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Strengthening Applicability in Qualitative Nursing Research Using the Multi-Case Narrative Approach: A Methodological Insight

Dr. Amira El-Shenawy[1], Dr. Mahmoud Abdelrahman[2]
[1]Faculty of Nursing, Cairo University, Cairo, Egypt
[2]Department of Nursing, Alexandria University, Alexandria, Egypt
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Abstract

PCOS is a common endocrine disease in the reproductive-aged women, which is usually insulin resistant, hyperandrogenism and metabolic imbalance. SodiumGoeslugar-glucose Cotransporter -2 (SGLT2) inhibitors as a primary agent in management of type 2 diabetes have been considered useful agents in PCOS management including insulin sensitization, weight reduction and cardiometabolic effects. In this systematic review, some clinical and preclinical studies on the applicability and safety of SGLT2 inhibitors to manage PCOS are critically evaluated. The results indicate that SGLT2 inhibitors can enhance insulin sensitivity, decrease androgen level, induce weight loss, and possibly restore ovulatory activity; nevertheless, the literature is lacking and rather heterogenic. Future superior randomization controlled trials should be conducted to demonstrate their role and standardize treatment regimes in management of PCOS.

Keywords: ***Polycystic Ovary Syndrome, SGLT2 Inhibitors, Insulin Resistance, Hyperandrogenism, Metabolic Syndrome, Female Reproductive Health, Type 2 Diabetes Mellitus, Endocrine Therapy, Cardiometabolic Risk, Weight Loss Therapy.***

1.Introduction

PolyCystic Ovary Syndrome (PCOS) represents one of the most complicated and prevalent endocrine mimics, which is estimated by 5-10 percent of women in the reproductive period in the whole world. Being described by a constellation of symptoms including hyperandrogenism, menstrual irregularities, and ovulatory dysfunction along with insulin resistance and various metabolic alterations, PCOS is a significant public health issue. Notably, in addition to the reproduction issues, PCOS greatly predisposes one to diabetes type 2, heart disease, non-alcoholic fatty liver disease, and carcinoma of the endometrium throughout life. The pathophysiology of PCOS is multifactorial, and includes genetic predispositions, environmental factors and severe metabolic dysfunction, the key elements in the endocrine dysfunction of PCOS and in the ability to in insights of metabolic dysfunction.

Although lifestyle interventions and weight loss are generally advised as the first line of treatment, pharmacologic interventions are generally necessary to exercise the attendant clinical bracket of PCOS. Combined oral contraceptives (COCs) have traditionally been the first-line treatment of control of menstrual cycles and suppression of hyperandrogenic effects(1). Simultaneously, insulin sensitizers, notably metformin, have often been subjected to use with an eye on the metabolic features including insulin resistance as well as glucose intolerance. Nonetheless, metformin is inhibited by the fact that it has not resulted in meaningful weight loss, enhancement of body composition, and sustained glycemic control in non-diabetic overweight PCOS women. There is also a recent indication of the plateau effect on the capacity of metformin to address fasting glucose level or fasting insulin level when used in such patients provided also by the recent meta-analyses.

Here, Sodium Glucose Cotransporter-2 inhibitors (SGLT2i), a group of antidiabetic agents developed to enhance glycemic control in type 2 diabetes mellitus (T2DM), are an upcoming option of PCOS. Such agents reduce the level of glucose in the blood without the participation of insulin by preventing its reabsorption by the kidneys causing glucosuria and small weight loss. They have also shown cardioprotective actions in subjects with and without diabetes thereby becoming appealing in disorders that are characterized by a high cardiometabolic risk including PCOS.

This interest in the repositioning of SGLT2 inhibitors to treat PCOS relates to the multi-faceted advantages of the drugs. First, SGLT2i is lessening visceral adiposity and core obesity, which are likely to fade insulin resistance, which contributes to PCOS hyperandrogenism and anovulation. Secondly, positive modulations of the hormones have been documented to include decreases in androgens; dehydroepiandrosterone sulfate (DHEAS) and total testosterone, which may translate into enhanced ovulatory behavior and hirsutism. And thirdly, they can be synergized with other agents such as glucagon-like peptide-1 receptor agonists (GLP-1RA) or metformin and

improve their metabolic and endocrine efficacy. These qualities highlight why SGLT2 inhibitors may constitute a possible non-hormonal pharmacological treatment of PCOS.

