

The Relation Between the Endocannabinoid System and Polycystic Ovary Syndrome

A Relação Entre o Sistema Endocanabinóide e a Síndrome do Ovário Policístico

La Relación Entre el Sistema Endocannabinoide y el Síndrome de Ovario Poliquístico

RESUMO

INTRODUÇÃO: A síndrome do ovário policístico é uma doença endócrina comum entre mulheres, caracterizada por irregularidades menstruais, alterações metabólicas e sintomas decorrentes de desequilíbrios hormonais. Estudos recentes sugerem que a redução da atividade da hidrolase de amida de ácido graxo, associada ao sistema endocanabinóide, pode interferir no funcionamento do eixo hipotálamo-hipófise-ovário. **OBJETIVOS:** Analisar a relevância de tratamentos não convencionais para a síndrome do ovário policístico, destacando benefícios, riscos e o estigma relacionado ao uso de canabinóides. **MÉTODO:** Foi realizada uma revisão integrativa, permitindo uma busca ampla na literatura. Foram incluídos quatorze artigos científicos e dois livros, publicados entre os anos de 1997 e 2024. **CONCLUSÃO:** Os resultados sugerem que canabinóides, especialmente o canabidiol, podem ajudar a regular o eixo hormonal reprodutivo, melhorar o fluxo menstrual, reduzir cólicas e favorecer a sensibilidade à insulina. A interação entre o sistema endocanabinóide e a síndrome do ovário policístico indica potenciais novas abordagens terapêuticas.

DESCRIPTORIOS: Saúde da mulher; Fitofármacos; Canabidiol; Sistema endocanabinóide; Síndrome do ovário policístico; ovário.

ABSTRACT

INTRODUCTION: Polycystic ovary syndrome is a common endocrine disorder among women, characterized by menstrual irregularities, metabolic changes, and symptoms resulting from hormonal imbalances. Recent studies suggest that reduced fatty acid amide hydrolase activity, associated with the endocannabinoid system, may interfere with the functioning of the hypothalamic-pituitary-ovarian axis. **OBJECTIVES:** To analyze the relevance of non-conventional treatments for PCOS, highlighting benefits, risks, and the stigma related to the use of cannabinoids. **METHOD:** An integrative review was conducted, allowing a broad search of the literature. Fourteen scientific articles and two books, published between 1997 and 2024, were included. **CONCLUSION:** The results suggest that cannabinoids, especially cannabidiol, may help regulate the reproductive hormonal axis, improve menstrual flow, reduce cramps, and promote insulin sensitivity. The interaction between the endocannabinoid system and polycystic ovary syndrome indicates potential new therapeutic approaches.

DESCRIPTORS: Women's health; Phytopharmaceuticals; Cannabidiol; Endocannabinoid system; Polycystic ovary syndrome; Ovary.

RESUMEN

INTRODUCCIÓN: El síndrome de ovario poliquístico es un trastorno endocrino frecuente en mujeres, caracterizado por irregularidades menstruales, alteraciones metabólicas y síntomas derivados de desequilibrios hormonales. Estudios recientes sugieren que la actividad reducida de la hidrolasa de amida de ácidos grasos, asociada al sistema endocannabinoide, puede interferir con el funcionamiento del eje hipotálamo-hipófisis-ovario. **OBJETIVOS:** Analizar la relevancia de los tratamientos no convencionales para la síndrome de ovario poliquístico, destacando los beneficios, los riesgos y el estigma relacionado con el uso de cannabinoides. **MÉTODO:** Se realizó una revisión integrativa, permitiendo una búsqueda exhaustiva en la literatura. Se incluyeron catorce artículos científicos y dos libros, publicados entre 1997 y 2024. **CONCLUSIÓN:** Los resultados sugieren que los cannabinoides, especialmente el cannabidiol, pueden ayudar a regular el eje hormonal reproductivo, mejorar el flujo menstrual, reducir los cólicos y promover la sensibilidad a la insulina. La interacción entre el sistema endocannabinoide y el síndrome de ovario poliquístico indica posibles nuevos enfoques terapéuticos.

