Influence of Dyslipidemia on the Quality of Sexual Life in Women in the Menacme using a Combined Oral Contraceptive

Influência da dislipidemia na qualidade de vida sexual de mulheres na menacme usando contraceptivos orais combinados

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Abstract

Purpose Female sexual dysfunction is a complex and common condition that affects women, and the relationship between sexual function and dyslipidemia is poorly studied. This study aims to assess this relationship in the reproductive life women in the menacme who use combined oral contraceptives (COCs).

Methods A total of 49 healthy women who were sexually active received COC pills that contained ethinylestradiol 30 mcg (EE30) plus levonorgestrel 150 mcg (LNG150). The women were divided into two groups according to their lipid profiles. Dyslipidemia was defined as a high-density lipoprotein (HDL) level $<$ 50 mg/dL or a low-density lipoprotein (LDL) level $>$ 130 mg/dL. Sexual function was assessed using the Female Sexual Function Index (FSFI) Questionnaire. Lipid and lipoprotein parameters were obtained at baseline and after the sixth cycle.

Results After six cycles of the COCs, the total cholesterol and LDL cholesterol levels in the women with a LDL level $>$ 130 mg/dL decreased by 14.7% and 22.1% respectively. In the women with a HDL level $<$ 50 mg/dL at baseline, the HDL level increased by 15.5% at the end of the study. The arousal and orgasm domains and the FSFI total scores significantly increased in women with and without dyslipidemia. The desire and satisfaction domains increased only in the group without dyslipidemia at the end of the treatment period.

Conclusions The EE30/LNG150 formulation increased the sexual function and it was only positively correlated with the HDL cholesterol level. These data indicated a low correlation between sexual function and the changes in the lipid and lipoprotein metabolism.

Keywords
- combined oral contraceptive
- quality of sexual life
- female sexuality
- sexual function questionnaire
- dyslipidemia

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Resumo

Objetivo Disfunção sexual feminina é uma condição complexa e comum que acomete as mulheres, e a relação entre a função sexual e a dislipidemia é muito pouco estudada. Este estudo objetivou avaliar esta relação em mulheres na menacme que fazem uso de contraceptivos orais combinados (COCs).

Métodos Um total de 49 mulheres saudáveis com vida sexual ativa receberam pílulas anticoncepcionais contendo etinilestradiol 30 mcg (EE30) associado a levonorgestrel 150 mcg (LNG150). As mulheres foram divididas em dois grupos, de acordo com o perfil lipídico. Dislipidemia foi definida como nível de lipoproteína de alta densidade (HDL) $<$ 50 mg/dL, ou nível de lipoproteína de baixa densidade (LDL) $>$ 130 mg/dL. A função sexual feminina foi avaliada utilizando o questionário de Índice de Função Sexual Feminina (IFSF). O IFSF e os parâmetros lipídicos e lipoproteicos foram obtidos no início e após o sexto ciclo do estudo.

Resultados Após seis ciclos de uso dos COCs, as mulheres com LDL $>$ 130 mg/dL, tiveram redução dos níveis de colesterol total e colesterol LDL de 14,7% e 22,1% respectivamente. Nas mulheres com níveis HDL $<$ 50 mg/dL no momento basal, o nível de HDL aumentou 15,5% ao final do estudo. Os domínios de excitação, orgasmo e os escores totais do IFSF aumentaram significativamente nas mulheres com e sem dislipidemia. Os domínios de desejo e satisfação aumentaram no final do período de tratamento exclusivamente no grupo sem dislipidemia.

Conclusões A formulação EE30/LNG150 aumentou a função sexual das mulheres, sendo positivamente correlata somente com os níveis de colesterol HDL. Estes achados demonstram baixa correlação entre a função sexual e as alterações no metabolismo lipídico e lipoproteico.

