

EP12. SILENT AND METASTATIC PHEOCHROMOCYTOMA IN A SDHB-MUTATED PATIENT: CHALLENGES IN FOLLOW-UP

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Introduction: Pheochromocytomas are rare neuroendocrine tumours, for which surgical resection is the standard treatment. These tumours seldom display evidence of metastatic spread, but this risk persists in the long term and higher for patients with genetic syndromic diseases.

Case Report: This case describes a woman who underwent a left adrenalectomy at 26 years of age in the context of a 10 cm pheochromocytoma, without mitosis or vascular invasion. The genetic testing confirmed a deletion in one of the alleles of *SDHB* gene. Seven years after surgery, a follow-up magnetic resonance imaging showed signs of relapse in the surgical *loca*, with rapid growth during the following two years. At the age of 35, she was re-operated with removal of a 10 cm retropancreatic tumour with immunohistochemistry features of a pheochromocytoma relapse. There was vascular invasion, Ki67 10% and 8 mitosis per 10 high power field. After two years, there is no evidence of disease on imaging studies. Of notice, there was never clinical or biochemical evidence of catecholamines secretion.

Conclusion: This case emphasizes the importance of long term follow-up, particularly in high risk patients, and the challenges of silent tumours - which are frequent in *SDHB*-mutated patients - where imaging is the only useful follow-up method to monitor relapses.

Keywords: Pheochromocytoma

EP14. EUGLYCEMIC DIABETIC KETOACIDOSIS IN A PATIENT WITH VERY HIGH CARDIOVASCULAR RISK

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Introduction: SGLT2 inhibitors are a pharmacological class associated with euglycemic diabetic ketoacidosis.

Case Report: A 46-year-old woman with a history of type 2 diabetes mellitus, proliferative diabetic retinopathy and two episodes

of acute coronary syndrome, the last in July 2018. One month later, she went to the emergency department for nausea and vomiting with 1 day of evolution. She was medicated with insulin detemir 50U at breakfast and 36 U at dinner and metformin 1000 mg / dapagliflozin 5 mg bid, with interruption of the basal-bolus regimen about 1 month ago. It had capillary blood glucose of 223 mg/dL, ketonemia of 4.4 mmol/L, metabolic acidosis (pH 7.34, pCO₂ 30.4 mmHg, HCO₃⁻ 16.5 mEq/L, lactates 1.09 mmol/L), and initiated fluid therapy. By worsening of the health state repeated gasometry: pH 7.25; pCO₂ 23.1 mmHg; HCO₃⁻ 9.8 mEq/L; glycemia 164 mg/dL; lactates 1.03 mmol/L and ketonemia of 6.7 mmol/L. Initiated continuous intravenous infusion of insulin with clinical and biochemical improvement. She was discharged with intensive insulin therapy and discontinued dapagliflozin.

Conclusion: This case demonstrates that the abrupt reduction of insulin doses and the acute coronary syndrome may be precipitating factors of this complication. Their identification is difficult due to the absence of significant hyperglycemia.

Keywords: Blood Glucose; Diabetic Ketoacidosis; Sodium-Glucose Transporter 2 Inhibitors

EP16. DIABETIC PATIENTS ADMITTED FOR HYPOGLYCEMIA IN HOSPITALS IN THE NORTH OF PORTUGAL: HIPOS-WARD STUDY RESULTS

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Introduction: Hypoglycemia remains a limiting factor in achieving glycemic control and often related to poor clinical outcomes in people with diabetes.

Objective: Characterization of diabetic patients admitted for hypoglycemia in hospitals in the North of Portugal and compared to the rest of the country.

Materials and Methods: HIPOS-WARD is an observational, cross-sectional study designed to evaluate adult diabetic patients treated with anti-hyperglycemic agents hospitalized due to a hypoglycemia. This study included patients admitted in 16 national hospitals, 7 in the North of Portugal (considered at north of Coimbra, inclusive) for a hypoglycemic episode for a period of 21 months (Nov16-Aug18).

Results: From a total of 176 patients enrolled, 66 were from the North (38%), mean age of 70 years, most female (58%) and higher body mass index (BMI) (mean 26.9 vs 25.45 kg/m², $p=0.01$). The main probable causes of hypoglycemia were: higher insulin treatment (47.7% vs 26.4%, $p=0.005$), less carbohydrate deficit (43.8% vs 60.0%, $p=0.042$) and secondary acute illness (39.1% vs 40.9%, $p=0.873$). A higher percentage (44.6% vs 26.4%, $p=0.038$) had had a hypoglycemic event in the last 12 months and 65.5% of these in the previous 30 days.

Conclusion: The results obtained in North Portugal are consistent with a predominantly senior overweight population, where severe hypoglycemia still represents a relevant burden.

Keywords: Diabetes Mellitus, Type 2; Hospitalization; Hypoglycemia

EP17. OSTEOPOROTIC BONE FRACTURE HIDING A RARE SEX CHROMOSOME DISORDER: CASE REPORT

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Introduction: The XXYY syndrome is an extremely rare sex chromosomal disorder characterized by the presence of extra X and Y chromosomes, and clinically by tall stature, dysfunctional testes associated with infertility and hypogonadism, cognitive, affective and social functioning impairments, global developmental delay, and an increased risk of congenital malformations.

Case Report: A 46-year-old man was referred to the Fracture Osteoporosis Outpatient Clinic because of an osteoporotic left hip fracture.

He had a history of epilepsy, hypothyroidism, esophagitis, dyslipidemia, cognitive deficit, and a previous osteoporotic right hip fracture at 43 years-old.

Central obesity, reduced facial and body hair, poor muscle development, gynecomastia and testicular atrophy were observed.

The analytical evaluation showed normal thyroid function, P1NP 70.8 ng/mL, 25(OH)D 18.1 ng/mL, FSH 18.7 U/L, LH 14.8 U/L, total testosterone 46.6 ng/dL. A karyotype study revealed a 48, XXYY syndrome.

He was started on intravenous zoledronic acid, intramuscular testosterone and oral calcium and vitamin D supplementation.

Conclusion: The 48 XXYY syndrome, previously considered as a variant of Klinefelter syndrome, is nowadays described as a distinct clinical and genetic entity, as the medical problems and more complex psychological and neurodevelopmental involvement are usually present. The hypogonadism predisposes these patients to osteoporosis and fragility fractures.

