Development of Online Modules for Intensive Insulin Dose Adjustment Education for Parents of Children with Type 1 Diabetes

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Background: British Columbia Children's Hospital (BCCH) developed a new on-line learning module ‘Getting the Most out of Insulin Pump Therapy’. Traditional classroom or paper-based teaching lack accessibility, flexibility, interactivity and consistent delivery of information. The e-learning format is a good fit for teaching advanced pump therapy.

Aims: The aim of this pilot descriptive study was to obtain feedback on program strengths, areas for improvement and changes in learner knowledge and confidence.

Methods: Participants included 10 parents of children and 3 teens using insulin pumps. They attended a 2.5 hour session to complete the module. Module content is interactive, self-paced, and includes pattern management, fine-tuning basal and bolus insulin and using advanced pump features. Participant knowledge, confidence, and insulin pump adjustment behaviours were assessed pre and post education module. The session concluded with a focus group discussion to explore program strengths and areas for improvement.

Results: All participants were making at least some adjustments on their own before doing the module. Pre and post module questionnaires indicate that 12/13 participants had increased knowledge and the number of participants who felt confident to adjust pump settings on their own increased from 7/13 to 13/13. In the focus group, participants gave minor suggestions for changes in graphics and wording of the module.

Conclusions: Participants found the program content engaging and liked the e-learning format. Focus group input was used to make changes to the final module. The focus group format was useful for obtaining feedback from participants and contributed to a stronger final product. This format will be used again as further modules are developed.

Clinical Implications: Insulin/pump dose adjustment is one of the most powerful self-care skills for diabetes management but is challenging to provide ongoing education in diabetes centers. Online learning is an effective format for endocrine nurses to meet this need. This module is accessible on the hospital website http://endodiab.bcchildrens.ca and is used by BCCH patients, diabetes educators and other diabetes programs. BCCH has also completed basic insulin dose adjustment modules available on the website. Modules on carbohydrate counting and multiple daily injections are in development.
002 - Using Art to Assess Emotions and Learning in Newly Diagnosed Children with Type 1 Diabetes
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Background: Drawing is an intimate, child appropriate form of communication, linked to expression of personality, emotion and ideas. Most healthcare professionals consider children’s drawing to be a normal extension of play and do not appreciate the value of art expression as a tool for assessment and evaluation. The developmental stages of children’s drawings follow similar stages to cognitive and motor development. These include the scribble, pre-schematic, schematic, dawning realism and pseudorealism stages. Children may go back and forth between stages, and can show fluctuations in artistic development when under emotional stress.

Purpose: The purpose of this project was to assess the usefulness of the art of children newly diagnosed with type 1 diabetes in revealing how they are coping with and learning about diabetes.

Description: This project involved newly diagnosed children with type 1 diabetes aged 5-12, who came in to the BC Children’s Hospital diabetes education program for teaching with their families. They were asked to ‘draw a picture of diabetes’ at the start of education and again upon completion of the education program.

Clinical Implications: Looking at the before and after drawings revealed that they were useful for assessing emotions, and in many cases, were also a tool to evaluate learning. Often, even when a child appeared not to be listening or paying attention, the drawings revealed that, in fact, they were! Even in cases where no useful information was obtained, the children had so much fun drawing that the exercise was deemed useful. Children love to draw and will often keep drawing long after the requested artwork is completed. Although there are standard emotional indicators for analyzing children’s drawings, they are not diagnostic tools. They can, however, be a source of information. Based on this experience, the use of art as part of the education process for children with diabetes should be encouraged, and would be an interesting and innovative area for future research.

003 - An Innovative Approach to Outpatient Diabetes Management in a Pediatric Population
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Background: We believe giving adolescents with type 1 diabetes mellitus (T1DM) a notebook containing sections related to education, nutrition, school care plans, current and past medications, medical history and clinic appointments to guide them and then offering an incentive (gift card) will improve compliance with prescribed insulin regimen, therefore improving HbA1c and giving them ownership of their diabetes.

Purpose: The purpose is to study compliance and diabetes management in the adolescent population between the ages of 12-16 years with T1DM by using the Diabetes Care Notebook (DCN) and offering an incentive for their participation.