Although there are theoretical benefits, available and current evidence of the application of SGLT2 inhibitors in PCOS is rather young and non-homogenous. The current clinical studies have been heterogeneous with regards to combinations of drugs, dose, duration of treatment, outcome measures and comparators arms. Few randomized controlled trials (RCTs) have shown the efficacy of particular SGLT2i, including empagliflozin, canagliflozin, dapagliflozin and licogliflozin, as monotherapy and/or combination with other drugs in patients with PCOS. They have included insulin resistance indices (e.g., HOMA-IR), body composition (e.g., waist circumference, fat mass) and lipid profile outcomes or hormonal related measures (e.g. testosterone and DHEAS)(2).

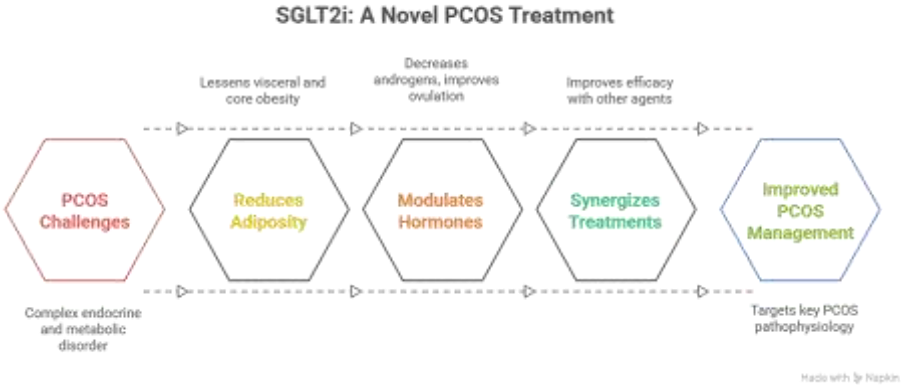

FIGURE 1 SGLT2i: A Novel PCOS Treatment

The systematic review used in the case constitutes the synthesis of results of five randomized control trials, which involve 269 overweight or obese women with prime- cutaneous alopecia syndrome. All these studies report an improvement in various metabolism parameters with use of SGLT2 inhibitors including: fasting plasma glucose levels, HOMA-IR, body mass index (BMI), and waist circumference among others. Remarkably, the augury of SGLT2i and GLP-1RA was associated with better outcomes of fat mass levels and glycemic management and redistribution of fat in android to gynoid bodies that reflects a pathway to a more healthy body shape. In the meantime, SGLT2i combination therapy with metformin seemed to be more advantageous in terms of affecting the hormonal profile of patients, particularly through lowering the androgen level and improving the menstrual cycle regularity.

The incidences related to SGLT2i use among PCOS populations have been mild and most often included genital infections. The results favor the acceptability of the treatment in the given population. But the evidence also demonstrates significant limitations, and these are low sample sizes, the limited period of the study (down to two weeks in the case of certain trials), and poor standardization of the clinical elements, such as hirsutism levels or the frequency of ovulation. Moreover, other trials could not find placebo-controlled groups, or they were not of sufficient size to discriminate clinically meaningful changes in all outcomes that are relevant in PCOS.

On the whole, this emerging body of evidence supports an optimistic role of SGLT2 inhibitors in treating PCOS, particularly in the overweight and obese individuals. These agents have the potential to support or even replace current treatment, including metformin, offered to individuals by targeting the most key attributes of PCOS pathophysiology, including insulin resistance and adiposity. Nevertheless, there is an urgent necessity of larger, longer, placebo-controlled RCTs, which will with certainty evaluate their effectiveness in metabolic, reproductive, and clinical areas(3). These trials will play a paramount role in defining the role of SGLT2 inhibitors as therapeutic options in the PCOS clinical paradigm as well as formulating new clinical guidelines.

To sum up, existing evidence is more promising, but it should be interpreted more as a ground than as a conclusion. The capacity of SGLT2 inhibitors in PCOS remains an avenue that can be explored in the therapy. Healthcare providers and investigators would have to combine their efforts to produce top-notch evidence that would fill existing gaps, extend safety in the long term, and determine the population of patients who are the best candidates to use this new pharmacologic method.

