Abstract: Polycystic ovarian syndrome (PCOS) is one of the common endocrine diseases that lead to female reproductive dysfunction. Up to 75% of PCOS patients have endocrine and metabolic abnormalities such as obesity, hyperinsulinemia and hyperandrogenemia. As a classic PCOS drug, CPA/EE is mainly used to adjust estrogen and progesterone levels and menstrual cycle. Recent studies have found that this drug may worsen blood lipids and reduce insulin sensitivity. On the other hand, studies have found that reproductive disorders secondary to metabolic disorders can be improved by correcting metabolic disorders. glucagon-like peptide1 receptor agonist (GLP-1 RA) is a new type of glucagon-like glucagon-like peptide1 receptor agonist, which has a significant effect on the improvement of metabolic disorders in obese patients. This topic aims to study.To observe the effects of metformin combined with CPA/EE or GLP-1RA on blood glucose, blood lipids, sex hormone levels and menstrual cycle in overweight PCOS patients.

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Research department/project leader	Endocrinology Department / Min Long
Research category	Clinical research, source: self raised
Title of the study	The Effect of GLP-1 Agonists Versus OCs on Reproductive Disorders and Cardiovascular Risks in Overweight PCOS
NTC Number	NCT03151005
Research duration	3 years
Number of research and design cases in this center	60 cases
Study design	All subjects underwent height, weight, waist and hip, hip circumference, blood pressure, hairy score, blood biochemistry (blood routine, liver and kidney function, electrolyte, thyroid function, fasting blood glucose, glycated hemoglobin, insulin release test, inflammatory markers, sex hormones, eight items), gynecologic color Doppler ultrasound and glucose clamp examination before admission. After informed consent was obtained, 1ml of the remaining plasma was collected and frozen in the refrigerator at -80℃. Patients with BMI≥24kg/m² or waist circumference ≥85cm were randomly assigned to GLP-1RA+ metformin or Diane-35 + metformin. After 1 month, all subjects were examined: height, weight, BMI, waist circumference, hip circumference, waist-to-hip ratio, menstrual history, hirsutism score, diet, exercise frequency and intensity, blood pressure and blood biochemistry. After 3 months, the general condition of all subjects and general biochemical tests such as blood lipid, liver and kidney function, fasting blood glucose, glycated hemoglobin, insulin release test, inflammation markers and gynecological color ultrasound were tested again, and 1ml of plasma was collected and frozen in the refrigerator at -80℃.
Trial objective	1. Provide new treatments for overweight or obese patients with PCOS. 2. Improve PCOS and establish regular menstrual cycles by reducing weight and correcting metabolic disorders.
Name and specifications of the required drugs or equipment Grid, manufacturer, and quantity	Metformin enteric coated tablets: Hebei Tiancheng Pharmaceutical Co., Ltd., trade name: Junshida, dosage: 0.5g orally 3/day; Liraglutide injection: Novo Nordisk, Denmark, trade name: Novo Nordisk, dosage: 0.6mg subcutaneous injection once a day, increased to 1.2mg after 1 week, maximum dose is 1.8 mg/d; Acetylenylestradiol cycloproterenone tablets: Bayer AG, Germany, trade name: Diane-35, dosage: 1 tablet taken orally starting from the first day of the menstrual cycle,Take 1 tablet daily for 21 consecutive days, discontinue for 7 days。
Inclusion and exclusion criteria	**Inclusion criteria :** a) clinical diagnosis of PCOS according to the Rotterdam criteria based on the presence of two of three criteria (3) , oligomenorrhoea, clinical or biochemical hyperandrogenism, and polycystic ovaries on ultrasound after exclusion of other endocrine causes of hyperandrogenism; b) participants had no concurrent illness and were not on any prescription or over-the-counter medication that was likely to affect insulin sensitivity or lipids for the preceding 12 weeks; c) participants were advised not to change physical activity or dietary habits during the study period; d) given that all subjects were of Asian ethnicity, overweight was defined as BMI ≥ 24 kg/m2. e.) all subjects had normal thyroid-stimulating hormone and prolactin levels. **exclusion criteria :** a) age below 18 years or over 50 years; b) uncontrolled hypertension (blood pressure ≥160/100 mmHg); c) signs of liver or renal failure or active liver disease (alanine transaminase (ALT) > 2.5× the upper limit of normal values); d) patients who were postmenopausal or pregnant; e) alcohol intake greater than 20 g/day; f) patients who could not complete the intervention or had other conditions that made them ineligible for participation. For example, patients taking glucocorticoid steroids or under treatment for a malignant tumor were excluded.

Subject benefits and possible risks and compensate	This study is an intervention clinical observation trial. Due to the needs of the treatment of their own diseases, the subjects need to collect venous blood for blood sugar, insulin and other tests. After informed consent, the researchers will collect 1ml of the remaining serum, 1m of plasma and 1ml of urine after testing in the laboratory, so as to avoid repeated blood extraction of the subjects and protect the interests of the subjects to the greatest extent. The drugs used in the study were all conventional treatment drugs for newly diagnosed polycystic ovary syndrome. For the survey subjects, through baseline examination and follow-up, the drug response of patients and the therapeutic effect of improving metabolic and reproductive disorders can be clarified, providing a basis for the postoperative treatment of patients and the selection of drugs for the prevention and treatment of complications. In addition, survey subjects can also pass after 3 months.Follow-up examination to understand the efficacy and safety of its treatment.
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