Palavras-chave

- contraceptivo oral combinado
- qualidade de vida sexual
- sexualidade feminina
- questionário de função sexual
- dislipidemia

Introduction

Female sexual dysfunction (FSD) is recognized as a widespread problem in society that is influenced by both health-related factors and psychosocial factors, and consists of multiple disorders that are classified into diagnostic categories, including desire, arousal, orgasm and pain.[1]

While the pill has been misrepresented in the social context, ironically, it is also misunderstood with regard to its impact on the quality of the sexual life of women. Despite scientific studies that examined the various aspects of the pill, surprisingly, few have assessed its impact on female sexual function.[2] Most reports focus on safety and efficacy, weight gain, bleeding irregularities, nausea and effects on mood.[3] However, there is a paucity of literature that describes the relationship between dyslipidemia and the quality of sexual life in women using combined oral contraceptives (COCs). In Brazil, the pill is used by $\sim$ 30% of fertile women.[4]

Hormones are only one component of the many factors that contribute to normal sexual function in women.[5] The decline in sex hormone levels that accompanies women throughout their lives has substantial effects on the tissues of the urogenital system.[6] Estrogen administration to women generally results in a favorable lipid profile, and may have a beneficial effect on the cardiovascular system.[7] The effect of progestogens on lipid profiles is related to the intrinsic androgenicity of the progestogen and the dose-ratio of estrogen to the progestogen in combined preparations.[8,9]

Dyslipidemias are frequently associated with sexual dysfunction, which has been attributed to the impairment of blood flow by the endothelium-dependent relaxation of the smooth muscle cells.[10] Human studies suggest that the vascular pathophysiology in women may be similar because the first phase of the female sexual response is mediated by a combination of vasocongestive and neuromuscular events that include increased clitoral length, vaginal lubrication, wall engorgement and luminal diameter.[11]

To the best of our knowledge, there are no reported studies that have assessed the relationship between female sexuality and dyslipidemia in healthy women who use COC pills and who previously presented normal sexual function. Therefore, the aim of this study was to determine whether changes in the lipid and lipoprotein profiles would be associated with a reduction in sexual function domains in a sample of sexually active women in reproductive age with and without dyslipidemia.

Methods

This study had an open, prospective design, and was conducted at the Family Planning Sector of the Department of Gynecology and Obstetrics of Faculdade de Medicina do ABC, in Santo André, Brazil. The protocol and all of the procedures were approved by the local research ethics committee, and all of the women read and signed an informed consent statement before their inclusion in the study.

The inclusion criteria were women with a desire to use an oral contraceptive method who were 18–40 years of age, had a stable sexual relationship for at least 1 year with the same partner, and had regular menstrual periods. The exclusion criteria were as follows: the presence of contraindications for the use of oral combined hormonal contraceptives according to the World Health Organization medical eligibility criteria for contraceptive methods;[12] the use of hormonal contraceptives during the preceding three months; current breastfeeding; complaints of pain or diminished sexual desire, arousal, vaginal lubrication or satisfaction during sexual intercourse; psychiatric disorders of any nature or previous diagnoses of premenstrual dysphoric disorders; the use of antidepressant medications, or of any drugs that affect sexual function; alcohol abuse, use of illegal drugs; use of sexual steroids or anabolizing substances; and a body mass index (BMI) > 30 kg/m^2.

Evaluations for inclusion in the study were conducted on 51 women. The patients received contraceptive pills that were composed of ethinylestradiol 30 mcg (EE30)/day + levonorgestrel 150 mcg (LNG150)/day, which were administered using a regimen of 21 days, followed by a 7-day interval between packs for 6 cycles. Before the administration of this contraceptive composition, the women did not use any other kind of COC.

The criteria for a diagnosis of dyslipidemia were based on low-density lipoprotein (LDL) cholesterol levels ≥ 130 mg/dL, a high-density lipoprotein (HDL) cholesterol level < 50 mg/dL, or triglyceride levels > 150 mg/dL according to the Adult Treatment Panel III.[13]

Sexual function was assessed at the study onset and at the end of the treatment period (six cycles) using the Female Sexual Function Index (FSFI). This measure instrument is a 19-item, self-administered questionnaire that assesses sexual function in women using 6 separate dimensions (desire, arousal, lubrication, orgasm, satisfaction and pain) to provide a total score.[14] The version of FSFI was validated for the Portuguese language.[15] All of the women who completed the FSFI were sexually active with the same partner, and answered the questionnaire alone in a quiet environment without interruptions. The FSFI cut-off score was set at 26 because a cut-off FSFI full scale score of 26 or less is currently being accepted for the diagnosis of sexual dysfunction in women.[16]