Description: The DCN will be given to patients admitted inpatient with a diagnosis of T1DM as well as those who have been previously diagnosed and are currently seen in our clinic. After informed consent, we will record the HbA1c for each participant before the DCN (baseline) and at six month intervals for eighteen months to see if the DCN is impacting compliance and
diabetes management. Because the DCN has the different sections related to education, nutrition, school care plans, current and past medications, medical history and clinic appointments, we believe that they will use the DCN at home as an informational tool in the management of their diabetes. The expectation is that patients will bring the DCN to clinic and HbA1c will improve at each visit. The patients will be rewarded with a nominal gift card for complying with each of these expectations.

Clinical Implications: This is a nursing piloted project by two pediatric nurses. We believe the clinical implications for this study will be better patient and family compliance and overall ownership of diabetes management. This involvement with nursing staff helps to create and develop a foundation of trust between family/patient and clinic nursing staff.

004 - Adrenal Insufficiency: Causes of Adrenal Insufficiency and Prevention of Adrenal Crisis
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Background: Adrenal insufficiency (AI) is defined as the body’s inability to produce enough adrenal hormones. Cortisol and aldosterone maintain normal physiologic functions in the body such as blood pressure, glucose levels and sodium/water balance in the body. Adrenal insufficiency can be primary or secondary, congenital or acquired. The most common form of primary adrenal insufficiency in children is congenital adrenal hyperplasia (CAH), with an incidence of about 1 in 15,000. A much more common cause of acute adrenal insufficiency is glucocorticoid withdrawal in patients being treated with chronic pharmacologic doses of steroids. The prevalence of secondary adrenal insufficiency is 150-280 per million. Causes of permanent AI include: Addison disease, CAH, complete removal of pituitary gland, surgical removal of the adrenal gland. Temporary causes are surgical removal of tumor from the pituitary gland, removal of cortisol producing tumors, medical treatments that lower cortisol levels to treat Cushing syndrome, and taking steroids for prolonged periods.

Purpose: The purpose of this poster is to identify and explain the causes of adrenal insufficiency, explain the daily management versus the illness regimen, and review the sick day rules and injection teaching of intramuscular hydrocortisone to prevent adrenal crisis.

Description: Nursing interventions to prevent adrenal crisis are to educate parents about sick day rules and provide intramuscular injection teaching to parents of children on glucocorticoid therapy. Even though there are adequate treatments for adrenal crisis, it continues to be a cause of morbidity and mortality in children. Children are at increased risk during times of illness and surgical procedures.

Clinical Implications: There are many children taking glucocorticoid therapy for multiple diseases. Giving exogenous glucocorticoids turns off the body’s natural ability to produce extra cortisol in times of physiologic stressors. Prevention of the crisis with correct dosing for physiologic stressors such as fever or trauma is an important goal. Pediatric endocrine nurses can provide patients and their families with the tools to prevent crisis by knowing the symptoms, causes, and tools to use in case of emergency.

005 - Defining the Unique Roles and Responsibilities of the Pediatric Endocrine Nurse in the Clinical Research Setting
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Background: The Clinical Center (CC) at the National Institutes of Health (NIH) opened in 1953, and since that time more than 400,000 patients from the US and around the world have participated in clinical research essential to developing novel treatments, minimizing side effects
of current therapies, and improving patient care. Medical milestones resulting from the clinical research include the development of chemotherapy for cancer, demonstration that lithium helps depression, and the first treatment of human immunodeficiency virus with azidothymidine. The inclusion of pediatric patients in clinical research is vital for having novel therapies available to pediatric patients. Nurses providing care to these patients play a key role maintaining the integrity of data collected, and ensuring the patients’ safety and protection. In 2010 the CC Nursing Department reported results of a three-year study, with the purpose of defining the role of the clinical research nurse, and developing a consensus definition leading to eventual specialty certification.

**Purpose:** Using roles and responsibilities identified in the NIH CC’s Nursing Model of Care 2010 as a template, the specialized role of the clinical research nurse for pediatric endocrine patients will be analyzed and defined.