DESCRIPTORIOS: Salud femenina; Fitofármacos; Cannabidiol; Sistema endocannabinoide; Síndrome de ovario poliquístico; Ovario.

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INTRODUCTION

Polycystic ovary syndrome is an endocrine disorder that, according to the Ministry of Health⁽¹⁾, affects 10% of Brazilian women in 2023. Polycystic ovary syndrome, also known as PCOS, is characterized by the presence of small cysts on the ovaries, which consequently cause irregularities in the menstrual cycle. Patients with PCOS have reduced expression of fatty acid amide hydrolase (FAAH), suggesting that there is a dysfunction of the endocannabinoid system (O'llenecia; Alison; Sandeep, 2019²). The endocannabinoid system, in turn, is a biological system composed of endocannabinoids. Endocannabinoids are endogenous retrograde neurotransmitters based on lipids and fatty acids that act on the central nervous system (CNS) by binding to cannabinoid receptors and receptor proteins (Fonseca et al., 2013³).

The main objective of this scientific article is to demonstrate the importance and stigma surrounding other types of unconventional treatments, disseminating the benefits and harms of both treatments.

METHOD

Divided into six stages, the integrative review was based on data collection from secondary sources through

bibliographic surveys, which aim to synthesize the existing literature on a given topic in a comprehensive manner. It allowed the inclusion of studies with different methodologies, providing a broader and more complete view of the subject presented.

"Integrative review is a method that provides the synthesis of knowledge and the incorporation of the applicability of significant study results into practice." (Souza, Marcela Tavares; Silva, Michelly Dias da; Carvalho, Rachel de; 2010⁴).

The first step consists of developing the guiding question, which is the first phase of the integrative review that consists of clearly defining the topic of interest and formulating the research question that will guide the entire review. It also determines which studies will be included and the information selected.

The second stage involves searching the literature, which consists of conducting a comprehensive search of scientific databases and relevant reliable sources to prepare an academic research paper. The literature search can be conducted using books, newspapers, magazines, and articles.

Data collection is the third stage, where a diverse collection of research and data found in the literature is carried out. The search must be done carefully to ensure the accuracy and veracity of the information shared.

"The data should include: definition of subjects, methodology, sample size, measurement of variables, method of analysis, and underlying concepts employed." (Albert Einstein Hospital, São Paulo, 2010⁵)

The fourth step is the analysis of the included studies, which consists of reviewing all the material found. The quality, relevance, and accuracy of the included studies must be evaluated.

The fifth step is the discussion of the results, which involves comparing the results obtained. It is necessary to identify gaps and review the analysis of the theoretical framework, paying attention to possible errors.

The sixth and final stage consists of presenting the integrative review, which is the last phase of the research. It must be complete and comprehensive, containing essential information for the reader's understanding. The author has an obligation to certify the data collected, without omitting any evidence.

RESULTS

The table below shows five articles from 2005 to 2024 that confirm what was addressed in this study. It is evident that the use of cannabinoids has therapeutic effects on the female reproductive system as well as on pain management, psychological well-being, and insulin sensitivity.