The laboratory assays were performed using blood samples that were collected at baseline and at the end of the treatment, between days 2 and 4 of the menstrual cycle, in the morning after 12 hours of fasting had been observed, and were collected in tubes containing anticoagulant and immediately stored at a temperature of between 2 and 8°C. The Friedewald formula (total cholesterol – HDL cholesterol – triglycerides / 5) was used to calculate the LDL cholesterol levels.[17]

The sample size was calculated based on the results from Guida et al[18] using the Power and Sample Size Program software, version 2.1.31, from Dupont and Plummer.[19] This calculation indicated that a sample of 45 patients would be needed because the standard deviation (SD) of the average difference between the FSFI total scores at baseline and at the end of the study was 1.26. This study had a power of 80% to detect variations in the FSFI total scores that were ≥ 0.52, and this study had a type I error (α) of 5%.

All of the clinical parameters were obtained from the patients at baseline and at the end of the treatment period. The anthropometric measures, weight and height, were recorded with an attached stadiometer when the patients were wearing lightweight clothing and no shoes. The BMI was calculated as the weight in kilograms divided by the square of the height in meters (Kg/m^2).

Statistical Analysis

The data were presented as the mean $\pm$ SD unless otherwise stated. The Mann-Whitney U test was used to compare the continuous numerical variables. For the categorical variables, the chi-squared and Fisher's exact tests were used. The Kolmogorov-Smirnov test was used to analyze the other differences between the groups of women. The Wilcoxon test was used to analyze the intragroup comparison. Univariate correlation analysis was performed with Pearson's correlation coefficient between the sexual function domains and the other independent variables. Multiple regression analyses were performed using the stepwise method with the "total score" at the end of the treatment period as the dependent variable and the following independent variables: the anthropometric measures at baseline and the lipid and lipoprotein variations at the end of the study. All of the analyses were conducted using the WinSTAT® software program, version 2007.1, for Microsoft® Excel®, and a value of $p < 0.05$ was considered significant.

Results

A total of 51 women who were included in the EE30/LNG150 group received combined oral contraceptives. There was one loss to follow-up, and one patient dropped out of the study because she had headaches after using the COC pills. Therefore, total 49 women completed the six cycles of treatment, and were included in the analysis of the results.

Using the criteria for a diagnosis of dyslipidemia, the sample was divided into additional groups. One group had LDL cholesterol levels ≥ 130 mg/dL and another did not have dyslipidemia when their LDL cholesterol levels were < 130 mg/dL. Another comparison group had HDL cholesterol levels < 50 mg/dL, and one did not have dyslipidemia when their HDL cholesterol levels were ≥ 50 mg/dL.

►**Table 1** shows the baseline characteristics of the women who participated in the study. There were no differences between the groups, excluding ethnicity, total cholesterol, LDL cholesterol and HDL cholesterol. Total cholesterol and LDL cholesterol levels were statistically significant when compared with those in the LDL group at baseline. In addition, the HDL cholesterol levels were statistically significant when compared with those in the HDL group at baseline.

The distributions of weight, BMI, abdominal circumference, fasting glucose, lipids and lipoprotein abnormalities

Table 1 Baseline characteristics of the study population, expressed as means ± SD or as frequencies and percentages (%), for each of the groups

