Young People With PCOS And T2DM: Case Studies On Public Health Care

Jovens Com SOP E DM2: Estudo De Casos Sobre Atendimento Público Em Saúde

Jóvenes Con Sop Y Dm2: Estudio de Caso Sobre Atención En Salud Pública

RESUMO

Objetivo: Descrever a relação da síndrome do ovário policístico (SOP) com a diabetes mellitus tipo 2 (DM2), seus fatores de risco, bem como opções terapêuticas e as consequências desse distúrbio sobre a saúde da mulher. Método: Foi realizada a análise de quatro prontuários de pacientes portadoras da SOP no município de Joinville. Resultado: Entre 469 mulheres com SOP e DM2, 4 atendiam os critérios. Observa-se que a metformina pode ser menos eficaz para o hirsutismo em certos subgrupos, enquanto estudos indicam que o tratamento com metformina e ACH melhora parâmetros bioquímicos, mas não obesidade. Isto implica que a escolha do tratamento deve ser baseada nos sintomas, observando benefícios bioquímicos do tratamento combinado; visando os principais distúrbios endócrinos: hiperinsulinemia e hiperandrogenismo. Conclusão: Observou-se a correlação entre SOP e obesidade no desenvolvimento de diabetes e a necessidade de se estabelecer um tratamento para benefício tanto do sistema reprodutor quanto para o cardiovascular.

DESCRITORES: Síndrome do ovário policístico; Diabetes Mellitus tipo 2; Obesidade; Metformina.

ABSTRACT

Objective: To describe the relationship between polycystic ovary syndrome (PCOS) and type 2 diabetes mellitus (T2DM), its risk factors, as well as therapeutic options and the consequences of this disorder on women's health. Method: Four medical records of patients with PCOS in the city of Joinville were analyzed. Result: Among 469 women with PCOS and T2DM, 4 met the criteria. It was observed that metformin may be less effective for hirsutism in certain subgroups, while studies indicate that treatment with metformin and ACH improves biochemical parameters, but not obesity. This implies that the choice of treatment should be based on symptoms, observing biochemical benefits of combined treatment; targeting the main endocrine disorders: hyperinsulinemia and hyperandrogenism. Conclusion: A correlation between PCOS and obesity in the development of diabetes was observed and the need to establish a treatment to benefit both the reproductive and cardiovascular systems.

DESCRIPTORS: Polycystic ovary syndrome; Diabetes Mellitus type 2; Obesity; Metformin.

RESUMEN

Objetivo: Describir la relación entre el síndrome de ovario poliquístico (SOP) y la diabetes mellitus tipo 2 (DM2), sus factores de riesgo, así como las opciones terapéuticas y las consecuencias de este trastorno sobre la salud de la mujer. Método: Se realizó el análisis de cuatro expedientes de pacientes con SOP en el municipio de Joinville. Resultado: De las 469 mujeres con SOP y DM2, 4 cumplían los criterios. Se observa que la metformina puede ser menos eficaz para el hirsutismo en ciertos subgrupos, mientras que los estudios indican que el tratamiento con metformina y anticonceptivos hormonales (ACH) mejora los parámetros bioquímicos, pero no la obesidad. Esto implica que la elección del tratamiento debe basarse en los síntomas, observando los beneficios bioquímicos del tratamiento combinado, dirigido a los principales trastornos endocrinos: hiperinsulinemia e hiperandrogenismo. Conclusión: Se observó la correlación entre SOP y obesidad en el desarrollo de la diabetes, y la necesidad de establecer un tratamiento que beneficie tanto al sistema reproductivo como al cardiovascular.

DESCRIPTORES: Síndrome de ovario poliquístico; Diabetes mellitus tipo 2; Obesidad; Metformina.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent disease and represents the main endocrine-metabolic disorder in women of childbearing age. [1] Studies indicate that women with PCOS have an increased chance of developing type 2 diabetes mellitus (DM2) and glucose intolerance; in addition, in some cases, they are overweight. This topic is relevant due to the early risk of DM2 in this patient profile, as well as high body mass index – BMI – which contributes to the increased risk of insulin resistance (IR).