**Description:** Specific attention will be given to unique nursing care processes for pediatric endocrine patients. Additionally, it is important to describe a typical pediatric endocrine research study visit and how nurses contribute to the successful participation of the pediatric patient/family in this context. Experiences from pediatric endocrine nurses and advanced practice nurse colleagues who care for thousands of pediatric patients and their families participating in endocrine studies will be surveyed to form this role definition.

**Clinical Implications:** Providing a thorough description of a pediatric endocrine clinical research nurse’s role is critical. Appropriate support by management can then be allocated to allow these nurses to support the pediatric research study patient in the context of the broader acute care hospital setting. Defining their role will enhance the quality of clinical research in pediatric endocrine patients, and encourage pediatric endocrine nurses to influence the development of new medical treatments.

**CASE PRESENTATIONS**

**006 - Severe Insulin Resistance in a Pediatric Patient: Key Areas to Address in the Screening**

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**Demographics:** DP is a 14-year old African American female with a recent history of severe insulin resistance, hyperglycemia, fatigue, polyuria and polydipsia.

**Clinical Presentation:** She has significant darkening to the skin fold areas. She has increased hair growth to the face and chin. She is overweight (BMI 95%ile) and has not had a menstrual period in 2 years. Post-prandial blood sugars are 200-400mg/dL. She takes 2 gms metformin daily.

**Past History:** The patient reports having breast buds at age 8, and pubic hair developed shortly afterwards. She had a history of hypoglycemic episodes, with morning blood sugars frequently 40-50 mg/dL, prior to starting metformin a year ago. She has a strong family history for type 2 diabetes mellitus on both the maternal and paternal lineages.

**Evaluation:** During the screening visit, weight is 65.6 kg (90%ile) and height is 154cm (10%ile). Blood pressure is 141/78. She is tanner stage 4 with mild clitoromegaly. Baseline results were a fasting glucose of 153 mg/dL and the 2-hour glucose of 333 mg/dL. The fasting insulin was extremely elevated at 175.7 uIU/mL and c-peptide was 6.3 ng/mL. HgbA1c was 7%. GAD and anti-islet cell antibodies were negative. Lipid panel showed total cholesterol of 137 mg/dL, triglycerides low at 47 mg/dL, HDL of 45 mg/dL and LDL of 83 mg/dL. The patient underwent autoimmune and inflammatory work-up and results were unremarkable. DEXA scan showed 25.5% body fat. Bone age of the left hand/wrist read a skeletal age of 17 years. Ultrasound showed mild fatty liver disease, and enlarged ovaries.
Interventions: Oral contraceptive pills were started for amenorrhea. Genetic samples were sent to a National Institutes of Health collaborative laboratory to screen for insulin receptor mutations. Serum was sent for insulin receptor antibodies and adiponectin level.

Discussion/Recommendations: The prevalence of type 2 diabetes is increasing. Now 1/3 of children are overweight or obese. The pediatric endocrine nurse must be knowledgeable of insulin resistance, the metabolic syndrome, etiologies, and manifestations. This case presents an example of Type A insulin resistance and demonstrates screening tests to distinguish inherited defects in insulin action and endocrinopathies associated with hyperglycemia from type 2 diabetes.

007 - Syndrome of Inappropriate Antidiuretic Hormone (SIADH) Associated with Carbamazepine Use in a Patient with Central Diabetes Insipidus
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Patient Demographics: 15-year 4-month-old Aboriginal female
Clinical Presentation: She presented with status epilepticus secondary to hyponatremia, with sodium 120 mmol/l. It was hypothesized that her desmopressin dose and fluid intake were slightly too high resulting in a gradual decline in her sodium level until it hit a threshold. Episodes of hyponatremia persisted and four months later she was admitted to hospital for evaluation.

Past Relevant History: Patient has a history of septo-optic dysplasia, panhypopituitarism, cortical blindness, schizencephaly, developmental delay & seizures. She was diagnosed with diabetes insipidus at age 4 years, confirmed by water deprivation test during which her sodium rose to 153 mmol/l (nl 133-148) and serum osmolality rose to 307 mmol/kg (nl 283-292).