2.Methods

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To assess the outcomes of the effects of sodium-glucose cotransporter-2 inhibitors (SGLT2i) on women with polycystic ovary syndrome (PCOS), this systematic review was carried out. The study design was well-planned and corresponded to the Preferred Reporting Items in Systematic reviews and Meta-Analyses (PRISMA) protocol, and was transparent and reproducible, securing scientific integrity. The protocol of this review was registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO) with unique identifier CRD42024560088.

2.1 Strategy of literature search

The procedure conducted a systematic but thorough search at various electronic databases, such as PubMed and the ClinicalTrials.gov, to find the relevant randomized controlled trials (RCTs) since their inception until March of 2024. The searching strategies included Medical Subject Headings (MeSH) and free-text words. The Boolean search string was created with the aim of being sensitive and required combinations of terms including:
polycystic ovary syndrome" OR PCOS" SPLC and sglt2 inhibitors or sglt2i or Canagliflozin or Dapagliflozin or Empagliflozin or licogliflozin or Sotagliflozin.
Moreover, manual search using reference lists of eligible full-text articles was performed to improve the capture of the studies that would not be found by database algorithms(4). Articles written in English were used only. They excluded abstracts, grey literature, conference proceedings and other ongoing clinical trials whose results had not been published as long as there were some desired methodological and outcome data.

TABLE 1 Summary of Methodological Framework

Component	Description
Review Protocol	Registered in PROSPERO (ID: CRD42024560088); PRISMA guidelines followed
Databases Searched	PubMed, ClinicalTrials.gov
Search Period	Inception to March 2024
Keywords Used	“Polycystic Ovary Syndrome,” “PCOS,” “SGLT2 inhibitors,” “Canagliflozin,” “Dapagliflozin,” etc.
Study Type Included	Randomized Controlled Trials (RCTs)
Participants	Women aged 18–45 with PCOS (Rotterdam or NIH criteria); non-diabetic; overweight/obese
Interventions	SGLT2i (monotherapy or with metformin/GLP-1RA)
Comparators	Placebo or non-hormonal agent (e.g., metformin, GLP-1RA)
Primary Outcomes	Insulin resistance (HOMA-IR), BMI, androgen levels (testosterone, DHEAS), body composition
Secondary Outcomes	Lipid profiles, menstrual regularity, glycemic control, adverse events
Exclusion Criteria	Diabetes, other endocrine disorders, recent hormonal therapy, animal/in vitro studies
Data Synthesis	Qualitative/narrative synthesis only (no meta-analysis due to heterogeneity)
Risk of Bias Tool	Cochrane RoB tool (RevMan v7.2); multiple domains assessed
Number of RCTs Included	5 trials with 269 total participants

2.2 Exclusion Criteria

The studies included were after meeting the following criteria: (1) trials were randomized controlled and involved women aged 1845 years, diagnosed with PCOS based on either Rotterdam condition or National Institutes of Health (NIH) guidelines; (2) the participants were overweight and obese but not having type 2 diabetes mellitus; (3) the intervention included any SGLT2 inhibitors that were either taken as a single agent or a combination with a non-hormonal comparator drug, such as metformin or glucagon-like peptide-1 re
Research papers which involved diabetic and other endocrine (simulating PCOS) cases such as Cushing syndrome, congenital adrenal hyperplasia, patients taking insulin or hormonal contraceptives within three months of the study

were also not included. The article was also excluded in trials on animal models, vice observational designs, or with proper control arms. Inadequate outcome reporting and shorter outcome reporting than two weeks were not considered as a matter of study(5).

2.3 Selection Process of Study

The screening of the titles and abstracts was done by the two reviewers independently to obtain the initial eligibility. The full-text articles of potentially relevant studies were then downloaded and, through the pre-determined criteria, they were finally included. The differences in the selection procedure were reconciled on a consensus basis or with a third reviewer. Cases of missing critical data were followed up, by trying to get access to study authors, to clarify or have access to complete datasets.

Five randomized controlled trials with 269 subjects were selected and consequently included into the final quality synthesis since they fulfilled all their eligibility criteria. These trials tested a number of SGLT2 inhibitors as monotherapies or with metformin or GLP-1RA: canagliflozin, empagliflozin, dapagliflozin, licogliflozin. The complete study identification and selection process drawings took the form of a PRISMA flow diagram.