Keywords: Osteoporotic Fractures

EP18. A MENOPAUSAL WOMEN WITH DWARFISM AND OSTEOPOROSIS: CONSEQUENCES OF A CONGENITAL HYPERGONADOTROPHIC HYPOGONADISM LATE DIAGNOSIS

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Introduction: Turner syndrome (TS) is characterized by the monosomy of the X chromosome. The mosaic 45,X/46,XX prevalence is 36%. TS's clinical features are highly variable, but the most common are short stature and ovarian failure.

Case Report: A 65-year-old woman, with valvular heart disease,

heart failure, atrial fibrillation and pacemaker carrier, was sent to the Endocrinology department due to hyperthyroidism [TSH:0.09 mUI/mL(0.38-5.33); T4L:1.47 ng/dL(0.54-1.24) and thyroid ultrasound: a micronodule]. Reported menarche at age 15, unknown age of menopause. She had a sister with short stature. On physical examination she had a proportionate dwarfism. Analytically: TSH 0.73 mUI/mL, T4L 1.17 ng/dL, T3L 3.98 ng/dL(2.5-3.9); FSH 88.5 mUI/mL, LH 25 mUI/mL, estradiol 24 pg/mL, GH 1.37 ng/mL(0.06-10), PTH 79.3 pg/mL(15-65), calcium 4.5 mE/L(4.3-5.1), phosphorus 3.5 mg/dL(2.7-4.5), D vitamin 15 nmol/L(>75). Bone densitometry: osteoporosis (score: lumbar spine: -4.8, femoral neck: -3.8). Peripheral blood lymphocytes karyotype showed mos:45,X[10]/46,XX[40]. Therapy with zoledronic acid, calcium and D vitamin was initiated and maintained follow up.

Discussion: This case report of a late diagnosis of TS. Most cases are detected during childhood or adolescence. When detected after menopause, the treatment with growth hormone or hormone replacement therapy, does not have benefit. However women with TS have a reduced life expectancy, so screening for known associations carries the advantage of preventive measures.

Keywords: Dwarfism; Osteoporosis; Turner Syndrome

PRÊMIO DR. LUÍS MARQUES / INTERNO DE ENDOCRINOLOGIA DO CHUSJ

EP03. ⁶⁸GA-DOTANOC AND ¹⁸F-FDG PET/CT IN METASTATIC MEDULLARY THYROID CARCINOMA: NOVEL CORRELATIONS WITH TUMORAL BIOMARKERS

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Objective: Metastatic disease is common in medullary thyroid carcinoma (MTC) and it presents with raising calcitonin and carcinoembryonic antigen (CEA) levels. Nuclear medicine imaging like ⁶⁸Ga-DOTANOC PET/CT and ¹⁸F-FDG PET/CT can be helpful in lesion detection but there is no consensus on which one performs better.

Methods: Cross-sectional study including 13 patients with MTC diagnosis.

Results: ⁶⁸Ga-DOTANOC PET/CT identified MTC metastases in 2 patients that were ¹⁸F-FDG-negative (sensitivity 69.2% vs 53.9%, respectively). ⁶⁸Ga-DOTANOC PET/CT also detected a higher number of lesions than ¹⁸F-FDG PET/CT in 7 patients. Both differences lacked statistical significance ($p=0.50$ and $p=0.86$, respectively) but ⁶⁸Ga-DOTANOC PET/CT better performance allowed changes in patients' management. ⁶⁸Ga-positive/¹⁸F-FDG-negative patients were the ones with the lowest calcitonin doubling time and presented a CEA doubling time >24 months, while the patient with more ¹⁸F-FDG-positive lesions was the one with the highest CEA/calcitonin ratio. The number of lesions found in ⁶⁸Ga-DOTANOC PET/CT were correlated with calcitonin levels ($r=0.73$; $p<0.01$) but not with CEA ones ($r=0.42$; $p=0.15$) and the opposite pattern was observed for ¹⁸F-FDG ($r=0.48$; $p=0.09$ and $r=0.60$; $p<0.05$, respectively).

Conclusion: This is the first study to describe a positive correlation between ⁶⁸Ga/¹⁸F-FDG-positivity and calcitonin/CEA levels, respectively. Tumoral markers pattern could help clinicians to decide which exam to perform first.

EP04. METASTATIC MEDULLARY THYROID CARCINOMA: 20 YEARS OF FOLLOW-UP

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Introduction: Medullary thyroid carcinoma (MTC) is a rare tumor and can either be sporadic or hereditary. It typically extends locally, to the surrounding tissues and may metastasize at distance.

Case Report: A 34-year-old woman was sent to our hospital in 1997, after a total thyroidectomy and lymph node dissection due to a MTC. The germline *RET* mutations screening was negative and sporadic MTC was confirmed. In 1999, for keeping persistently high calcitonin and CEA levels, the patient underwent abdominal magnetic resonance imaging, bones scan and cervical and thoracic computed tomography. These were compatible with hepatic metastasis, confirmed by biopsy. As she was asymptomatic, a watchful approach was adopted. From 2004-2006, multiple ganglionic, pulmonary and bone metastases were confirmed. The patient was stable until 2015, when because of clinical, biochemical and radiological progression of the disease, she started vandetanib 300 mg/day, after confirming a somatic *RET* mutation (c.2753 T>C; p.M918T). Side effects lead to a dose reduction (100 mg/day) that she nowadays maintains. Since then, the patient went through a symptomatic improvement, calcitonin and CEA levels reduction and radiological stabilization of the disease.

Discussion: The clinical behavior of sporadic MTC is unpredictable. Treatment with tyrosine kinase inhibitors is already approved and promising to advanced progressive MTC.

Keywords: Medullary Thyroid Carcinoma

EP07. BARIATRIC SURGERY CARDIOMETABOLIC OUTCOMES: IS PATIENT AGE A FACTOR TO CONSIDER?

Fernando Mendonça¹; Maria Manuel Silva¹; Maria João Ferreira¹; Daniela Salazar¹; Jorge Pedro¹; João Sérgio Neves¹; Vanessa Guerreiro¹; Sara Viana²; Ana Varela¹; Sandra Belo¹; Paula Freitas¹; Davide Carvalho¹

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Introduction: Despite the abundant data addressing the influence of patient age on surgery-related complications, its impact on several cardiometabolic outcomes following metabolic surgery has been overlooked.

