ference (6.27 vs 6.30 correspondingly, p=0.374). **Conclusion.** The use of the application helped to increase the length of monitoring period, the amount of data that patients perceived in the diary and improved glycemic control. This can be due to an increased motivation to keep records and to a reduction of burden associated with traditional diaries. More detailed analysis on achieving BG goals and delivery outcomes will be held in further studies.

KEYWORDS: gestational diabetes, mobile app.

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EFFECT OF FAMILY INTERVENTION TO CONTROL TYPE 2 DIABETES IN YOUNG: A CONTROLLED CLINICAL TRIAL

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Introduction. With the increasing number of young type 2 diabetes mellitus (T2DM) patients in India, it has become a great challenge for clinicians to achieve strict glycemic control and prevent complications in this population of patients. We studied the effectiveness of a family oriented intervention designed to improve glycemic control of these patients in a specialised diabetes clinic. There are very few studies have ever been done on this aspect on type 2DM. **Aim.** Our aim of this study was to see the effect of family intervention in these patients on glycemic control as reduction of HbA_{1c} to ⩽6.5 % over and above standard care. **Material and methods**. Young (18—25 years) newly diagnosed ,drug naïve T2DM patients from our clinic were selected for the study as per patient'. Patients were selected with type 2DM with HbA_{1c} between >7% to < 9% and living with at-least one family member(not alone). One group (A) of patients received the family oriented intervention; patients from the other group (B) received standard care. The intervention involved family members which included one amongst "father ,mother, wife or husband " and included family counselling during clinic visits, family meetings and home visits by a dedicated diabetes educator . The primary outcome was HbA_{1c}, measured at 6 and 12 months. **Result**. A total of 205 patients were enrolled and they were divided into group A (n=103) and group B (n=102). All patients completed the study. The HbA_{1c} from baseline to 12 months was a significantly different between groups (p<0.005). During the later period (6—12 months), when the patients in the group A showed further improvement in their HbA_{1c} reduction (p<0.001) compared to Group B patients. **Conlcusions.** In T2DM in young patients a significant reduction in HbA1c was seen when the family intervention was provided over standard intervention.

KEYWORDS: young type 2 diabetes mellitus, diabetes clinic, family intervention.

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ASSOCIATIONS OF THE POLYMORPHISMS KCNJ11, ADIPOQ, ADIPOR2, IGF1B2 OF THE GENES WITH INSULIN RESISTANCE AND FUNCTIONAL ACTIVITY OF PANCREATIC B-CELLS IN WOMEN WITH METABOLIC SYNDROME

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Purpose. To evaluate the association of alleles and genotypes of the polymorphisms KCNJ11 ADIPOQ, ADIPOR2, IGFBP2 genes with insulin resistance and functional activity of pancreatic β-cells in women with metabolic syndrome. **Material and methods.** A survey of women in the Russian population with obesity and metabolic syndrome. Insulin resistance (IR) and functional activity of pancreatic β-cells were determined using the HOMA-IR ⩾2.77 and HOMA-β ⩾180% indices (D. Matthews et al., 1985). The polymorphisms of the genes candidate for IR and insulinopenia were determined: rs16928751 of the *ADIPOR2* gene, rs2241766 of the *ADIPOQ* gene, rs5219 of the *KCNJ11* gene, rs4402960 of the *IGFBP2* gene. Genotyping of the polymorphisms of candidate genes of IR and insulinopenia was carried out on the basis of the Laboratory of Molecular Diagnostics and Genomic Dactyloscopy of the State Scientific Center of the Russian Federation «GosNIIGenetika», Moscow (Doctor of Biological Sciences, professor V.V. Nosikov). **Results.** Higher values of the HOMA-IR index [6.3 (3.6, 10.8)] in women with the Lys/Lys genotype of the polymorphism rs5219 of the *KCNJ11* gene were determined than in the carriers of the genotypes Glu/Glu and Glu/Lys 3,8 (2,2, 7,0) and 3,6 (2,3, 5,6) (p<0,01). It was established that HOMA-β index ⩾180% is more often detected in carriers of genotypes G/A + A/A (34.2%) than in persons with genotype G / G of the polymorphism rs16928751 of the *ADIPOR2* gene (18.8%) (p=0.04). The homozygous carrier of the T/T genotype of the polymorphism rs2241766 of the *ADIPOQ* gene was more often detected in obese and MS patients (94.3%) than in healthy individuals (72.1%)) (p=0.009). In women with obesity and IR, the carrier of the T allele and the T/T genotype of the polymorphism rs2241766 of the *ADIPOQ* gene increases (OR=3.21 95% CI 1.01—10.24; p<0.05 and OR=6.39 95% CI 1.32—30.86; p=0.009), and the carriage of the G allele and the G/T genotype of rs2241766 of the *ADIPOQ* gene reduces the risk of developing IR (OR=0.31 95% CI 0.10—0.99; p<0.05 and OR=0.04 95% CI 0.1—0.80; p=0.009). Carriers of the T/T genotype of the polymorphism rs4402960 of the *IGF1B2* gene had a higher HOMA-IR index, along with a low HOMA-β index of 7.0 (5.9; 8.9) and 59.1% (37.7; 153.8%) than individuals with genotypes G/G and G/T [3.9 (2.3, 7.4), 105.3 (53.1, 157.50 and 3.4 (2,2; 4.9), 121.3 (76.3, 170.9; p<0.05)]. **Conclusions.** These data suggest that the relationship between insulin resistance and the functional activity of β-cells of the pancreas of the polymorphisms rs5219 KCNJ11, rs2241766 *ADIPOQ*, rs4402960 *IGF1B2*,

rs16928751 *ADIPOR2* genes in women of the Russian population.