Characteristics	LDL Group ($n = 49$)			HDL Group ($n = 49$)		
	LDL < 130 mg/dL ($n = 34$)	LDL ≥ 130 mg/dL ($n = 15$)	p	HDL ≥ 50 mg/dL ($n = 31$)	HDL < 50 mg/dL ($n = 18$)	p
Age (years)	27.6 ± 6.4	31.2 ± 7.4	0.087	28.2 ± 7.1	29.7 ± 6.4	0.456
Ethnicity (Caucasian)	17 (69.3%)	12 (30.7%)	0.049	21 (63.2%)	8 (36.8%)	0.110
Smoking (%)	8 (23.5%)	3(20.0%)	0.549	5 (16.1%)	6 (33.3%)	0.150
Duration of relationship (years)	5.9 ± 4.8	8.9 ± 7.1	0.138	7.4 ± 6.3	5.9 ± 4.5	0.723
Weight (kg)	60.7 ± 10.4	60.3 ± 9.0	0.893	60.1 ± 8.9	61.4 ± 11.7	0.654
BMI (kg/m^2)	23.8 ± 3.2	24.3 ± 2.6	0.616	23.8 ± 2.8	24.3 ± 3.3	0.569
Abdominal circumference (cm)	79.5 ± 9.8	81.1 ± 8.1	0.598	78.5 ± 8.5	82.5 ± 10.3	0.153
Fasting glucose (mg/dL)	82.8 ± 9.3	79.3 ± 8.5	0.221	81.8 ± 9.8	81.5 ± 8.2	0.911
Total cholesterol (mg/dL)	175.2 ± 21.2	223.9 ± 18.7	< 0.001	190.5 ± 29.3	189.3 ± 33.1	0.894
LDL cholesterol (mg/dL)	99.7 ± 19.6	145.3 ± 15.1	< 0.001	113.8 ± 29.5	113.3 ± 25.8	0.952
HDL cholesterol (mg/dL)	53.4 ± 11.0	52.1 ± 7.7	0.700	58.7 ± 7.3	43.1 ± 5.2	< 0.001
Triglycerides (mg/dL)	103.3 ± 53.6	127.1 ± 77.0	0.224	91.9 ± 32.8	142.7 ± 84.8	0.087

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.
Note: Significant values appear in boldface.

over time for each group with or without dyslipidemia are shown in ►**Table 2**. There was a statistically significant decrease in the total cholesterol by 14.7% and LDL cholesterol levels by 22.1% in the group with dyslipidemia (LDL ≥ 130 mg/dL). The HDL cholesterol levels increased by 15.5% in the group with HDL levels < 50 mg/dL, and there was a statistically significant increase in the triglyceride levels in the group HDL ≥ 50 mg/dL after 6 cycles of treatment.

►**Table 3** shows that the FSFI lubrication score was significantly higher in the patients with LDL levels ≥ 130 mg/dL according to the intergroup comparison at baseline. The FSFI total score was increased with statistical significance in women with and without dyslipidemia after six cycles of treatment. However, there was a statistically significant improvement in the "desire" domain only in the group with LDL levels < 130 mg/dL. In the intragroup comparison, the "orgasm" domain and the FSFI total score were statistically significantly increased in all the groups of women, regardless of LDL or HDL cholesterol levels. However, the individual analysis of the different domains revealed statistically significant improvements in the "arousal" and "satisfaction" domains in both LDL and HDL groups after six cycles of treatment respectively, independently of cholesterol levels. There were no improvements in the pain domain in either group after the COC treatment.

Pearson's correlation was performed between the sexual function domains and the following variables at baseline and at the end of the treatment period: age, smoking, anthropometric measures, fasting glucose levels, lipid levels and lipoprotein levels. At baseline, smoking was negatively correlated with the total FSFI score (r = -0.264, $p = 0.032$), the lubrication domain (r = -0.282, $p = 0.024$) and the orgasm domain (r = -0.207, $p = 0.030$). The BMI was negatively correlated with the arousal domain (r = -0.323, $p = 0.011$). The abdominal circumference was negatively correlated with the arousal domain (r = -0.505, $p < 0.001$), the orgasm domain (r = -0.360, $p = 0.005$), the satisfaction domain (r = -0.483, $p < 0.001$) and the total FSFI score (r = -0.399, $p < 0.001$). After six cycles of the COC treatment, the HDL cholesterol levels were positively correlated with the lubrication domain (r = 0.255, $p = 0.038$), the orgasm domain (r = 0.299, $p = 0.018$), and the total FSFI score (r = 0.267, $p = 0.031$). There was no correlation between any of the FSFI scores and the other independent variables after six cycles of the COC treatment.