Methods: Retrospective analysis of 1728 obese patients submitted to bariatric surgery. Patients were divided in three age groups according to their age at surgery: <40 (n=751), 40 to 59 (n=879) and ≥60 years (N=98). The groups were compared regarding multiple

cardiometabolic parameters such as body anthropometry measures, lipid profile and glycemic status, before and 24 months after surgery. A multiple linear regression was performed, adjusting differences between groups for sex, surgery type and body mass index (BMI) variation.

Results: The younger group (<40 years) presented more weight loss (-35.4 ± 9.0 kg, $p < 0.001$), greater BMI reduction (-15.78 ± 6.1 kg/m², $p < 0.001$) and bigger changes in waist (-34 ± 13.8 cm, $p < 0.001$) and hip circumferences (-28.7 ± 11.9 cm, $p < 0.05$).

The ≥60 years group showed the biggest reduction in fasting plasma glucose (-23.3 ± 11.0 mg/dL, $p < 0.001$) and HbA1c (0.7 ± 1.0, p adjusted <0.001), having also a tendency to have the highest changes in systolic blood pressure (SBP-14.7 ± 8.7 mmHg, $p = 0.071$).

Conclusion: Older patients (≥60 years) benefit from the greatest changes on cardiometabolic parameters 24 months after surgery, showing higher reductions in glucose, HbA1c and a tendency to an higher decrease in SBP. No differences in lipid profile were observed between groups.

Keywords: Age; Bariatric Surgery; Blood Pressure; Glycemic Status; Lipid Profile

EP08. PATIENT'S EDUCATION LEVEL AS A PREPONDERANT FACTOR IN THE SUCCESS OF SURGICAL TREATMENT OF OBESITY

Daniela Salazar¹; João Sérgio Neves¹; Maria João Ferreira¹; Jorge Pedro¹; Vanessa Guerreiro¹; Sara Viana²; Mendonça Fernando¹; Maria Manuel Silva¹; Sandra Belo¹; Ana Varela¹; Paula Freitas¹; Davide Carvalho¹

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Introduction: Bariatric surgery is the most effective treatment of morbid obesity, with a demonstrated benefit in the control of associated comorbidities. The objective of this study was to evaluate the importance of patient education level in the remission of obesity and consequently in the metabolic profile of the patients.

Methods: Retrospective study of 1287 patients undergoing bariatric surgery between 2010 and 2017. Patients were divided according to the attained body mass index (BMI) at 2 years: Obesity persistence (BMI ≥ 30 kg/m²) and remission (<30 kg/m²).

Results: Remission group (n=713) presented lower values of systolic ($p < 0.001$) and diastolic blood pressure ($p < 0.001$), fasting plasma glucose ($p < 0.001$), HbA1c ($p < 0.001$), uric acid ($p < 0.001$), and HOMA-IR ($p < 0.001$), and better lipid profile (total cholesterol ($p < 0.001$), LDL ($p < 0.001$), HDL ($p < 0.001$), triglycerides ($p < 0.001$). We found a 6.5% reduction in the risk of maintaining a BMI > 30 kg/m² for each year of patient education level, even after adjusting for baseline BMI, sex, age and type of surgery (OR=0.935, $p = 0.002$).

Conclusion: The metabolic benefits of bariatric surgery are superior with the remission of obesity, and the education level of the patient presents as a limiting factor to remission, which reinforces the importance of background education of the patient for the success of this treatment.

Keywords: Bariatric Surgery; Obesity

EP09. MAGNESIUM SUPPLEMENTATION IS ASSOCIATED WITH A LOWER RISK OF CARDIO-METABOLIC RISK FACTORS IN PATIENTS SUBMITTED TO BARIATRIC SURGERY

Maria Manuel Silva¹; Maria João Fonseca²; Fernando Mendonça¹; Maria João Ferreira¹; Daniela Salazar¹; Jorge Pedro¹; Vanessa Gonçalves¹; João Sérgio Neves^{1,3}; Sara Viana⁴; Eva Lau^{1,3}; Sandra Belo^{1,3}; Ana Varela^{1,3}; Paula Freitas^{1,3}; Davide Carvalho^{1,3}

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Introduction: Magnesium is an essential mineral for human health and several studies have demonstrated an inverse relation between Mg consumption and cardiovascular risk, with higher doses exerting protection on the development of type 2 diabetes (DM2), arterial hypertension (HTA) and dyslipidaemia.

Objective: To analyse cardio-metabolic risk factors of bariatric patients and the effect of magnesium supplementation on them.

Methods: We performed a cross-sectional analysis of 1884 obese patients who were submitted to bariatric surgery. Data was assessed preoperatively and yearly during a 4-year follow-up.

Results: Mg deficiency was more common among patients who were not supplemented during each year of follow-up ($p < 0.05$). Patients who had magnesium deficiency had higher prevalence of DM, HTA and dyslipidaemia. Among those who underwent Mg supplementation, the percentage of DM, HTA or dyslipidaemia was significantly lower. At the first year, the supplementation group had a lower risk of DM2 (OR=0.305, $p < 0.0001$), dyslipidaemia (OR=0.509, $p < 0.0001$) and HTA (OR=0.466, $p < 0.0001$). The OR for having these metabolic comorbidities persisted lower during the 4 years' follow-up.

Conclusion: Mg supplementation had a protective effect on the development of DM2, HTA and dyslipidaemia in these post-bariatric individuals. There is a need to understand the optimal Mg intake to achieve cardiovascular protection.

Keywords: Bariatric Surgery; Cardiovascular Diseases; Magnesium, Malabsorption Syndromes

EP11. ADRENOCORTICAL CARCINOMAS: TREATMENT AND SURVIVAL ANALYSIS OF A REFERENCE CENTRE

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Introduction: Adrenocortical carcinomas are rare aggressive tumours that may exhibit functional autonomy.

Methods: Cross-sectional study of 25 patients diagnosed with

adrenocortical carcinoma. Survival analysis was performed using Kaplan-Meier curves.