Evaluation: She was on desmopressin 0.15 mg BID, as well as carbamazepine 200 mg BID and naproxen at the time of her evaluation. Due to hyponatremia, her desmopressin dose was gradually decreased over four months until it was no longer needed. A water deprivation test was performed off desmopressin and confirmed the resolution of diabetes insipidus after 22 hours fasting with urine osmolality 607 mmol/kg (nl 50-1400mmol/kg), serum osmolality 287 mmol/kg, sodium 141 mmol/l, and a decrease in urinary output. Episodes of hyponatremia persisted.

Intervention: The possibility of a tubulopathy and salt wasting as a cause for the hyponatremia secondary to naproxen was entertained, therefore naproxen was discontinued. Sodium rose to normal but hyponatremia (Na 127 mmol/l) reoccurred within a short time. At age 17 years 1 month, SIADH was considered. Two months later, clobazam was restarted and she was gradually weaned off the carbamazepine over the next three to four months. Four months later, she was admitted with another hyponatremic seizure. While hospitalized, another water deprivation test showed peak sodium 152.3 mmol/l, serum osmolality 315 mmol/kg, and urine osmolality 126 mmol/kg, indicating the diabetes insipidus had returned and desmopressin was restarted at 5 micrograms intranasally daily.

Discussion/Recommendations: The recurrent episodes of hyponatremia, followed by the confirmation of resolution of DI after starting carbamazepine and the subsequent recurrence of DI after discontinuing carbamazepine, supports the association of SIADH with carbamazepine. Therefore patients requiring both medications should be monitored for hyponatremia. Frequent contact with the family ensured accurate monitoring of the patient’s fluid balance, sodium levels and desmopressin requirements.

008 - The Use of Leptin Therapy in the Treatment of Extreme Metabolic Abnormalities in a Girl with Congenital, Generalized Lipodystrophy
Patty Graves MS, RN, CPNP, CDE
**Demographics:** H.J. is a 15 year old African American female with lipodystrophic diabetes, hypertriglyceridemia, and amenorrhea.

**Clinical Presentation:** H.J. developed diabetes at 13 years of age and initiated basal/bolus insulin therapy. Her diabetes was not optimally controlled due to poor compliance, extreme hunger, and high insulin requirements.

**Past History:** H.J. was diagnosed at 2 months of age with lipodystrophy. She was noted to lack subcutaneous fat, had elevated triglycerides and failure to thrive. An oral glucose tolerance test at 15 months of age showed normal glucose levels and insulin resistance.

**Evaluation:** Her highest HbA1c reached 11%. Her lowest HbA1C (8.3%) was after starting pump therapy. Other diagnostic studies showed a leptin level of 1.9 ng/ml (normal 3.3-18.3). A lipid profile showed triglycerides 1604 mg/dL (normal < 150), cholesterol 460 mg/dL (normal < 200), HDL normal at 35.9 umol/L; the LDL unable to calculate due to her elevated triglycerides.

**Interventions:** At 15 years of age, she was transitioned to pump therapy allowing more flexibility and improving glucose control. Due to high insulin requirements (exceeding 2 units/kg), she was converted to U-500 insulin. Her hyperlipidemia was treated with a statin and niacin. The family was encouraged to enroll in a National Institutes of Health study using Leptin which has been successfully used in treating metabolic abnormalities of lipodystrophy. She received twice daily Leptin injections and within two months discontinued insulin. Her most recent HbA1c was 6.8%. She continues on treatment of her abnormal lipid profile but her levels have improved considerably. Her appetite is estimated to be half of pretreatment and her menses are regular. She continues the leptin injections.

**Discussion/Recommendations:** Lipodystrophies are heterogeneous, genetic, or acquired disorders characterized by loss of body fat and insulin resistance. The extent of fat loss determines the severity of the metabolic complications such as diabetes mellitus, hypertriglyceridemia, and amenorrhea. Because of the loss of adipose tissue, levels of the adipocyte-secreted hormone leptin are low. Leptin therapy has been successful in ameliorating associated metabolic abnormalities. The role of the endocrine nurse is essential in the extensive counseling, patient education, and coordination of care needed for successful management of these patients.