The multiple regression analysis revealed that the "FSFI total" at the end of the treatment was statistically significant for the smoking coefficient = -3.841(95% confidence interval [CI]: 2.801–4.881), $p < 0.001$ and the BMI coefficient= 0.766 (95%CI: 0.546–0.986), $p = 0.001$. These two variables accouted for 46% of the variations in the total FSFI scores at the end of the study (R2 = 0.0460). None of the others variables were statistically significant.

Discussion

Many factors that contribute to female sexual satisfaction have been discussed, and they include interactions between metabolic diseases, sex hormones, neurotransmitters, marital status, social factors, age, personality and affective disorders.[20,21] Currently, little is known about the relationship between sexual function and obesity or lipid metabolism.[22]

Table 2 Behavior of weight, BMI, abdominal circumference, glucose, lipids, lipoprotein profile and triglycerides in the groups over the treatment period, expressed as means

Characteristics	LDL Group ($n = 49$)			HDL Group ($n = 49$)		
	LDL < 130 mg/dL ($n = 34$)	LDL ≥ 130 mg/dL ($n = 15$)	*p (intergroup comparison)*	HDL ≥ 50 mg/dL ($n = 31$)	HDL < 50 mg/dL ($n = 18$)	*p (intergroup comparison)*
Weight (kg)						
Baseline	60.7 ± 10.4	60.3 ± 9.0	0.893	60.1 ± 8.9	61.4 ± 11.7	0.654
After six cycles	60.6 ± 10.3	60.5 ± 9.5	0.979	60.4 ± 8.8	61.0 ± 12.0	0.838
Intragroup comparison	$p = 0.713$	$p = 0.586$		$p = 0.317$	$p = 0.205$	
BMI (kg/m^2)						
Baseline	23.8 ± 3.2	24.3 ± 2.6	0.616	23.8 ± 2.8	24.3 ± 3.3	0.569
After six cycles	23.8 ± 3.1	24.4 ± 2.7	0.531	23.9 ± 2.8	24.2 ± 3.5	0.808
Intragroup comparison	$p = 0.872$	$p = 0.574$		$p = 0.242$	$p = 0.243$	
Abdominal circumference (cm)						
Baseline	79.5 ± 9.8	81.1 ± 8.1	0.598	78.5 ± 8.5	82.5 ± 10.3	0.153
After six cycles	79.4 ± 11.3	79.1 ± 7.3	0.923	77.6 ± 8.4	82.1 ± 12.4	0.136
Intragroup comparison	$p = 0.804$	$p = 0.060$		$p = 0.116$	$p = 0.761$	
Fasting glucose (mg/dL)						
Baseline	82.8 ± 9.3	79.3 ± 8.5	0.221	81.8 ± 9.8	81.5 ± 8.2	0.911
After six cycles	82.0 ± 4.6	82.7 ± 4.6	0.610	83.3 ± 4.7	80.3 ± 3.8	0.026
Intragroup comparison	$p = 0.622$	$p = 0.170$		$p = 0.350$	$p = 0.616$	
Total cholesterol (mg/dL)						
Baseline	175.2 ± 21.2	223.9 ± 18.7	< 0.001	190.5 ± 29.3	189.3 ± 33.1	0.894
After six cycles	176.4 ± 22.5	191.2 ± 19.6	0.032	183.2 ± 20.1	176.9 ± 26.5	0.348
Intragroup comparison	$p = 0.759$	$p < 0.001$		$p = 0.131$	$p = 0.050$	
HDL cholesterol (mg/dL)						
Baseline	53.4 ± 11.0	52.1 ± 7.7	0.700	58.7 ± 7.3	43.1 ± 5.2	< 0.001
After six cycles	54.1 ± 7.4	56.2 ± 11.0	0.429	57.6 ± 8.3	49.7 ± 6.9	0.001
Intragroup comparison	$p = 0.623$	$p = 0.115$		$p = 0.469$	$p = 0.001$	
LDL cholesterol (mg/dL)						
Baseline	99.7 ± 19.6	145.3 ± 15.1	< 0.001	113.8 ± 29.5	113.3 ± 25.8	0.952
After six cycles	101.6 ± 21.0	113.2 ± 23.3	0.092	105.3 ± 22.3	104.9 ± 22.5	0.948
Intragroup comparison	$p = 0.542$	$p < 0.001$		$p = 0.075$	$p = 0.115$	
Triglycerides (mg/dL)						
Baseline	103.3 ± 53.6	127.1 ± 77.0	0.224	91.9 ± 32.8	142.7 ± 84.8	0.087
After six cycles	105.6 ± 39.3	115.9 ± 34.5	0.384	103.9 ± 35.3	117.1 ± 41.6	0.244
Intragroup comparison	$p = 0.630$	$p = 0.564$		$p = 0.008$	$p = 0.109$	