Results: The mean age at diagnosis was 56.4 ± 12.5 years-old and most patients were women (64%). Adrenal incidentaloma (40%), abdominal/back pain (24%) or hormonal hypersecretion (24%) were the most frequent clinical presentations. Nine patients (36%) presented hormonal autonomous production: hypercortisolism (88.9%) and androgen excess (33.3%). Metastasis (stage IV disease) were frequent at diagnosis (40%), mainly involving lungs (70%). The remaining patients presented at stage I (8%), stage II (28%) and stage III (24%). Surgery was performed in 68% of the cases. Other treatment regimens like mitotane (32%), radiotherapy (12%) and chemotherapy (16%) were also pursued. Among those undergoing surgery without any adjunctive therapy, the majority (55.6%) presented relapse during follow-up. Recurrence occurred even in patients with stage I/II disease, R0 resection and low proliferative indexes. A median overall survival-time of 4.62 years was observed. Disease staging ($p=0.001$) and proliferative indexes ($p=0.02$) significantly affected survival.

Conclusion: This study reinforces the ominous prognosis of adrenocortical tumours and the need for considering adjunctive therapy regimens after surgery even in deceptively more favorable settings.

Keywords: Adrenocortical Carcinoma

EP13. PITUITARY INCIDENTALOMAS IN PAEDIATRIC AGE: EXPERIENCE OF A TERTIARY CENTRE

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Purpose: Guidelines on pituitary incidentalomas are limited to adults since there are no data in the paediatric population.

Methods: We have included 41 children diagnosed with pituitary incidentalomas.

Results: Most patients were females (62.4%) and the mean age at diagnosis was 12.0 ± 4.96 years-old. Headaches were the main reason that led to image acquisition (51.2%) and magnetic resonance imaging was the imaging method that detected the majority of the incidentalomas (70.7%). The most prevalent lesion was pituitary hypertrophy (29.3%), which was mainly diagnosed in female adolescents (91.7%), followed by arachnoid cysts (17.1%), pituitary adenomas (14.6%) and Rathke's cleft cysts (12.2%). Most patients (90.2%) did not present clinical or laboratorial findings of hypopituitarism or hormonal hypersecretion. Four patients presented endocrine dysfunction: three had growth hormone deficiency and one had a central precocious puberty. Twenty-three patients (56.1%) underwent imagiological reevaluation during a median follow-up time of 24.6 months. None of them presented dimensional progression.

Conclusion: To the best of our knowledge, this is the first series of pituitary incidentalomas in pediatric age. Comparing our series with those conducted in adults, we have observed a higher preponderance of pituitary hypertrophy over adenomas, a lower prevalence of hormonal hyper/hyposecretion and lower risk of dimensional progression during follow-up.

Keywords: Child; Incidental Findings; Pituitary Neoplasms

EP15. MALIGNANT INSULINOMAS: CLINICOPATHOLOGICAL CHARACTERISTICS

Vanessa Guerreiro^{1,2,3}; João Neves^{1,2,3}; Ana Isabel Oliveira¹; Eva Lau^{1,2,3}; Luís Graça⁴; José Manuel Lopes⁵; Luís Teles⁶; Paula Freitas^{1,2,3}; Davide Carvalho^{1,2,3}

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Introduction: Malignant insulinomas are extremely rare. There are little data regarding features of the malignant ones. The aim of this study was to describe features of patients with malignant insulinomas.

Methods: We retrospectively analyzed patients clinical records with insulinoma resected in our hospital from 1980 to 2018 and identified 29 cases. We compare malignant with benign insulinoma clinicopathological data.

Results: Malignant insulinomas represent 13% of the patients (Table 1), with median age at diagnosis of 49 years (35-57 years). All presented with metastasis at diagnosis. The major sites of metastasis were the abdominal lymph nodes (100%) and liver (25%). All patients except for one had a solitary pancreatic primary lesion; all benign insulinomas were single tumors. Malignant insulinoma patients displayed neurogenic symptoms in 50% and neuroglycopenic symptoms in 33%. The maximal diameters of the primary

Features	Malignant insulinomas	Benign insulinomas
Total, n (%)	4 (13)	25 (87)
Age, years - average	48.75 + 9.60	45.95 + 15.18
Female, %	50	64
Diameter, cm – average (range)	3.7 + 2.51 (1.2 to 6.5)	1.92 + 0.94 (0.6 to 4.0)
Single, n (%)	3 (75)	25 (100)
Neuroglycopenic symptoms, %	33	91
Neurogenic symptoms, %	67	61
Diagnosis		
– Abdominal CT (%: performed, sensitivity)	100 (75)	84 (90)
– Abdominal MRI (%: performed, sensitivity)	25 (100)	24 (67)

lesions in patients with malignant insulinomas ranged between 1.2 and 6.5 cm (average 3.7 ± 2.51 cm). All patients with malignant insulinoma had an abdominal computed tomography (CT) performed, contributing to the location of the tumor in 3 patients (75%). Abdominal magnetic resonance imaging (MRI) localized the tumor in one patient. All patients were submitted to surgery. Malignant insulinomas recurred in 50% of the cases (3 and 6 years later). None of the patients had evidence of the multiple endocrine neoplasia syndrome.

Conclusion: Our data highlight the heterogeneity of these tumors and its rarity makes difficult to predict their natural history.

Keywords: Insulinoma

EP19. HYPOPHOSPHATEMIA AND PITUITARY TUMOR: A CASE REPORT

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Introduction: Phosphorus is the second most abundant mineral in the human body and it is highly reactive. Nearly all of the inorganic phosphorus is present in the form of phosphate. Chronic hypophosphatemia leads to complications such as childhood rickets, osteomalacia, and skeletal muscle myopathy. Hypophosphatemia can result from hereditary hypophosphatemia or tumor induced osteomalacia (TIO), a paraneoplastic syndrome associated with FGF23-producing tumors.