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**009 - A Case of a Pre-Adolescent Female with a Triad of Bone Diseases**

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**Demographics:** 12 year 8 month old Caucasian female

**Clinical Presentation:** CM presented to the endocrinology clinic at age 10 years 3 months with lumbar and lower thoracic vertebral compression fractures. She was referred from the orthopedic clinic for endocrine evaluation of back pain and osteoporosis. She had spine x-rays and MRI which indicated severe osteoporosis, and significant loss of vertebral body height in the thoracolumbar region.

**Past History:** She was the product of fraternal twin gestation, with birth weight of 5 pounds, 11 ounces. Previous fractures of the clavicle and finger have been reported. She has central obesity with BMI 26.6 kg/m² (>97%). She drinks little milk, does not take vitamins, and participates in age-appropriate activities. Twin is unaffected.

**Evaluation:** Height 135 cm (10-25%ile), weight 48.4 kg (75-90%ile). Physical exam reveals a buffalo hump on the upper back, without abdominal striae. Laboratory assessments include:
IGF-1 71 (117-771 ng/mL), 25-hydroxy vitamin D 20 ng/mL, alkaline phosphatase 216 (80-240 units/L), thyroid function studies normal, parathyroid hormone normal, morning cortisol 19.0 (2.9-19.4 µg/mL), urinary free cortisol 10.3 (1.0-45.0 µg/24 hr), growth hormone stimulation test using arginine and insulin with growth hormone maximum 0.8 ng/mL, and genetic testing for collagen mutation revealed a COL1A2 mutation consistent with osteogenesis imperfecta (OI). Radiologic assessments include: bone age 11 years at 10 years 3 months, and pituitary MRI normal. DEXA scan revealed bone mineral density (BMD) significantly below the expected range for the patient age.

**Interventions:** CM was started on vitamin D supplementation 2000 IU/day for vitamin D deficiency. She was begun on growth hormone therapy at a dose of 0.3 mg/kg per week for severe growth hormone deficiency. Two years post therapy reveals no back pain, decreased fracture rate, increase in height to the 50th percentile, normal IGF-1, significant improvement in BMD, and repair of compressed vertebrae.

**Discussion:** Both growth hormone deficiency and OI can contribute to loss of bone integrity, resulting in osteopenia or osteoporosis. The combination of these two conditions has resulted in significant impact upon the bony structure. Replacement with growth hormone only has demonstrated significant improvement in her medical condition.

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**010 - Identifying Depression in an Adolescent Diabetic Patient: A Case Study Depicting the Use of the Patient Health Questionnaire-9 Depression Screen**

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**Demographics:** WA is a 13 year 5 month old Hispanic female, who lives with her mother and sister. She is a ninth grade honor student and active in track.

**Clinical Presentation:** Presented at diabetes clinic with a HbA1c 10.1% (normal <6.5%). Although pleasant and cooperative, she admits to not always checking her blood sugar as instructed. Well-healed lacerations noted on left forearm.

**Past History:** Diagnosed with Type 1 diabetes at age 8 years. Past HbA1c results range 9.5-10.4%, indicating poor glycemic control. Started on a Lispro/NPH regimen at diagnosis, switched to a basal/bolus regimen 6 months prior. Hospitalized with DKA (diabetic ketoacidosis) one month after starting the basal bolus regimen. Started Lisinopril for proteinuria eight months ago.

**Evaluation:** The Patient Health Questionnaire-9 (PHQ-9) depression screen was administered by her diabetes team. Her PHQ-9 score was 13, which is positive (scores of 5, 10, 15 and 20 represent mild, moderate, moderately severe and severe depression, respectively). Upon discussion, patient cried that two weeks ago she “wanted to die” and made superficial cuts on her forearm. She was not in counseling and has no prior mental health history. Mother and sister were aware but did not report the incident.

**Interventions:** WA met with a social worker and was cleared of an active suicide risk. She was referred for psychiatric counseling. Patient returned to clinic in 8 weeks with PHQ-9 score improved at 5. She had been meeting with a school counselor, and had no further self-inflicted cutting, nor thoughts of suicide. HbA1c worsened at 12.2%. Efforts to improve her glycemic control through nursing support and diabetes education are ongoing. She was again referred for psychiatric counseling.