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.
Note: Significant values appear in boldface.

Table 3 Total score and domains scores for the FSFI questionnaire in the LDL and HDL groups at baseline and after six cycles of treatment, expressed as means ± SD

Domain (range of score)	LDL Group ($n = 49$)			HDL Group ($n = 49$)		
	LDL < 130 mg/dL ($n = 34$)	LDL ≥ 130 mg/dL ($n = 15$)	*p (intergroup comparison)*	HDL ≥ 50 mg/dL ($n = 31$)	HDL < 50 mg/dL ($n = 18$)	*p (intergroup comparison)*
FSFI-Desire (1.2–6.0)						
Baseline	3.9 ± 0.7	3.8 ± 0.5	0.781	3.8 ± 0.6	3.9 ± 0.7	0.712
After six cycles	4.1 ± 0.7	3.8 ± 0.6	0.185	4.0 ± 0.7	4.1 ± 0.7	0.966
Intragroup comparison	$p = 0.013$	$p = 0.673$		$p = 0.058$	$p = 0.093$	
FSFI-Arousal (0.0–6.0)						
Baseline	3.9 ± 1.0	3.9 ± 0.9	0.991	3.9 ± 1.0	3.8 ± 1.1	0.551
After six cycles	4.0 ± 0.9	4.1 ± 0.8	0.913	4.1 ± 0.8	3.9 ± 0.9	0.378
Intragroup comparison	$p = 0.008$	$p = 0.043$		$p = 0.005$	$p = 0.068$	
FSFI-Lubrication (0.0–6.0)						
Baseline	4.9 ± 1.2	5.5 ± 0.8	0.034	5.1 ± 1.2	5.0 ± 1.1	0.559
After six cycles	5.0 ± 1.1	5.5 ± 0.8	0.081	5.1 ± 1.0	5.1 ± 1.0	0.806
Intragroup comparison	$p = 0.052$	$p = 0.655$		$p = 0.345$	$p = 0.273$	
FSFI-Orgasm (0.0–6.0)						
Baseline	4.7 ± 1.3	4.8 ± 1.2	0.800	4.8 ± 1.3	4.6 ± 1.2	0.454
After six cycles	5.0 ± 1.0	5.0 ± 0.8	0.648	5.1 ± 1.0	5.0 ± 1.0	0.609
Intragroup comparison	$p = 0.004$	$p = 0.04$		$p = 0.010$	$p = 0.012$	
FSFI-Satisfaction (0.8–6.0)						
Baseline	4.5 ± 1.1	4.7 ± 1.1	0.541	4.7 ± 1.0	4.3 ± 1.3	0.407
After six cycles	4.9 ± 0.9	4.9 ± 0.9	0.825	5.0 ± 0.8	4.7 ± 1.0	0.393
Intragroup comparison	$p < 0.001$	$p = 0.093$		$p < 0.001$	$p = 0.004$	
FSFI-Pain (0.0–6.0)						
Baseline	5.2 ± 1.2	5.7 ± 0.6	0.224	5.4 ± 1.0	5.2 ± 1.2	0.448
After six cycles	5.3 ± 1.1	5.7 ± 0.6	0.301	5.5 ± 0.9	5.3 ± 1.2	0.772
Intragroup comparison	$p = 0.068$	$p = 1.000$		$p = 0.285$	$p = 0.109$	
FSFI-Total Score (2.0–36.0)						
Baseline	27.0 ± 5.3	28.3 ± 3.0	0.688	27.7 ± 4.6	26.9 ± 5.1	0.507
After six cycles	28.5 ± 4.5	29.0 ± 2.8	0.888	28.9 ± 3.9	28.3 ± 4.4	0.648
Intragroup comparison	$p < 0.001$	$p = 0.004$		$p < 0.001$	$p < 0.001$	

Abbreviations: BMI, body mass index; FSFI, Female Sexual Function Index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.
Note: Significant values appear in boldface.