2.4 Data Extraction

A prepared standardized extraction form was applied to collect pertinent material of each of the included studies. Data extracted consisted of characteristics of the studies (authors, year of publication, study locality, study design), characteristics of the participants (sample size, age, body mass index), method of diagnosing PCOS, form and strength of the SGLT2 inhibitor and other characteristics.

Interests of outcomes were classified as primary and secondary ones. Main outcome measures were alterations in insulin resistance (e.g. HOMA-IR), serum androgens (total testosterone, DHEAS) and body mass index (BMI), waist and total body fat percentages(). Second outcomes included an improvement in lipid profiling (triglycerides, LDL-C, HDL-C), the regularity of the menstrual cycle, the occurrence of ovulations, glycemic parameters (HbA1c, fasting plasma glucose) and the adverse events.

2.5 Risk of Bias Assessment

The used tool was the Cochrane Risk of Bias Tool (version 7.2.0) that was used to evaluate each of the included studies independently. The instrument assesses risk in seven domains; random sequence generation, allocation concealment, blinding outcome assessors, blinding of participants and personnel, incomplete outcome data, selective reporting, and other sources of bias. Each domain was rated as low, unclear or high risk.

The majority of studies have low risk of bias of randomization and reporting data, but there is often a high performance and detection bias; that is, because of an open-label design of many of these trials. The rate of attrition-related bias was quite low in most of them and there were no signs of significant reporting bias based on included trials.

2. 6 Data Synthesis

The non-homogeneity in study design, treatment duration (between 2 weeks and 24 weeks), kinds of SGLT2i intervened, and differences in how to define outcomes did not allow performing a meta-analysis. Rather, it was decided to utilize a narrative synthesis strategy that is used to synthesise the results and compare them with other studies. Data were summarized to note whether there was consistency of effect sizes or there was a deviation of the same, especially in regards to the insulin sensitivity, androgen concentrations, body composition and menstrual functioning(6).

Mean changes and the 95% confidence intervals (CIs) were retrieved where the numerical data were obtained. The reports on the same combination of drugs with similar conditions were united into one group and discussed in detail.

3.Results

Summary of the studies Reviewed

There were five randomized controlled trials (n total = 269) included in the systematic review, all of which were overweight or obese women aged 18 to 45 years who were diagnosed with polycyclic ovarian syndrome (PCOS) either using Rotterdam or NIH criteria. The SGLT 2 inhibitors evaluated were canagliflozin, dapagliflozin, empagliflozin and licogliflozin. These agents were examined by themselves or combined with other non-hormonal agents as metformin or exenatide. The interventions lasted between 2 and 24 weeks. The anthropometric, metabolic and hormonal results have been evaluated in every study, and the adverse events and clinical characteristics like the regularity of menstrual periods were documented in some studies.

Volume 2, Issue 2 | October-2025
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Outcome results in Anthropometric and Body Composition Measures

Majority of the trials indicated the declining weight and body mass index of the study population treated with SGLT 2 inhibitors. The study by Cai et al. showed that both canagliflozin and metformin monotherapy treatment presented a relevant but similar weight reduction (2.82kg vs 2.68kg) and BMI. Conversely, Elkind-Hirsch et al. demonstrated that dapagliflozin and exenatide reduction of weight (6.0 kg) and BMI (3.2 kg/m 2) was more pronounced than that of either dapagliflozin alone or dapagliflozin combined with metformin.

As discovered by Javed et al., the use of empagliflozin was much more successful in decreasing the levels of central obesity markers such as waist circumference in comparison to metformin. Another trial conducted by Zhang et al. revealed that both canagliflozin and metformin combination plus metformin alone caused a decrease in body weight and BMI; however, merging of groups was not statistically significant. Body weight was not affected significantly in a two-week trial with licogliflozin perhaps owing to inadequate treatment duration(7).

With regard to body composition the combination regimen of dapagliflozin-exenatide had superior results as others do in minimizing total body fat percent, android-to-gynaoid ratio (AGR) and trunk-to-leg fat ratio (TLR). Canagliflozin also lowered visceral and subcutaneous fat, but not to the extent as metformin. Empagliflozin was linked to a decrease in total fat mass and better retention of lean mass as compared with metformin.