Case Report: A 62-year-old woman was referred to the endocrinology consult with a pituitary tumor and a history of bone pain in her hips that made her needs a wheelchair. She had been diagnosed with rickets during childhood. She showed no significant alteration at physical examination, with the exception of bone abnormalities. Analytically: calcium 4.2 mEq/L (N 4.2-5.1), phosphorus 1.3 mg/dL (N 2.7-4.5), 25-OH-vitamin-D 16 ng/mL (N > 30); PTH 145 pg/mL (N 10-65); 24 hours urine: phosphorous 793 mg/L, 635 mg/24 hours, creatinine 1.1 mg/24 hours. Her bone densitometry showed a T score of -1.3 in the lumbar spine and -0.4 in the femur. She underwent a magnetic resonance imaging that showed: “Extensive osteonecrosis of both femoral heads (...) fractures in both iliopubic and ischio-pubic branches (...)”. She initiated therapy with disodium phosphate, 1,25-dihydroxycholecalciferol and 25-hydroxyvitamin D. The endocrine evaluation did not reveal any other abnormality. She underwent transphenoidal surgery with partial removal of the tumour, which histology was of a non-functioning pituitary tumour. Under phosphate treatment she was able to walk without any help.

Conclusion: Patients with HHR typically present during childhood with skeletal abnormalities, osteomalacia with hypophosphatemia, normal calcium, normal-augmented PTH and normal 25-hydroxyvitamin D. Although late, correct diagnosis and therapy allowed the patient to significantly improve her quality of life.

Keywords: Hypophosphatemia; Pituitary Neoplasms

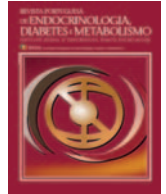


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Resultados de Ensaios Clínicos

A Rev Port Endocrinol Diabetes Metab apoia iniciativas que contribuam para uma melhor divulgação de resultados ensaios clínicos. Estas incluem o registo prospectivo de ensaios clínicos em bases de dados públicas adequadas. De acordo com as recomendações do ICMJE, a Rev Port Endocrinol Diabetes Metab exige o registo de todos os ensaios clínicos cujos dados sejam incluídos em trabalhos submetidos para publicação nesta revista.

O ICMJE adopta a definição da Organização Mundial de Saúde de ensaio clínico, que é “qualquer estudo de investigação que prospectivamente atribua a participantes humanos, individualmente ou em grupo, uma ou mais intervenções relacionadas com a saúde, com o objectivo de avaliar os seus resultados relacionados com a saúde”. Esta definição inclui ensaios das fases I a IV. O ICMJE define intervenções relacionadas com a saúde como “qualquer intervenção usada para modificar um resultado biomédico ou relacionado com a saúde” e resultados relacionados com a saúde como “qualquer medida biomédica ou relacionada com a saúde obtida em doentes ou participantes”.

Registo de Ensaio Clínicos

O registo numa base de dados pública de ensaios clínicos é condição necessária para a publicação de dados de ensaios clínicos na Rev Port Endocrinol Diabetes Metab, de acordo com as recomendações do International Committee of Medical Journal Editors (ICMJE, <http://www.icmje.org>). Os ensaios devem ser registados anteriormente ou no início do período de recrutamento de doentes. Um ensaio clínico é definido como qualquer estudo de investigação que prospectivamente atribua a participantes humanos, individualmente ou em grupo, uma ou mais intervenções relacionadas com a saúde, com o objectivo de avaliar os seus resultados relacionados com a saúde. As intervenções relacionadas com a saúde incluem qualquer intervenção usada para modificar um resultado biomédico ou relacionado com a saúde (por exemplo, fármacos, procedimentos cirúrgicos, dispositivos médicos, tratamentos comportamentais, intervenções nutricionais e alterações do processo de prestação de cuidados). Os resultados relacionados com a saúde incluem qualquer medida biomédica ou relacionada com a saúde obtida em doentes ou participantes, incluindo medidas farmacocinéticas e eventos adversos. Os estudos puramente observacionais (aqueles em que a atribuição de uma intervenção médica não é do critério do investigador) não exigem registo.

O número de registo do ensaio clínico (TRN) bem como a data desse registo devem ser referidos no final do resumo do artigo.

Disponibilização dos Dados

A Rev Port Endocrinol Diabetes Metab sugere fortemente que todos os conjuntos de dados nos quais se baseiam as conclusões de um artigo sejam disponibilizados para os leitores. Sugere-se assim aos autores que assegurem que os seus dados ficam disponíveis em repositórios públicos (sempre que estes estejam disponíveis e sejam adequados), que sejam apresentados no manuscrito principal ou em arquivos adicionais, sempre que possível em formato tratável (por exemplo, em folha de cálculo e não em pdf).

A Rev Port Endocrinol Diabetes Metab exige uma declaração de disponibilização dos dados, presente no final de cada manuscrito. Para ensaios de fármacos ou dispositivos médicos, a declaração deve referir, pelo menos, que os dados relevantes de cada doente, devidamente anonimizados, estão disponíveis mediante pedido justificado aos autores.

Sugerem-se formulações para a referida declaração: “Disponibilização dos dados: os dados individuais dos doentes [e/ou] o conjunto completo de dados [e/ou] o anexo técnico [e/ou] as especificações da análise estatística, estão disponíveis em [/doi] [com acesso livre/com as restrições] [do autor correspondente em]. Os participantes deram o seu consentimento informado para disponibilização de dados [ou... não foi obtido consentimento dos participantes, mas os dados apresentados estão anonimizados e o risco de identificação é reduzido... ou não foi obtido consentimento

dos participantes, mas os benefícios potenciais da disponibilização destes dados justificam os prejuízos potenciais, uma vez que ...]”

Se os dados não estiverem disponíveis, deve ser referido o seguinte: “Disponibilização dos dados: não estão disponíveis dados adicionais.”

Esta opção não se aplica a ensaios clínicos de fármacos ou dispositivos médicos.

Podem ser solicitados aos autores que disponibilizem os dados brutos em que basearam o seu artigo durante o processo de revisão e até 10 anos após a publicação.

Submissão dos Trabalhos

A submissão de um manuscrito implica que o trabalho descrito não tenha sido publicado previamente (excepto na forma de um resumo ou como parte de uma palestra publicada ou de uma tese académica), e que não está sendo considerado para publicação em outra revista, que o manuscrito foi aprovado por todos os autores e, tácita ou explicitamente, pelas autoridades competentes onde o trabalho foi realizado e que, se for aceite para publicação, não será publicada em outro lugar na mesma forma, em inglês ou em qualquer outra língua, incluindo electronicamente.