**Discussion/Recommendations:** Depression is three to four times as common in diabetic adolescents as in the general population. Depression and diabetes are associated with a ten-fold increase in suicide and suicidal ideation. The PHQ-9 is a nine question, easy to score assessment.
A tool that can be used in adolescents to diagnose depression. WA’s positive depression screen and subsequent disclosure of suicidal thoughts were surprising, and discovered via the depression screen. This case study supports the need for formal depression screening to become standard of care in our adolescent diabetes clinics.

011 - Individualized Gonadotropin-Releasing Hormone Agonist Therapy in Young Male with Central Precocious Puberty
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Demographics: A 3.6-year-old Caucasian male presented with early puberty.
Clinical Presentation: Parents noticed his deepening voice, facial hair, pubic hair, and penile growth 1-2 months before evaluation. Height was +2.9 s.d., weight +3.8 s.d., BMI >97th percentile, testes Tanner stage (TS) 2 (6 mL), pubic hair TS 3, and penile length 9.5 cm.
Past History: There was no exogenous hormone exposure. Growth velocity (GV) was 13.1 cm/year. There was no family history of precocious puberty or short stature. Mid-parental height was 184.2 cm. Paternal grandfather had a pituitary tumor.
Evaluation: Bone age (BA) was 7 years. Bayley-Pinneau predicted adult height (PAH) was 161.3 cm. Random luteinizing hormone 4.9 mIU/mL, follicle stimulating hormone 4.5 mIU/mL, and testosterone 780 ng/dL were elevated. Adrenal steroids, chemistries, human chorionic gonadotropin tumor marker, carcinoembryonic antigen, and thyroid stimulating hormone were normal. MRI of head and CT of chest, abdomen, and pelvis were normal.
Interventions: At 3.8 years, he started leuprolide acetate depot-ped 11.25 mg IM every 28 days. At 4.1 years, GV was 16.6 cm/year, BA 11.5 years, and PAH 156.2 cm. Leuprolide was increased to 15 mg IM every 28 days. At 4.3 years, penile length was 10.5 cm. At 4.6 years, he had increased aggression and mood swings, GV 11.2 cm/year, BA 11.75 years, and testes 8 mL. Leuprolide was increased to 15 mg IM every 25 days, tolerated well, and continued until age 11 years when BA was 14.5 years, height 165.7 cm, and TS 2 testes and pubic hair. At 11.8 years, BA was still 14.5 years, height 170.3 cm, and TS 4 testes and pubic hair. At 12.5 years, height was 175.9 cm and GV 8.1 cm/year.
Discussion/Recommendations: His low PAH was likely overestimated since BA was advanced by 3.4 years at presentation and then advanced by 7.4 years after three months’ treatment. However, increasing the frequency of leuprolide depot injections slowed bone age progression significantly. Recent stature was near target height range. This case demonstrates benefits of individualizing gonadotropin-releasing hormone agonist therapy until pubertal suppression is achieved. No literature was identified on increased injection frequency when standard therapy fails to suppress puberty, therefore further study is needed.

012 - Severe Hypoglycemia as a Presenting Symptom of Celiac Disease in an Adolescent with Type 1 Diabetes
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Patient Demographics: CS is a 15 year old female with type 1 diabetes for twelve years. She also has a history of autoimmune thyroiditis, insulin resistance, vitamin D deficiency, and hypertriglyceridemia.
Clinical Presentation: Patient presented with a hypoglycemic seizure (glucose 39 mg/dl) and recovered uneventfully. Over the next four days, CS continued to demonstrate persistent profound hypoglycemia despite serial reduction in her insulin doses. Basal insulin was completely discontinued with occasional prn doses of rapid-acting insulin required for glucose values > 200 mg/dl.
Past History: HbA1c levels had ranged from 9.4 to 10.3% over the last 12 months. CS had negative celiac screening 9 months previously and had a negative small bowel biopsy 18 months ago secondary to gastritis.

Evaluation: Patient was evaluated in clinic and had a 250 mcg ACTH stimulation test to evaluate for Addison’s disease. The peak cortisol value was 35.8 mcg/dl (nl >20). Insulin autoantibody was negative. Thyroid studies were within normal limits. Random insulin level was 20.3 uIU/ml. Anti-human tissue transglutaminase IgA was positive at 129 U/ml, anti-endomysial IgA was positive, and gliadin IgA was positive. Serum IgA was normal at 82 mg/dl. HbA1c was 8.7%, which was down from 9.4% three weeks before.