As patients diagnosed with PCOS are generally younger patients, the development of early T2DM can also cause women to present common complications of diabetes earlier, such as macrovascular (acute myocardial infarction, peripheral arterial disease, stroke) and microvascular (retinopathy, neuropathy and nephropathy).

Some patients with PCOS have obesity as a comorbidity. This is a factor that increases IR and can make the patient develop DM 2 more easily. In this sense, it is important to have interdisciplinary support for patients with PCOS, since monitoring by a nutritionist, physical educator, doctor and even a psychologist is necessary. Prevention of this disease is essential, and the earlier it is started, the greater the benefits will be. However, pharmacological intervention ends up being the main one, being the fomenter of the guiding question of this research: What reflections can be made about the pharmacology used in women with PCOS and DM2 - under 30 years of age and overweight - without generalizing the results - in public health care?

Although it is extremely necessary, many women are unable to receive multidisciplinary care for non-pharmacological treatment, since it is necessary to receive treatment from gynecologists, endocrinologists, nutritionists and, often, also from psychologists. Therefore, it is known that the SUS is unable to meet the needs of all patients and a large proportion of these patients do not have the financial resources to receive treatment privately.

Furthermore, some of the medications prescribed to patients with PCOS and DM2, which reduce peripheral insulin resistance and promote weight loss, are very expensive, making it difficult for patients to adhere to treatment. Thus, the possibility of creating support groups for PCOS and DM2 is highlighted, thus reducing costs and enabling the coverage of more women, and giving women the possibility of psychological support.

However, poor adherence to PCOS and DM2 treatment is often noted, often due to side effects of the medications and the lack of willingness of patients, as it requires a specific routine of better nutrition and regular, daily physical exercise. However, it is extremely important that

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the doctor-patient relationship be of high quality, to show patients the importance of adherence to pharmacological treatment and especially to non-pharmacological treatment, such as more restrictive diets and regular physical activity.

METHOD

The research was conducted through a case study, based on the work of Yin [2], in which a group of women was selected through secondary data, from medical records obtained from public health services in the city of Joinville SC (CAAE 26899319.7.0000.5366 CEPE - Universidade da Região de Joinville - Univille), from January to December 2020.

For the purpose of guiding the research, the guiding question was created based on the PICo method, as shown in table 1:

Table 1: elaboration of the guiding question

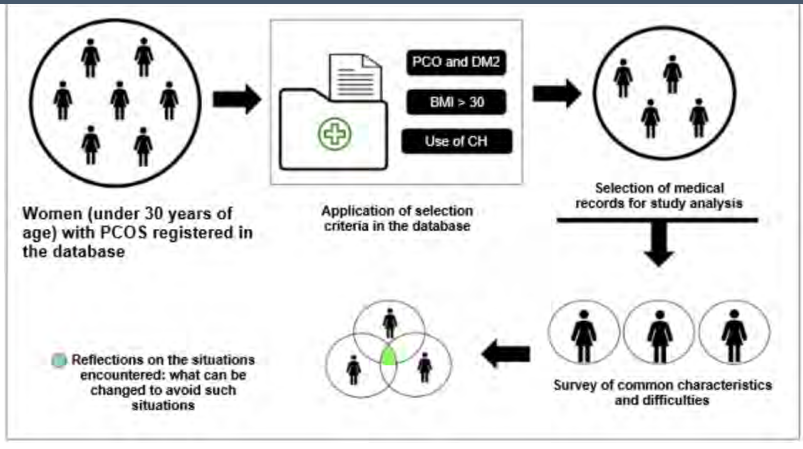
Population	Intervention	Context
Women with PCOS and DM2 under 30 years of age who are overweight	*Pharmacological therapy*	*Public care*

Source: The authors, 2024.

Therefore, the guiding question was defined as: What reflections can be made regarding the pharmacology used in women with PCOS and DM2 - under 30 years of age and overweight - without generalizing the results - in public health care?