Todos os manuscritos devem ser acompanhados por uma carta de apresentação. Deve ser dada garantia na carta de apresentação de que o manuscrito não está sob consideração simultânea por qualquer outra revista. Na carta de apresentação, os autores devem declarar seus potenciais conflitos de interesse e fornecer uma declaração sobre a autoria.

Para verificar a originalidade, o artigo pode ser verificado pelo serviço de detecção de originalidade.

As submissões que não estejam em conformidade com estas instruções podem ser devolvidas para reformulação e reenvio.

Submissão do Manuscrito

Submeta o seu manuscrito em: <http://spedmjjournal.com/>

Contacto

Em caso de dúvidas durante a submissão, contacte: scientific.landscape@gmail.com

Preparação do Manuscrito

Uso de programa de processamento de texto

É importante que o arquivo seja guardado no formato nativo do processador de texto usado. O texto deve estar no formato de coluna única. Mantenha o *layout* do texto o mais simples possível.

Para evitar erros desnecessários, aconselhamos o uso das funções “verificação ortográfica” e “verificação gramatical” do seu processador de texto.

Tipologia dos Artigos

A Rev Port Endocrinol Diabetes Metab aceita a seguinte tipologia:

- a) Artigos originais reportando investigação clínica ou básica;
- b) Artigos de revisão (incluindo sistemáticas revisões e meta-análises);
- c) Estudos de Caso/Casos Clínicos;
- d) Imagens em Endocrinologia;
- e) Editoriais, que são escritos a convite do Editor-Chefe e consistem em comentários sobre artigos publicados na revista ou sobre temas de relevância particular;
- f) Cartas ao Editor, que consistem em pareceres concisos sobre artigos recentemente;
- g) Perspectivas

h) *Guidelines*.

Os autores devem indicar na carta de apresentação qual o tipo de manuscrito que está a ser submetido para publicação.

Na primeira página/ página de título:

I. Título

Título em português e inglês, conciso e descritivo, sem abreviaturas e não excedendo os 120 caracteres. O título pode incluir um complemento de título com um máximo de 40 caracteres (incluindo espaços).

II. Autores e afiliações

Na linha da autoria, liste o Nome de todos os Autores (primeiro e último nome) e respectiva afiliação (departamento, instituição, cidade, país).

III. Subsídio

Todos os subsídio(s) ou bolsa(s) que contribuíram para a realização do trabalho.

IV. Autor Correspondente

Indicar claramente quem vai lidar com a correspondência em todas as fases de arbitragem e publicação, também pós-publicação. Endereço postal e *e-mail* do Autor responsável pela correspondência relativa ao manuscrito.

V. Resumo e Keywords

Um resumo conciso e factual é requerido. Um resumo é frequentemente apresentado separadamente do artigo, por isso deve ser capaz de ficar sozinho.

Resumo escrito em português e inglês. Nenhuma informação que não conste no manuscrito pode ser mencionada no resumo. O resumo não pode remeter para o texto, não podendo conter citações nem referencias a figuras.

No fim do resumo devem ser incluídas um máximo de 5 *Keywords* em inglês utilizando a terminologia que consta no Medical Subject Headings (MeSH), <http://www.nlm.nih.gov/mesh/MBrowser.html>,

VI. Resumo Estruturado

Um resumo estruturado, com as etiquetas de secção apropriadas, deve fornecer o contexto e objectivo do estudo, procedimentos básicos (seleção dos sujeitos de estudo ou animais de laboratório, métodos observacionais e analíticos), principais resultados (significância estatística, se possível) e principais conclusões. Deve enfatizar aspectos novos e importantes do estudo ou das observações. Secções: Introdução, Métodos, Resultados e Conclusões.

VII. Os autores também incluirão nesta página de título, sob a designação “Considerações éticas” a declaração de “**Protecção de pessoas e animais**”, **Confidencialidade dos dados e consentimento informado e Conflitos de interesse**.

Prémios e Apresentações prévias

Devem ser referidos os prémios e apresentações do estudo, prévias à submissão do manuscrito

Texto**Artigos Originais**

Os artigos originais devem incluir as seguintes secções: Introdução, Material e Métodos, Resultados, Discussão e Conclusão, Agradecimentos (se aplicável), Referências, Tabelas e Figuras.

Os artigos originais não devem exceder 4000 palavras, até 6 tabelas ou figuras e até 60 referências. Um resumo estruturado com o máximo de 350 palavras.

Article structure**Introduction**

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Material and methods

Provide sufficient detail to allow the work to be reproduced.

Article type	Abstract	Keywords	Main text structure	Max. words	Tables/figures	References
Original Article	Max. 350 words; structured (Introduction and Objectives, Methods, Results and Conclusion(s)) Portuguese and English	Up to 6 Portuguese and English	Introduction; Methods; Results; Discussion; Conclusion(s); Acknowledgments, if any; References; and figure legends, if any	4000	Total up to 6	Up to 60
Review Article	Max. 350 words; unstructured Portuguese and English	Up to 6 Portuguese and English	Introduction; thematic sections at the discretion of the authors; Conclusion(s); Acknowledgments, if any; References; and figure legends, if any	4000	Total up to 6	Up to 100
Systematic Review	Max. 350 words; structured Portuguese and English	Up to 6 Portuguese and English	PRISMA	4000	Total up to 6	Up to 100
Case Report	Max. 150 words; unstructured Portuguese and English	Up to 6 Portuguese and English	Introduction; Case report; Discussion; Conclusion(s) (optional); References; and figure legends, if any	2000	Total up to 4	Up to 25
Images in Endocrinology	None	Up to 6 Portuguese and English	Unstructured	500	Total up to 4	Up to 5
Editorial	None	None	Unstructured	1500	Total up to 2	Up to 20
Letter to the Editor	None	Up to 6 Portuguese and English	Unstructured	600	Total up to 1	Up to 10
Current Perspectives	None	Up to 6 Portuguese and English	Unstructured	1200	Total up to 2	Up to 10

Methods already published should be indicated by a reference: only relevant modifications should be described.

Results

Results should be clear and concise.