Metabolic and Glycemic Parameters

Insilin resistance and glycemic control was measured in all five trials. The majority of the reported decreased HOMA-IR, fasting insulin levels, and fasting plasma glucose (FPG) was significant after the use of SGLT2i. Cai et al. revealed that canagliflozin no longer inferior than metformin in decreasing HOMA-IR, insulin, and FPG by after 12 weeks. On the same note, Zhang et al. established that combination of canagliflozin and metformin decreased FPG, glucose AUC and insulin AUC substantially during OGTT.

In a study by Elkind-Hirsch et al., it was demonstrated that the dapagliflozin-exenatide combination had the greatest effect on mean plasma glucose and the insulin sensitivity indices compared to the effect of monotherapy of dapagliflozin and metformin. Remarkably, Javed et al. did not reveal any meaningful difference in insulin indices when using either empagliflozin or metformin which indicates the failure of all agents and populations. There was a prominent decrease in insulin crest, AUC after two weeks of licogliflozin, implying quick and insulin-indefinite glycemic activity.

TABLE 1 Summary of Results from SGLT2 Inhibitor Trials in PCOS

Study (Year)	Drug(s) Used	Key Anthropometric Findings	Metabolic Outcomes	Hormonal Effects
Cai et al. (2022)	Canagliflozin vs Metformin	↓ Weight (~2.8 kg), ↓ BMI, ↓ WC (non-inferior to metformin)	↓ HOMA-IR, ↓ FPG, ↓ Insulin (similar to metformin)	↓ DHEAS; no significant change in testosterone or FAI
Elkind-Hirsch et al. (2021)	Dapagliflozin ± Exenatide	Greatest weight/BMI loss in dapagliflozin + exenatide group	↓ HOMA-IR, MPG improved most in combo group	↓ Total testosterone & FAI most with dapagliflozin monotherapy
Javed et al. (2019)	Empagliflozin vs Metformin	↓ Central obesity, ↑ lean mass (empagliflozin better)	No significant changes in insulin sensitivity markers	↑ SHBG, estradiol; no change in testosterone, FAI or DHEAS
Zhang et al. (2022)	Canagliflozin + Metformin vs Metformin	↓ Weight, ↓ BMI (similar), improved menstrual regularity	↓ FPG, ↓ AUC glucose/insulin (better in combo group)	↓ Testosterone, ↓ FAI (significant in combo group)
Tan et al. (2021)	Licogliflozin vs Placebo	No weight change (2-week study)	↓ HOMA-IR, ↓ Insulin peak, ↓ AUC insulin (rapid effects)	↓ DHEAS, ↓ Testosterone, ↓ Androstenedione (all significant)

Effects of Lipid Profile

There was mixed effect on lipid metabolism. There was a modest decline in triglycerides with most studies, and an increment in LDL-C with some SGLT2 inhibitors. Cai et al. identified that canagliflozin and metformin decreased triglycerides but not meaningfully different LDL-C or HDL-C. Elkind-Hirsch et al. concluded that

dapagliflozin+exenatide had a moderate decrease in LDL-C (6mg/dl), whereas dapagliflozin alone or with metformin only increased LDL-C. Zhang et al. reported that canagliflozin/metformin showed a significant decrease in triglycerides and total cholesterol versus In general, SGLT2i were associated with neutral or modestly beneficial impacts on the lipid profiles according to the combination therapy received.

Hormonal and Reproductive Results

The results of evidence on androgen levels and reproductive outcome were inconsistent. Canagliflozin caused a statistically significant decrease in the DHEAS but not in the total testosterone or free androgen index (FAI). Dapagliflozin monotherapy-induced the largest decrease in total testosterone, and FAI, compared to exenatide, in a study by Elkind-Hirsch et al. Combination treatment did not work as well as was surprising and has to be analyzed further(8).

According to Zhang et al., combination of canagliflozin with metformin considerably weakened FAI and total testosterone as compared to metformin alone. Both treatment groups showed improvement in regularity of menstrual periods. Javed et al. reported that SHBG and estradiol had elevated levels with empagliflozin but no significant changes in major hormones than metformin. Licogliflozin demonstrated the greatest decreased DHEAS (-24%) only within 2 weeks, but it is unclear clinically relevant.