The selection criteria were: Having PCOS and DM2 concomitantly, and being under 30 years of age (Figure 1)

Figure 1: Methodological path



Source: The authors, 2024.

Exclusions were related to factors linked to the development of DM2, such as [1] family history and [2] specific eating habits, as well as the presence of DM1.

According to Yin (2017) (2), the Case Study as an empirical research aims to investigate contemporary phenomena within a real-life context, used especially when the boundaries between the phenomenon and context are not very evident, such as the issue of the use of certain contraceptives and the risk of weight gain in young people under 20 years old with PCOS and DM2 (Figure 2).

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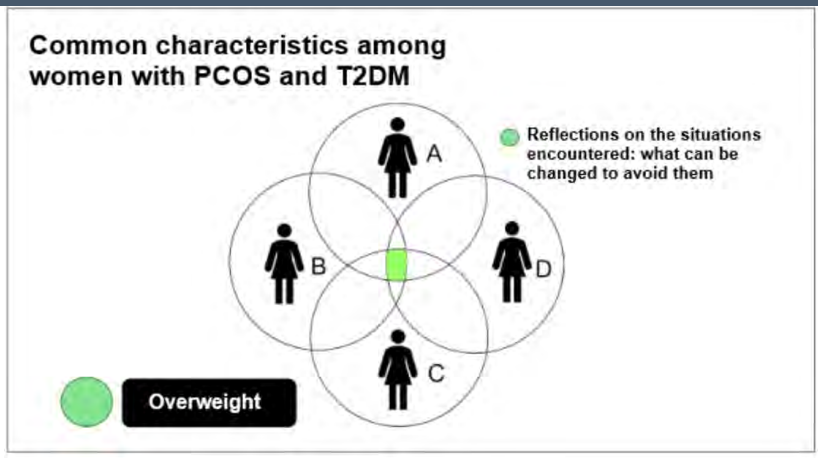
Figure 1: Methodological path



Source: The authors, 2024.

The aim was to simultaneously emphasize the unity and globality of this theme. The focus was on aspects that are relevant to the issue of whether or not hormonal contraceptives influence excess weight, which would also affect DM2, over a given period of time, to allow a clearer view of the phenomena through a dense description, as determined by Stake (2010). (3)

The therapeutic path was analyzed in the cases, including [1] medication indicated for PCOS in the medical records, the HC (hormonal contraceptive) used, visits to a nutritionist and whether there was an attempt at weight control (pharmacological or non-pharmacological).

RESULTS

Of a total of 469 women with PCOS and DM2, 4 met the criteria for age, BMI, and use of HC (hormonal contraceptive), as shown in Table 2.

Table 2: Characteristics extracted from the medical records of the selected patients. 1 year period (2020)

Pacient	Age (years)	Medication for PCOS	HC	bmi	Weight loss medication	Nutritional care	Weight control
A	*23*	*Metformina*	*Desogestrel 75 mcg*	*30*	*Nenhuma*	*Não*	*Não*
B	*20*	*Não*	*Ciproterona 2,0 mg + etinilestradiol 0,035 mg*	*34*	*Nenhuma*	*Sim*	*-5 kg*
C	*29*	*Metformina*	*Gestodeno 75 mcg+ etinilestradiol 0,03 mg*	*44*	*Buspropiona + Orlistat*	*Não*	*-6 kg*
D	*26*	*Metformina*	*Ciproterona 2,0 mg + etinilestradiol 0,035 mg*	*32*	*Nenhuma*	*Não*	*Não*

Source: INOVA SMS System Joinville SC.

The description of the cases follows below, in which the patients chosen for this case study were identified by the initial letters of the alphabet. The description of the cases includes: ID (identification), TP (treatment performed for PCOS – as described in the medical records), RF (risk factors), OC (observations and complaints), GPNPT (general pharmacological and non-pharmacological treatment).