Literature Review

Pompeo V, el Hkaim S

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AUTHORS	JOURNAL - YEAR	METHODOLOGY	CONCLUSION
Jason W Busse, Patrick Vankrunkelsven, Linan Zeng, Anja F. Heen, Arnaud Merglen, Fiona Campbell, Lars-Petter Granan, Bert Aertgeerts, Rachele Buchbinder, et al.	BMJ -2021	Integrative Review	Use of cannabinoids is effective in treating chronic pain
Saeed Zavareh, Zacareh Mirseyyed, Meysam Nasiri e Hamid Hashemi-Moghaddam	National Library of Medicine PMC Center -2024	In vitro studies	The use of therapeutic doses of THC for the treatment of polycystic ovary syndrome reduces weight and improves insulin sensitivity
Piotr Przybycien, Danuta Gasior-Perczak e Wojciech Placha	MDPI - 2022	Integrative Review	Interaction of cannabinoids with the endocrine system positively affects lipid metabolism in adipose tissue, consequently affecting also the ovary
Maria Scherma, Paolo Masia, Matteo Deidda, Walter Fratta, Gianluigi Tanda e Paola Fadda	MDPI- 2018	Integrative Review	Cannabinoids such as CBD and delta-9THC are used as treatment for some psychological disorders. The correlation between the endocannabinoid system and psychological disorders indicates anandamide dysfunction anandamide
Samara Yarak, Ediléia Bagatin, Karime Marques Hassun, Meire Odete Américo Brasil Parada e Sérgio Talarico Filho Buchinha; northern buchinha; São Paulo buchinha	Scielo - 2005	Integrative Review	A síndrome do ovário policístico está associada à hiperplasia adrenal e à hiperinsulinemia, causando morbidade metabólica e reprodutiva

DISCUSSION

A brief review of the literature on PCOS shows that sufferers of the syndrome may present signs and symptoms such as excessive cramping, irregular menstrual cycles, acne, infertility, obesity, hirsutism, diabetes, and in some cases depression. This occurs because more male hormones (androgen) are produced and there is a reduction in fatty acid amide hydrolase (FAAH). Traditional treatment involves the use of contraceptives (Albert Einstein Hospital, 2023⁶).

To simplify the endocannabinoid system, it is composed of two main endocannabinoids that act on the central nervous system: 2-arachidonylglycerol (2AG), which is biosynthesized from diacylglycerol (DAG) by the enzyme diacylglycerol lipase- α (DAGL α), and anandamide (AEA), synthesized from N-acyl-phosphatidylethanolamine (NAPE) by NAPE-specific phospholipase D (NAPE-PLD). The endocannabinoid system controls neurotransmission in case there is an excess of the respective neurotransmitter in the postsynaptic neuron, which releases 2AG and anandamide to return to the presynaptic neu-

ron and control excessive release. 2AG can be degraded or act on its receptors such as CB1, which blocks the release of neurotransmitters (FONSECA et al., 2013³).

The main basis for this review was the article in the Journal of Ovarian Research: "The role of the endocannabinoid system in female reproductive tissues" published online in 2019 by authors O'Llenecia S. O'Llenecia S. Walker, Alison C. Holloway, and Sandeep Raha².

Components of the endocannabinoid system (ECS) have been identified in female reproductive fluids and plasma in in vitro studies, animal studies, and some cannabis users. In 2009, El-Talatin⁷ reported the presence of CB1, CB2, FAAH, and NAPE-PLD within human ovarian follicles, a study conducted using immunohistochemical staining. It was also discovered that FAAH and NAPE-PLD are expressed in secondary and tertiary follicles, in the corpus luteum, and in the corpus albicans, suggesting that anandamide may be produced by follicular development.

An increase in the ovary at the time of ovulation has been reported, making it possible that endocannabinoid signaling

may help regulate follicular maturation and development. High intra-follicular levels of anandamide allow ovulation, while plasma and intrauterine levels must be reduced to allow implantation of a fertilized oocyte, acting on the hypothalamic-pituitary-ovarian axis.

CONCLUSION

The use of external cannabinoids such as CBD may help regulate the hypothalamic-pituitary-ovarian axis in some cases, promoting improvements in menstrual flow, cramps, insulin sensitivity, and other symptoms. The role of the nurse in taking the patient's history and collecting data is fundamental in order to provide and guide the patient in choosing the ideal and effective treatment for their respective pathology. It is of utmost importance that new therapeutic methods be explored in Brazil, given that according to a report by the National Cancer Institute (INCA)⁸, approximately 6% of Brazilian women over the age of 15 are smokers, and many are unaware of the risk of thrombosis when contraceptives are associated with tobacco or smoking.

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