Most trials failed to improve clinical manifestation of hyperandrogenism (hirsutism) despite androgen reductions. This can be ascribed to the short study periods and they are not enough to record any changes on hair growth cycles.

Cardiovascular and safety results

A number of trials included an account about blood pressure and cardiovascular risk indicators. The results revealed by Elkind-Hirsch et al. indicated that blood pressure bested in systolic and diastolic regions when connected to all treatment groups, and the biggest drop off was in DBP in the dapagliflozin exenatide population. There were no pronounced alterations in the endothelial function or inflammatory markers.

The adverse events (AEs) throughout trials were mild and usually self-limiting. The AEs related to the use of SGLT2i were a genital infection that occurred more frequently in cases of dapagliflozin monotherapy. Canagliflozin was linked with temporary pruritus vulvae and osmotic diuresis. Metformin groups had more GI AEs. No significant safety signals, or severe adverse events were reported in any trial(9).

4.Discussion

The systematic review assessed the new role of sodium glucose-cotransporter 2 inhibitor (SGLT2i) in the treatment of polycystic ovary syndrome (PCOS), specifically metabolic, hormonal, and clinical outcomes. According to the results of five randomized controlled trials (RCTs) covering 269 participants, SGLT2i has a significant potential to improve insulin resistance values, decrease body weight and visceral adipBiness or affect androgen profiles, therefore, covering the main aspects of PCOS pathophysiology. Such results become especially important in combination with a low number of effective therapy methods available to patients with PCOS who cannot be offered hormonal contraception and whose main symptoms are the presence of metabolic disturbances.

Reduction in weight, which is the most steadfastly noticed favorable impact of SGLT2i in all the examinations, is medically significant, since even a moderate diminishment of weight (~5 7) of any woman with PCOS promotes insulin sensitivity, ovulatory purpose, and androgen excess. Combination therapy with metformin or GLP-1 receptor agonists also caused a decrease in body mass index (BMI), waist circumference (WC) and fat mass. Remarkably, dapagliflozin in combination with exenatide showed the highest effect on fat mass and central adiposity, which may be attributed to a synergistic effect due to complementary action: glucosuria-induced calorie loss (SGLT2i) and feeling full (GLP-1RA)(10). These two-pronged interventions can possibly be particularly effective among overweight women having PCOS and comorbid prediabetes or insulin resistance.

Most studies also reported an improvement in insulin sensitivity measured using indicators including HOMA-IR and OGTT, among others. Canagliflozin and dapagliflozin proved to be at least as good as metformin in treating insulin resistance and fasting plasma glucose. The clinical trial using licogliflozin showed a quick effect of glycemic reduction in as fast as two weeks, which highlights the insulin-independent glucose-lowering effect of dual SGLT1/2 blocking. These findings are evidence in favor of the idea that SGTLT 2i can have powerful effects of controlling metabolism in non-diabetic women, but additional experiments conducted over a more extended period are necessary to provide the results of their long-term stability.

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Efficacy of SGLT2i on androgens and reproductive hormones was contradictory. Decreased DHEAS, total androgen and free androgen index (FAI) were observed in various trials and androgen-lowering outcomes were displayed by licogliflozin and dapagliflozin in the greatest magnitude. The decrease of DHEAS especially in tests with dual SGLT1/2 inhibitors (e.g. licogliflozin), makes one think that the synthesis of adrenal androgens could be indirectly modulated by SGLT1 inhibition. Nevertheless, the clinical significance of these changes--at least in regard to subjective and objective signs of hirsutism, acne, or ovulation-- was not clearly defined because of the durations of studies and absence of a full clinical scoring.

Concerning menstrual frequency and ovulatory activity, not all studies, and some of them, in particular, Zhang et al., provided normalization of the menstrual cycle with both SGLT2i and metformin. Less than a dozen subjects in the other trials conceived despite being treated, indicating reconstitution of ovulatory capacity though not the primary outcome. The tracking of ovulation was not performed in the majority of studies, which hinders the conclusion in this area. Interestingly, although some of the biochemical measures of hyperandrogenism were found to have improved, none of the clinical trials resulted in any effectiveness of reduction on hirsutism score probably due to a treatment period of less than a single hair growth cycle.