Description of cases of young patients with DM 2 and PCOS

PATIENT A

ID 23-year-old woman. TP She was undergoing contraceptive treatment for PCOS (2 years), but stopped because she wanted to get pregnant. It was during a consultation with a private gynecologist that she discovered the onset of DM2 and began treatment with metformin 500 mg. She underwent treatment for approximately 6 months, but stopped on her own. RF She weighs 75 kg and is 1.60 m tall (BMI: 30), which indicates overweight. Upon return, the tests showed insulin resistance and the presence of ovaries with a microcystic appearance. She is a non-smoker and does not consume alcohol. She takes relatively good care of her diet and is sedentary. OC She says she is very sleepy, more than usual. She uses HC

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and denied using other medications. She has irregular menstrual cycles. She complained of occasional greenish discharge, has a history of recurrent candidiasis; she is married and says she has sexual relations about twice a week. GPNPT The patient and her partner are prescribed metronidazole treatment and follow-up with a gynecologist; an ultrasound scan is requested and desogestrel 75 mcg is prescribed, as well as metformin 500 mg. Tranexamic acid 250 mg is prescribed for up to 5 days, as well as neomycin + bacitracin for skin lesions on the lower limbs. At the next follow-up, after evaluation of the exams, grade II hemorrhoids are found. The patient is advised to continue the treatments. Combined oral contraceptive pills (COCPs) are considered first-line treatment for the management of patients with polycystic ovary syndrome (PCOS) without reproductive needs. They are responsible for the management of hyperandrogenism, for the regulation of the menstrual cycles of these women and result in the decline of androgen production. Despite the great advantages of using the pills, there is still insufficient information on which COCP preparation is ideal, with all agents being very effective in improving the clinical condition of these patients.

PATIENT B

ID A 20-year-old woman sought the women's health unit complaining of polycystic ovaries and metrorrhagia for more than 3 months, associated with dyspareunia and weakness with pain on deep palpation in the lower abdomen. She reported irregular cycles, menarche at 13 years of age, and denied other complaints. A transvaginal ultrasound with Doppler was requested. The result of the examination showed a right ovary with a micropolycystic appearance and a right paraovarian cyst. She brought previous exams to the consultation with a fasting blood glucose index of 238, closing the diagnosis of DM 2. TP Uses 2.0 mg of cyproterone acetate and 0.035 mg of ethinylestradiol. RF Non-smoker; sedentary, obese, with a diet rich in carbohydrates and fats. Weight 92 kg and 1.63 cm tall (BMI: 34). OC Denies other complaints. GPNPT She was referred to a nutritionist and was prescribed metformin every 12 hours, advised to make lifestyle changes. Upon returning again, she showed a weight loss of 5 kg since the last evaluation, with dietary changes and initiation of regular physical activities and no other complaints.

PATIENT C

ID A 29-year-old woman sought medical attention complaining of an adverse reaction to metformin. The patient is prediabetic, has PCOS and hypertension. She is grade III obese (BMI 44). She wants to get pregnant. She reported irregular menstrual cycles and should stop taking metformin. She was advised to reduce the dose of metformin to 500 mg/day, and to have a fasting blood glucose test and to start nutritional monitoring and physical activity. She is taking Gestodene 75 mcg + ethinylestradiol 0.03 mg. TP Metformin at a dose of 1 g/day RF She denied smoking, was sedentary, and had a high-carbohydrate diet. She denied family history, BMI 44 OC. She denied other GPNPT complaints. Upon return, the patient presented fasting blood glucose of 119, high blood pressure, and weight loss of 3 kg, with the indication of a new fasting blood glucose test, glycated hemoglobin, and the prescription of bupropion, orlistat, and topiramate. The following month, the patient returned with fasting blood glucose test results of 116 and glycated hemoglobin of 5.7%. She started going to the gym, but reported not adhering to the indicated treatment due to financial difficulties. The prescription was renewed and metformin XR 1.5 g/day was prescribed. The following month, the patient presented weight loss of 6 kg while taking metformin XR 1.5 g/day and continued to have irregular cycles every 3 months. The patient returned to the health unit to schedule an appointment with a gynecologist complaining of vaginal itching. She was advised to take the preventive test.