KEYWORDS: obesity, metabolic syndrome, genotypes of the polymorphisms.

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FERTILITY RESTORATION IN A PATIENT WITH RESISTANT PROLACTINOMA AFTER COMPLEX THERAPY OF DOPAMINE AGONIST AND SELECTIVE ESTROGEN RECEPTOR MODULATOR

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Introduction. Prolactinomas are the most common pituitary adenomas and dopamine agonists (DA) still remain the first choice of treatment. Nevertheless it does not always exert an adequate effect and endocrinologists face the challenge of resistant prolactinomas more frequently. This problem is very important for women of reproductive ages who desire to recover fertility. We present a clinical case of a woman with DA resistant prolactinoma and primary amenorrhea who had recovered regular menstrual cycle and ovulation after one year of combination treatment with cabergoline and tamoxifen. **Clinical case.** In 2002 a 12-year old woman was referred to our tertiary care center with hyperprolactinemia (prolactin (PRL) level 5000 IU/l (90—540), no macroprolactinemia) and macroprolactinoma 10×18×10 mm by MRI. Administration of cabergoline with maximum dose 3.5 mg a week did not result in significant clinical or laboratory improvement. In 2004 transnasal transsphenoidal adenomectomy was performed. Postoperative prolactin levels remained high. For short period the patient received injections of octreotide without effect. In 2006 the repeat operation was conducted because of additional tumor tissue of 8×7×10 mm on MRI. After surgery PRL decreased to 3000 IU/l, cabergoline therapy was restarted in dose 1 mg per week with gradually increasing up to 4.5 mg that allowed to stabilize tumor growth, but without recovery of menstrual cycle. During examination in 2015 PRL level was 6000 IU/l, endoparasellar adenoma visualized on MRI and hypoplasia of the uterus with the lineal endometrium were detected. As an antitumor agent, the patient was assigned a treatment with selective estrogen receptors modulator (SERM) tamoxifen — in a dose 20 mg per day in combination with cabergoline in a dose 4.5 mg per week. After one year of such therapy the prolactin was 15000 IU/l, adenoma's MR-characteristics didn't reveal any negative trend. At the same time the patient noted that menstrual function restored in 3 months after starting tamoxifen. Ultrasound examination confirmed normal uterus size and adequate endometrial thickness; also, the left ovary contained corpus luteum. The therapy was prolonged with recommendations of careful ultrasound control of endometrium state and barrier contraception. **Conclusion.** This case demonstrates reversion of symptoms of hyperprolactinemic hypogonadism in a patient with DA resistant prolactinoma due to SERM treatment without prolactin level normalization. The pathophysiological mechanisms underlying the phenomenon are not clear but may be due to the changers in interactions of kisspeptin neurons involved in GnRH secretion due to modulation of negative and positive estrogen feedback.

KEYWORDS: hyperprolactinemia, plolactinoma, tamoxifen, cabergoline.

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EPIGENETIC ASPECTS OF BONE METABOLISM REGULATION IN PATIENTS WITH ENDOGENOUS HYPERCORTISOLISM

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Objective. To investigate mRNA and microRNA related to bone of remodeling in bone tissue samples from patients with Cushing's disease (CD). **Material and methods.** Patients with clinically evident and biochemically proven active CD and patients with hormonally inactive pituitary adenoma matched by age, sex and BMI were invited to participate. Bone samples were taken during transsphenoidal adenomectomy from the base of the sella-turcica, immediately placed in lysis buffer (QIAzol) and subjected to homogenization. 24h urine free cortisol (24hUFC) was measured by an immunochemiluminescence assay on a VitrosECi (60-413 nmol/24 h). Total RNA isolation from bone tissue with on-column digestion of the genomic DNA was carried out with miRNeasy Mini Kit on the automatic station «QIAcube». Reverse transcription was carried out using a High-Capacity RNA-to-cDNA Kit. Gene expression analysis was performed by Real-Time PCR on StepOnePlus instrument with Custom TaqMan Array 48 Plus plates. MicroRNA expression analysis was carried out by TaqMan Advanced miRNA Assays. **Results.** We enrolled 24 subjects (15 patients with CD and 9 with hormonally inactive pituitary adenomas); 18 females and 6 males, the mean age was 41 years (confident interval (CI) 95% 36—46) mean BMI — 29 (CI 95% 26—32) kg/m^2. There were no significant difference between the groups. Mean 24h UFC in subjects with CS — 1168 (CI 95% 702—1634) nmol/24h. Expression of osteoblast activity and bone formation genes was decreased in patients with CD: ALPL 0.34 (CI 95% 0.24—0.43; p<0.001), BGLAP 0.41 (CI 95% 0.28—0.54; p<0.001), COL1A1 0.26 (CI 95% 0.14—0.37; p<0.001), COL1A2 0.51 (CI 95% 0.33—0.69; p<0.001), MMP2 0.52 (CI 95% 0.41—0.62; p<0.001). The expression of SOST 5.3 (CI 95% 1.8—8.8; p<0.001), WNT10B 10.24 (CI 95% 5.26—15.22; p<0.001), WNT3A 1.44 (CI 95%