Interventions: The patient had small bowel endoscopy and biopsy performed which confirmed the diagnosis of celiac disease and she was started on a gluten-free diet. Her insulin doses were decreased by 25% and slowly titrated up to previous doses as her hypoglycemia resolved.

Discussion/Recommendations: Children and adolescents with type 1 diabetes are in close contact with their diabetes educator or nurse practitioner who are the first to encounter patients with hypoglycemia. Patients with type 1 diabetes and a sudden onset of hypoglycemia with decreasing insulin doses are often screened for Addison’s disease; however, the rate of Addison’s disease is only 2% in type 1 diabetes. Celiac disease has a much higher prevalence ranging from 5-10%. Patients with persistent or severe hypoglycemia should be screened for celiac disease even if previous screening labs have been negative.

PRODUCT-BASED RESEARCH

013 - Continuous Hormone Suppression and Improved Auxology Outcomes in Children with Central Precocious Puberty Who Received a Once-Yearly Histrelin Subcutaneous Implant for 4 Consecutive Years
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Background: Gonadotropin-releasing hormone analog (GnRHa) therapy is the standard of care for patients with central precocious puberty (CPP), defined as the reactivation of the hypothalamic-pituitary-gonadal (HPG) axis before age 8 in girls and age 9 in boys. Aims: To report on the prospective long-term extension of an extended-access, open-label phase 3 trial that evaluated the efficacy and safety of once-yearly histrelin therapy through 4 years.

Methods: Patients received 4 consecutive once-yearly histrelin implants. GnRHa-stimulated (peak) luteinizing hormone (LH), peak follicle-stimulating hormone (FSH), and basal estradiol levels were measured. Auxology outcomes including bone age/chronological age (BA/CA) ratio and Bayley-Pinneau–predicted adult height (PAH) were assessed. Adverse events were recorded.

Results: Thirteen children (12 girls; mean age at baseline [time of first implant] 6.6 years [range, 4.5–9.1 years]) received a fourth implant. Mean peak LH levels at 48 months were significantly suppressed compared with baseline (0.36 vs 13.71 mIU/mL; P=.014). Mean peak FSH levels at 48 months were also significantly suppressed compared with baseline (1.92 vs 11.27 mIU/mL; P=.005). Among the girls, mean estradiol level at 48 months was 5.22 pg/mL (vs 6.58 pg/mL at baseline; P=.285). Among all the patients, mean BA/CA ratio was significantly lower (1.16 vs 1.41; P<.001) and PAH was significantly increased (157.36 vs 150.05 cm; P=.015) at 48 months compared with baseline. During 4 years, the most frequently reported adverse event was implant site reaction (pain and discomfort), which occurred in 9 patients; majority of implant
site reactions occurred within 1 week of implant. No patient discontinued during the fourth year of histrelin implant therapy.

**Conclusions:** Four years of continuous histrelin implant therapy is effective in suppressing the HPG axis and improving auxologic outcomes in patients with CPP.

**Clinical Implications:** When indicated, long-term GnRHa therapy delivered by the once-yearly histrelin implant treatment for CPP provides continued efficacy through 4 years; biochemical suppression continues and PAH increases. This once-yearly GnRHa therapy option eliminates the need for intramuscular injections associated with other GnRHa therapies.

**015 - Long-Term Growth Hormone Therapy is Associated with a Dose-Dependent Increase in Height SDS and Insulin-Like Growth Factor-I SDS in Short Japanese Children Born Small for Gestational Age**

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**Background:** In children with short stature born small for gestational age (SGA), growth hormone (GH) treatment is associated with an acceleration of growth allowing most to achieve an adult height adequate for their target height. The pathophysiology of growth failure may arise from anomalies in the GH–IGF axis, including deficits in GH/IGF-I concentrations and/or GH/IGF-I sensitivity.

**Aims:** There is limited data on long-term GH therapy in Japanese children born SGA. This report investigates the relationship between GH dose, Δheight SDS (HSDS) and ΔIGF-I SDS.