PATIENT D

ID Woman, 26 years old. The patient sought the health unit complaining of a recurrent sebaceous cyst in the right armpit and erythema on the skin. TP She reported not using contraceptives for a year and two months, when she stopped taking medroxyprogesterone, and since then she has not had any more menstrual flow. She stated that before taking the medication she already had irregular cycles, but had never investigated them. The patient had already had two pregnancies with cesarean section, the last one 3 years ago, and had irregular cycles from then on. A transvaginal ultrasound was requested and she was prescribed 0.5 mg betamethasone + 1.0 mg gentamicin + 10 mg tolnaftate and 10 mg clioquinol cream. She was referred for minor surgery due to the presence of acrochordons in the left armpit. After returning with the ultrasound results, a diagnosis of polycystic ovary syndrome with the presence of secondary amenorrhea was confirmed, a 10 mg medroxyprogesterone tablet was prescribed for five days, Selene starting after the menstrual period; and routine laboratory tests were requested. RF Not described OC Not reported GPNPT At her next follow-up, the patient reported having used medroxyprogesterone 10 mg for the specified period and had not experienced a decrease in menstrual flow. She was referred to a gynecologist. After consulting with a gynecologist, she was referred to a nutritionist for weight loss due to changes in laboratory tests. She was advised to undergo a glucose tolerance test (GTT) and prescribed metformin 500 mg and spironolactone 25 mg once a day. She returned with a GTT result of 161.95, confirming the risk for DM. She was advised to continue taking the medication prescribed by the gynecologist.

DISCUSSION

It should be noted that the present study is based on only four cases, which limits the generalization of the results. It is not the objective of the study to represent the diversity of experiences and possible

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results in a broader population.

Reflections on the Pharmacotherapy used: use of metformin and hormonal contraceptives (HC)

It is noted that 3 women used metformin to treat PCOS. In a study conducted by Fraison (2020) [4]; which aimed to evaluate the efficacy and safety of metformin compared to ACH in improving the clinical, hormonal and metabolic characteristics of PCOS (alone or in combination); it was found that in adult women with PCOS, metformin may be less effective in improving hirsutism compared to CH in the BMI subgroup of 25 kg/m2 to 30 kg/m2 (i.e., in this range CH would be the best option), but there is no certainty as to whether there is a difference between metformin and ACH in the BMI < 25 kg/m2 and BMI > 30 kg/m2 subgroups. Therefore, these studies point to uncertainties about the therapeutic use of the medications in question when comparing them. [4]

Compared with CH, metformin may increase the incidence of serious gastrointestinal adverse events and decrease the incidence of other serious adverse events. Both metformin alone and CH alone may be less effective in improving hirsutism compared with metformin combined with CH [4], a situation in which patient B would be at a disadvantage in terms of treatment.

In the most up-to-date study on the issue just described, Melin (2023) [5]; carried out the evaluation of comparisons between CH, metformin and combined treatment (metformin and CH) to support the new International Evidence-Based Guidelines on the Evaluation and Management of Polycystic Ovary Syndrome – DIBESOP. [6] This study consisted of a systematic review and meta-analysis with women with PCOS; of randomized controlled trials (RCTs) selected in the last 10 years, considering different clinical characteristics. This research conducted by Melin et al (2023) [5] This study consisted of a systematic review and meta-analysis with women with PCOS; of randomized controlled trials (RCTs) selected in the last 10 years, considering different clinical characteristics. This research was conducted by Melin et al (2023) [6] so that CH is used for the treatment of irregular cycles and hirsutism in place of metformin, and metformin in place of CH for clinical indications related to metabolic issues in PCOS. [5,6]

This same study by Melin et al (2023) [5] indicates that combined treatment with metformin and CH improves [1] biochemical hyperandrogenism, [2] insulin levels and [3] insulin resistance more than CH alone. However, no difference was observed in clinical outcomes, including obesity and its control, a condition observed in 3 of the patients in this case study.