Discussion

This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Artigos de Revisão

Os artigos de revisão são artigos abrangentes que sintetizam ideias antigas e sugerem novas. Abrangem áreas amplas. Podem ser de ciência clínica, investigação ou básica. Embora geralmente por convite do Editor-Chefe, ocasionalmente aceitamos artigos de revisão não solicitados sobre assuntos importantes ou sobre avanços recentes. Antes de submeter uma revisão, pedimos que envie ao Editor-Chefe um breve esboço (não mais de 500 palavras) indicando a importância e novidade do assunto, e por que está qualificado para escrevê-lo. Um convite para submissão não garante aceitação.

Os artigos de revisão não devem exceder 4000 palavras, até 6 tabelas ou figuras e até 100 referências. Um resumo não estruturado com o máximo de 350 palavras.

Revisões Sistemáticas e Meta-Análises

As revisões sistemáticas podem ou não utilizar métodos estatísticos (meta-análises) para analisar e resumir os resultados dos estudos incluídos.

As Revisões Sistemáticas podem ser apresentadas no formato Introdução, Métodos, Resultados, Discussão. O assunto deve ser claramente definido. O objectivo de uma revisão sistemática deve ser produzir uma conclusão baseada em evidências. Nos Métodos devem fornecer uma indicação clara da estratégia de pesquisa da literatura, extracção de dados, classificação das evidências e análise. Deve ser seguida a normativa PRISMA (<http://www.prisma-statement.org/>).

O texto não deverá exceder 4000 palavras, excluindo um resumo estruturado (máximo de 350 palavras). Não poderá incluir mais de 10 referências, e até 6 tabelas ou figuras.

Caso Clínico

O relato de Casos Clínicos deve incluir as seguintes seções: Introdução, Caso Clínico e Discussão.

O texto não poderá exceder 2000 palavras, e não poderá exceder as 25 referências bibliográficas. Deve incluir um resumo não estruturado, que não exceda 150 palavras.

Deve ser seguida a normativa CARE (<http://www.care-statement.org/>).

Editoriais

Os Editoriais são da responsabilidade do grupo editorial ou solicitados por convite do Editor-Chefe e constituirão comentários sobre tópicos actuais ou comentários sobre artigos publicados na revista. Não devem exceder as 1200 palavras, um máximo de 20

referências bibliográficas e podem conter uma tabela e uma figura. Não têm resumo.

Cartas ao Editor

As cartas ao Editor consistem em comentários críticos sobre um artigo publicado na revista ou uma nota curta sobre um determinado tópico ou caso clínico. Cartas ao Editor não devem exceder 600 palavras e 10 referências e pode conter uma figura ou tabela. Não têm resumo.

Imagens em Endocrinologia

Esta secção destina-se à publicação de imagens clínicas, radiológicas, histológicas e cirúrgicas relacionadas com casos de endocrinologia, diabetes ou metabolismo.

O título não deve ter mais de oito palavras. Os autores devem ser no máximo quatro. As imagens devem ser de alta qualidade e valor educativo. São permitidas até 4 figuras. As legendas devem ser breves e informativas. Setas ou outros símbolos devem ser incluídos conforme necessário para facilitar a compreensão das imagens. O texto não deve exceder 500 palavras, até cinco referências, e deve incluir uma breve história clínica e dados relevantes do exame físico, testes laboratoriais e progressão clínica, conforme apropriado. Não têm resumo.

Perspectiva

Este é o tipo de manuscrito é submetido a convite do Conselho Editorial. Pode abranger uma ampla diversidade de temas relacionados com endocrinologia, diabetes, metabolismo e saúde: problemas atuais ou emergentes, políticas de gestão e saúde, história da medicina, questões de sociedade e epidemiologia, entre outros. Um Autor que deseje propor um manuscrito nesta secção deverá enviar um resumo ao Editor-Chefe, incluindo o título e a lista de autores para avaliação. O texto não deve exceder 1200 palavras, até 10 referências, e até 2 tabelas ou 2 figuras. Não têm resumo.

Guidelines

Os guias de prática clínica não devem exceder 4000 palavras, até 6 tabelas ou figuras e até 100 referências. Resumo até 350 palavras.

Referências

I. Citação no texto

Certifique-se de que todas as referências citadas no texto também estão presentes na lista de referências (e vice-versa). As referências devem ser listadas usando algarismos árabes pela ordem em que são citados no texto.

As referências a comunicações pessoais e dados não publicados devem ser feitas diretamente no texto e não devem ser numeradas. Citação de uma referência como “in press” implica que o item tenha sido aceite para publicação. Os nomes das revistas devem ser abreviados de acordo com o estilo da Medline.

As referências a artigos publicados em revistas devem incluir o nome do primeiro autor seguido dos nomes dos restantes autores, o título do artigo, o nome da revista e o ano de publicação, volume e páginas.

Certifique-se de que os dados fornecidos nas referências estão corretos. Ao copiar referências, tenha cuidado porque já podem conter erros.

A lista de referências deve ser adicionada como parte do texto, nunca como uma nota de rodapé. Códigos específicos do programa de gestão de referências não são permitidos.

II. Formato

Uma descrição detalhada dos formatos de diferentes tipos de referência pode ser consultada em ICMJE *Recommendations* (<http://www.icmje.org/recommendations/>). Liste todos os autores se houver seis ou menos. *Et al* deve ser adicionado se houver mais de seis autores. Título do artigo, nome da revista, ano, volume e páginas.

III. Estilo de referência

Texto: Indicar as referências no texto por número (s) em expoente. Os autores podem ser referidos, mas o número de referência deve ser sempre dado.

Lista: Ordene as referências na lista pela ordem em que aparecem no texto

Exemplos:

Referência de artigo:

1. Isidori AM, Sbardella E, Zatelli MC, Boschetti M, Vitale G, Colao A, et al. Conventional and nuclear medicine imaging in ectopic Cushing's syndrome: a systematic review. *J Clin Endocrinol Metab.* 2015;100:3231-44.

Referência de livro:

2. Ware JE, Kosinski M, Dewey JE. How to score version 2 of the SF-36 Health Survey: standard & acute forms. Lincoln: Quality Metric Incorporated; 2000.

Referência de capítulo de livro:

3. Castellano Barca G, Hidalgo Vicario M, Ortega Molina M. Transtorno del comportamiento alimentário. In: Castellano Barca G, Hidalgo Vicario M, Redondo Romero A, editores. *Medicina de la adolescência – atención integral.* 2ª ed. Madrid: Ergon; 2004. p.415-29.