**Methods:** Data were analyzed from a 156-week extension of a 104-week multi-center, randomized, double-blind, parallel group trial investigating the efficacy and safety of GH. Sixty-five children born SGA (age 3–8 years) received GH at 0.033mg/kg/day (n=31, 64.5% male, mean age 5.34 years) or 0.067mg/kg/day (n=34, 58.8% male, mean age 5.27 years). Changes from baseline in HSDS, IGF-I SDS, and bone age (BA) were recorded.

**Results:** After 260 weeks of GH treatment, ΔHSDS for chronological age (CA) was significantly positively correlated with ΔIGF-I SDS (n=57; r=0.664; p<0.0001). A greater increase in ΔHSDS and ΔIGF-I SDS was observed in the 0.067 than 0.033mg/kg/day group; a correlation between ΔHSDS and ΔIGF-I SDS was shown in both groups (0.067mg/kg/day: r=0.579; p=0.0010; 0.033mg/kg/day: r=0.715; p=0.0001). ΔHSDS was positively correlated with ΔIGF-I SDS in male (n=36; r=0.707; p<0.0001) and female (n=21; r=0.685; p=0.0006) patients. Mean bone age (BA) was delayed at baseline (BA/CA ratio <1) but increased during GH treatment. BA/CA ratio reached 1.01 in the 0.033mg/kg/day group and 1.09 in the 0.067mg/kg/day group at 260 weeks.

**Conclusions:** In short Japanese children born SGA, long-term GH therapy was associated with a dose-dependent increase in IGF-I that positively correlates with changes in HSDS. No acceleration of BA was noted in the low-dose group but a minor acceleration was seen in the high-dose group.

**Clinical Implications:** Long-term GH therapy in short Japanese children born SGA resulted in height gains that positively correlated with GH dose. Bone age advanced during the study but remained within normal limits.

**016 - Intuitiveness, Ease-of-Use and Dose Force in Two Growth Hormone Injection Devices**

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Background: Intuitive, easy-to-use devices with reduced dose force facilitate the self-administration of injectable medication and may therefore improve adherence.

Aims: Intuitiveness, ease-of-use and dose force are compared in two growth hormone (GH) injection devices: Norditropin FlexPro® (FP) (Novo Nordisk A/S, Denmark) and Genotropin GoQuick® (GQ) (Pfizer Inc., NY, USA).

Methods: Children treated with GH (≥6 months) were randomized to intuitiveness (INT, n=32; mean[SD]age, 13.1[2.1] years) or instruction (INS, n=32; age, 13.4[2.0] years) groups. The INT group received brief instruction on device use; the INS group received full instructions according to the patient user guide. The time taken to set a dose of 1.5mg and inject into an Eppendorf tube was recorded for each device. Intuitiveness/device preference was subsequently assessed by questionnaire. Maximum dose force was determined for a 1.5mg dose at speeds of 4, 6 and 8mm/s. Dose accuracy and precision were assessed at 0.1, 0.75 and 1.5mg doses.

Results: Dose delivery time was significantly lower with FP than GQ (INT, 40s vs. 66s; p=0.001; INS, 41s vs. 48s, p=0.026). Compared to GQ, FP was rated as the easiest-to-use, most intuitive, and device of overall preference. In the INT group, 97% reported that they felt confident operating FP without instruction (31% for GQ). Estimated relative dose force for FP was significantly lower than for GQ (3.6, 4.4, 5.2; p<0.0001) at all injection speeds (4, 6, 8mm/s). Dose accuracy at 0.10, 0.75 and 1.5mg doses was 97, 99 and 99% for FP and 100, 95 and 97% for GQ, respectively. Dose precision was 2.5, 0.8 and 0.8% for FP and 11.1, 2.6 and 1.6% for GQ.

Conclusions: FP is an intuitive, easy-to-use device with reduced dose force and improved dose precision compared with GQ. Patients felt confident using FP without instruction and reported a preference for the FP device over GQ.

Clinical Implications: Norditropin FlexPro® is an easy-to-use device with a reduced dose force and improved dose precision. This is relevant to pediatric patients and pediatric endocrinology nursing since patient preference for the FP device may improve adherence and compliance to treatment regimens, and lead to improved clinical efficacy.