This implies that the choice of treatment with metformin or CH should be based on symptoms, observing some biochemical benefits of combined treatment; targeting the two main endocrine disorders observed in PCOS: hyperinsulinemia and hyperandrogenism. [7].

Reflections on the use of hormonal contraceptives (HCC) in view of the diversity of these presentations

However, it is still necessary to consider the different types of existing CHs, including the dosage of ethinylestradiol (EE) as shown in Table 3. [8]

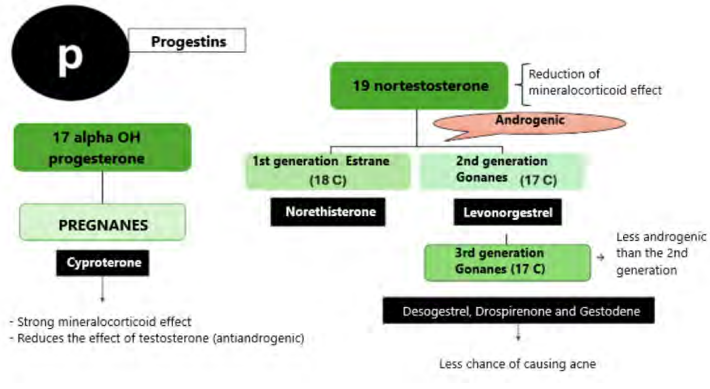
Table 3: Classification of CHs according to the dosage of Ethinylestradiol - EE

Ethinyl Estradiol Dosage Classification	Dosage Range in mcg
High	*50 mcg - > 50 mcg*
Medium [or standard]	*30 mcg – 35 mcg*
Low	*20 mcg*
Very low [or ultra low]	*< 20 mcg*

Source: Nelson & Cwiak, 2011.

As for progestins (PG), they have high variability in terms of origin and effects on the body, as shown in figure 3 [9]:

Figura 1: Caminho metodológico



Source: Speroff & Fritz, 2020. Art: The authors, 2024.

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Considering this reality, Forslund (2023) [10] sought to compare different CHs as part of the DIBESOP 2023 update [6] through a meta-analysis.

In this study, it was shown that very low-dose EE CHs associated with [1] Drospirenone (a PG from the third-generation gonane class); [2] drospirenone (another third-generation gonane) or [3] cyproterone (from the pregnane class) resulted in lower BMIs and lower testosterone levels in the women studied compared to medium-dose EE associated with Desogestrel or Gestodene (both third-generation gonanes), but no difference was observed regarding hirsutism. [10]

It is noted that patients B, C and D used medium-dose CH, which would then imply chances of high BMI and testosterone levels, even more so if associated with a third-generation gonane, as occurs in patient C, who, by the way, was the one who paid the most attention to weight, due to her BMI, being at a disadvantage in terms of an evidence-based approach. [6,7,10]

Reflections on the management of excess weight in the cases presented and comparison with the evidence

More specifically regarding obesity, it is worth mentioning the notes of Goldberg et al, (2023), in which they sought to evaluate the efficacy of anti-obesity agents for [1] hormonal, [2] reproductive, [3] metabolic and [3] psychological results in PCOS. This researcher found no difference between exenatide (GLP-1 receptor agonist) versus metformin for results on [1] weight, [2] biochemical hyperandrogenism and [3] metabolic. This study highlighted that there was a better response in the normalization of fasting blood glucose when metformin was used, the same not occurring with exenatide alone.

The use of orlistat together with CH for weight control did not show weight reduction, and did not improve metabolic aspects compared to CH. [11]

A visible gap is noted in the issue of pharmacological use for weight control in this group, and considering the cases under study, patient C used orlistat with CH, also using bupropion, but had slight weight loss; similar to patient B, who benefited from nutritional care and followed non-pharmacological treatments.