SGLT2i was found to have positive trends in the cardiometabolic risk markers, showing weight loss, improved diastolic blood pressure, and triglyceride levels, but inconsistent effects on LDL-C. The dapagliflozin abridged blood pressure, both systolic and diastolic, specifically in the combination with exenatide, and which may have long-term cardiovascular advantage in this high-risk group. In spite of the fact that cardiovascular experiences in none of the included trials were reported, previous evidence in diabetic populations indicates that SGLT2i is highly cardioprotective. These are yet to be tested whether they would equal those of PCOS populations with no diabetes.

SGLT2i safety experience in these trials did not differ with existing literature. Genital infections were the most frequently reported adverse events though they were mild in nature and self-limiting. Metformin arms had more gastrointestinal discomfort. TOTALLY, SGLT2i added to metformin or GLP-1RA did not cause an increase in the rate and severity of adverse events implying tolerability in the PCOS population.

However, this review has various limitations in spite of positive results. The sample size per study was small with the duration of the follow-up rather short (2-24 weeks). The studies were limited to one, with a placebo-controlled design and limited to two-weeks. Moreover, the study design, SGLT2i type, co-administration drugs, and the definition of the outcomes could not be directly compared or used in the pooled statistical analysis due to heterogeneity. The outcomes shown as clinically relevant endpoints in most trials are ovulation rate, live birth or complete androgenic symptoms scoring. These constraints pose some challenges on interpretation and create an urgent necessity in long-duration, placebo-controlled large-scale RCTs testing not only clinical but biochemical outcomes.

In a therapeutic perspective, SGLT2 inhibitors are potential alternative approach as a non-hormonal treatment in the management of PCOS in women that have metabolic phenotypes particularly the overweight, insulin-resistant or metformin-intolerant. They are promising in their potential to play a role in comprehensive PCOS management due to their insulin-independent activity, effects on visceral fat mass and the fact that they are favorable in cardiovascular regard. Nevertheless, they should only be used as adjunctive treatments, but not initial agents, at least as yet, until there is stronger evidence, preferably as an aspect of personalized therapy.

5.Conclusion and Future work

On the one hand, this systematic review supports the novel clinical promise of sodium-glucose cotransporter-2 inhibitors (SGLT2i) in the treatment of polycystic ovary syndrome (PCOS) in women with marked disturbances in metabolism. Five randomized controlled studies confirmed the efficacy of SGLT2i as monotherapy or in combination with other drugs such as metformin or GLP-1 receptor agonists in alleviating insulin resistance, lowering body weight, and central adiposity that holds the key to the pathophysiology of PCOS. Furthermore, multiple agents demonstrated positive although small effects on androgen levels, and there is some data of an improvement in the menstrual regularity and hormonal balance.

It also emerges in the review that SGLT2i have a manageable safety score, with adverse events being slight and confined mostly to mild infections in peoples genitals and temporary discomfort. The fact that they are insulin independent and reported to have cardiometabolic advantages makes them especially appropriate to be used in overweight or obese women with PCOS with poor tolerance or suboptimal response to standard pharmacological agents such as metformin or hormonal contraceptives.

But the existing evidence is still premature. The inadequate studies and trialed experiments also do not promote generality due to their small size, duration, and homogeneous structures. Also, some of the major clinical outcomes that have not been analyzed include the frequency of ovulatory occurrences, fertility indexes, and resolution of hyperandrogenic symptoms. Such gaps provide the rationale to conduct well-powered, long-term, placebo-controlled RCTs that should include both clinical and biochemical endpoints, in order to comprehensively explain the practice of SGLT2i in PCOS managing.

To summarize, SGLT2 inhibitors appear to be safe and effective as a new addition to the pharmacologic treatment of PCOS, particularly the metabolic manifestation of the condition. At present, however, despite initial results showing promise, these agents are not yet ready to be suggested on a regular basis because they require an adequate clinical trial. Their impact on the individualized treatment approaches (potentially in combination with other lifestyle intervention and/or other insulin-sensitizing agents) should also be studied to maximize the outcomes on both reproductive and meta-levels.

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Conflicts of interest

The authors have no conflicts of interest to declare

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