Referências Web:

4. No mínimo, o URL completo deve ser dado e a data em que o documento foi consultado. Qualquer outra informação, se conhecida (nomes de autor, datas, referência a uma publicação de origem, etc.), também deve ser dada.

Notas de Rodapé

As notas de rodapé devem ser evitadas. Quando imprescindíveis, devem ser numerados consecutivamente e aparecer ao pé da página apropriada.

Agradecimentos (facultativo)

Devem vir após o texto, e antes das referências, tendo como objectivo agradecer a todos os que contribuíram para o estudo mas que não têm peso de autoria. Nesta secção é possível agradecer a todas as fontes de apoio, quer financeiro, quer tecnológico ou de consultadoria, assim como contribuições individuais.

Abreviaturas

Não use abreviaturas ou acrónimos no título e no resumo e limite o seu uso. Abreviaturas não consagradas devem ser definidas na primeira utilização, por extenso, logo seguido pela abreviatura entre parênteses. A menos que a sigla seja uma unidade padrão de medição. Uso excessivo e desnecessário de acrónimos e abreviaturas deve ser evitado.

Unidades de Medida

Devem ser utilizadas as unidades Sistema Internacional de Unidades. As medidas de comprimento, altura, peso e volume

devem ser expressas em unidades do sistema métrico (metro, quilograma ou litro) ou seus múltiplos decimais. As temperaturas devem ser dadas em graus Celsius (°C) e a pressão arterial em milímetros de mercúrio (mm Hg) ou a hemoglobina em g/dL. Todas as medições hematológicas ou bioquímicas serão referidas no sistema métrico de acordo com o Sistema Internacional de Unidades (SI).

Nomes de Medicamentos

Identifique com precisão todos os medicamentos e produtos pelo nome genérico. Não é recomendável a utilização de nomes comerciais de fármacos (marca registrada), mas quando a utilização for imperativa, o nome do produto deverá vir após o nome genérico, entre parênteses, em minúscula, seguido do símbolo que caracteriza marca registrada, em sobrescrito (®).

Tabelas e Figuras

Tabelas/Figuras devem ser numerados na ordem em que são citadas no texto e assinaladas em numeração árabe e com identificação, Figura/Tabela.

Cada figura e tabela incluídas no trabalho têm de ser referidas no texto: Uma resposta imunitária anormal pode estar na origem dos sintomas da doença (Fig. 2). Esta associa-se a outras duas lesões (Tabela 1).

Figura: Quando referida no texto é abreviada para Fig., enquanto Tabela não é abreviada. Nas legendas ambas as palavras são escritas por extenso.

Cada tabela e figura deve ser acompanhada da respectiva legenda, sucinta e clara. As legendas devem ser auto-explicativas (sem necessidade de recorrer ao texto).

Em relação aos gráficos deve ser explícito se a informação inclui valores individuais, médias ou medianas, se há representação do desvio padrão e intervalos de confiança e o tamanho da amostra (n).

As fotografias deverão incluir identificadores (setas e asteriscos). Poderão ser publicadas fotografias a cores, desde que consideradas essenciais.

Cada tabela deve ser utilizada para mostrar resultados, apresentando listas de dados individuais ou sumariando os mesmos, não devendo no entanto constituir duplicação dos resultados descritos no texto. Devem ser acompanhadas de um título curto mas claro e elucidativo. As unidades de medida usadas devem ser indicadas (em parêntesis abaixo do nome que encabeça cada categoria de valores) e os números expressos devem ser reduzidos às casas decimais com significado clínico.

Para as notas explicativas nas tabelas devem ser utilizados os seguintes símbolos e sequência: *, †, ‡, §, ||, ¶, **, ††, ‡‡.

Se fotografias de doentes forem usadas, estas não devem ser identificáveis ou as fotografias devem ser acompanhadas de autorização por escrito para usá-las.

As imagens a cores são reproduzidas gratuitamente.

Princípios gerais:

- Numere as ilustrações de acordo com a sua sequência no texto.
- Forneça as legendas das ilustrações separadamente.
- Dimensione as ilustrações próximas das dimensões desejadas da versão publicada.
- Envie cada ilustração em ficheiro separado.

A inclusão de figuras e/ou tabelas já publicadas, implica a autorização do detentor de *copyright* (autor ou editor).

A submissão deve ser feita separadamente do texto, conforme as instruções da plataforma.

Os ficheiros das figuras devem ser fornecidos em alta resolução, 800 dpi mínimo para gráficos e 300 dpi mínimo para fotografias.

A publicação de ilustrações a cores é gratuita.

Material gráfico deve ser entregue em um dos seguintes formatos:

JPEG (. Jpg)

Portable Document Format (. Pdf)

PowerPoint (.ppt)

TIFF (. Tif)

Excel

Permissão para publicação: No caso de publicação de tabelas de livros ou revistas os autores são responsáveis por obter permissão, junto dos autores dos trabalhos de onde forem reproduzidos, para a referida publicação, e terão de a apresentar na submissão.

Ficheiros Multimedia

Os ficheiros multimedia devem ser enviados em ficheiro separado com o manuscrito. O material multimedia deve seguir os padrões de qualidade de produção para publicação sem a necessidade de qualquer modificação ou edição. Os ficheiros

aceitáveis são: formatos MPEG, AVI ou QuickTime.

Anexos/ Apêndices

Quando necessário, os anexos devem ser utilizados para apresentar inquéritos longos ou detalhados, descrições de extensos cálculos matemáticos e / ou listas de itens. Devem ser colocados depois da lista de referências, se necessário, com legendas. Anexos longos, tais como algoritmos, pesquisas e protocolos, serão publicados apenas *online*; o URL será fornecido no artigo impresso onde o anexo é citado.

Se houver mais de um apêndice, eles devem ser identificados como A, B, etc. As fórmulas e equações em apêndices devem ser numeradas separadamente: Eq. (A.1), Eq. (A.2), etc .; Em apêndice posterior, a Eq. (B.1) e assim por diante. Da mesma forma para tabelas e figuras: Tabela A.1; FIG. A.1, etc.

Estilo

Rev Port Endocrinol Diabetes Metab segue AMA Manual Style (10ª edição).

Última revisão **Maio 2017**