Reflections on how pharmacology has been used in women with PCOS and DM2 - under 30 years old and overweight - in public healthcare

It is important to note that this case series study is a delimited system and simultaneously emphasizes the unity and globality of this system. It is important to focus attention on the aspects that are relevant to the research problem, in the stipulated time, to allow a clearer view of the phenomena.

In short, the phenomenon represented here refers to not so successful attempts to deal with PCOS symptoms that contribute to difficult control of DM2, in which Fraison (2020) [4] warned in 2020 about the uncertainties regarding the interventions used in cases of women with BMI > 30, something that did not evolve until 2023, the date of the last DIBESOP. Here we have a question about how prepared the system is to deal with this clinical condition, given this particularity of the BMI value in young women. An issue limited to a small group, but which does require more comprehensive studies aiming at a more global understanding.

Regarding the use of CHs, the diversity of presentations and distinct actions within PCOS needs to be considered. This selection of 4 cases highlights another issue: access to those who have a better evidence profile on the conditions associated with PCOS.

Considerando os achados de Forslund (2023) [10] in which very low-dose EE CHs associated with gonans or foreign bodies resulted in lower BMIs and lower testosterone levels in women when compared to medium-dose EE, it must be considered that access via SUS in the city under study of CHs is limited to EE 0.03 mg associated with Levonorgestrel 0.15 mg - a second-generation gonan - classified as medium-dose. [12] The type of CH used by two patients is only available in the private system, which in certain cases can make access difficult. However, it is important to note that it is still a medium-dose presentation. [12]

Reflections on the interdisciplinary management of PCOS and the chances of interventions with a greater possibility of favorable outcomes

All these issues addressed here lead to the guiding question: What reflections can be made regarding the pharmacology used in women with PCOS and DM2 - under 30 years of age and overweight - without generalizing the results - in public health care?

Access to medicines and access to other professional categories that guarantee interdisciplinarity in health is crucial for weight control in women with polycystic ovary syndrome (PCOS) because it involves the integration of different areas of expertise to provide holistic and comprehensive care. [13]

Professionals from various specialties, such as endocrinologists, nutritionists, psychologists and physical educators, collaborate to address the multiple aspects of PCOS, which include hormonal dysfunctions, insulin resistance, psychological and behavioral challenges, and lifestyle issues. It is also worth noting that probiotic-based treatment has been an area of interest in terms of symptomatic management, as well as weight control in women with PCOS, and nutrition professionals are responsible for monitoring this issue. [14]

CONCLUSION

Polycystic Ovary Syndrome (PCOS) and Type 2 Diabetes Mellitus (T2DM) are health conditions that frequently coexist in young women, contributing to a significant increase in cardiovascular and metabolic risks. This case series study highlights the importance of an interdisciplinary and personalized approach in the management of these conditions, emphasizing both pharmacological and non-pharmacological interventions.

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The cases analyzed show that metformin, an insulin-sensitizing agent, is widely used in the treatment of women with PCOS and T2DM, demonstrating efficacy in reducing insulin resistance and glycemic control. However, adherence to treatment is often compromised by gastrointestinal side effects and financial challenges. In addition, the use of combined hormonal contraceptives (CHC) has been shown to be effective in regulating menstrual cycles and managing hyperandrogenism; however, the choice of the ideal type of CHC still lacks consensus.

Non-pharmacological interventions, including lifestyle changes focused on diet and physical activity, are also crucial. Interdisciplinary support involving nutritionists, physical educators, physicians, and psychologists can improve treatment adherence and outcomes. However, limited access to health services and lack of financial resources are significant barriers faced by many patients.

This study highlights the urgent need for public policies that facilitate access to effective and affordable treatments, as well as the creation of support groups that offer continuous and multidisciplinary monitoring. These initiatives can significantly improve the quality of life and health outcomes of women with PCOS and T2DM, reducing the long-term risks associated with these conditions.

Future studies should consider larger sample sizes, rigorous controls for intervening variables, and methodologies that allow for a more robust analysis of treatment efficacy to offer more conclusive and applicable conclusions.

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