This study investigated the effects of EE and LNG containing COC treatment on various parameters of lipid and lipoprotein metabolism, and showed that the androgenicity of the progestogen result in changes on lipids and on female sexual function. Our findings are in agreement with the results of a study that used contraceptive formulations with 25 mcg and 35 mcg of EE,[23] because the COC treatment was associated with a decrease in the total cholesterol (TC) and LDL levels, especially in the group who had the highest values at baseline. The changes in the TC and LDL levels were statistically significant in the intragroup and intergroup comparisons after six cycles of treatment.

A study by Tuppurainen et al[9] evaluated the effects of the combined contraceptive vaginal ring (NuvaRing®, CCVR, Organon Int., Oss, The Netherlands) and a COC treatment with levonorgestrel on various parameters of lipid metabolism. Neither the NuvaRing® nor the COC were associated with changes in TC; however, the COC treatment led to a reduction in HDL levels and a small increase in LDL levels.[9] In contrast to our findings in lipid metabolism, those were obtained with NuvaRing were consistent with lowere androgenicity of etonogstrel when compared with levonorgestrel.[12] Combined oral contraceptives with less androgenic progestogens demonstrate greater increases in HDL and lesser elevations in triglyceride levels compared with other formulations.[24] The statistically significant increase in the HDL levels in the group with HDL levels < 50 mg/dL after 6 cycles was not consistent with the greater intrinsic androgenicity of levonorgestrel.

On the most recent systematic review showed that the COC use among women with known dyslipidemia, discussed that generally EE tends to decrease LDL and increase both HDL and triglyceride levels, while progestogens exert antagonistic effects, resulting in increases in LDL and decreases in HDL and triglyceride levels.[25]

According to a study by Wallwiener et al,[26] women who take non-oral or oral hormonal contraceptives were at a high risk for sexual dysfunction. Sexual problems can have a negative impact on both the quality of life and emotional well-being of women, and the most common complaint is low desire.[27,28] However, other studies found that the use of contraceptives had no impact, and they have not observed an effect on sexual desire in women with or without hypoactive sexual desire disorder.[29,30] A more recent systematic review of the literature that evaluated the influence of different formulations of COC on female sexual desire concluded that the majority of COC users report no significant change in libido.[30] A study by Strufaldi et al[31] found that during the intake of a pill containing 30 mcg of EE and 150 mcg of LNG, plasma androgen levels decrease, but without any negative impact on sexual desire; however, with a lower estrogen dose of 20 mcg of EE and 100 mcg of LNG, sexual interest augmented.[31] The present study confirmed that the contraceptive pill did not have any negative effect on the lipid profile and on female sexual function after six cycles of treatment.

Recently, a trial by Caruso et al[29] investigated the effect of a four-phasic COC regimen with an oral contraceptive that contained estradiol valerate (E2V) and dienogest (DNG), for six cycles on quality sexual of life. The study demonstrated that the extended use of this COC formulation improved sexual enjoyment, arousal, orgasm and desire. In addition, the authors suggested that monophasic COCs may not have similar positive effects on sexuality.[29]

A systematic review found that BMI generally reflects the amount of fat in an individual; however, the accuracy of this parameter is limited, and all contraceptive methods are most effective when the recommended regimen is followed.[32] The relationship between sexual function and the amount of body weight and lipid or lipoprotein metabolism in females remains obscure.

A study by Esposito et al[33] that investigated the relationship between body weight, the distribution of body fat and sexual function in women demonstrated that obesity affected several parameters of sexuality according to the FSFI questionnaire.[33] Additionally, Ponholzer et al[34] suggested that metabolic syndrome is an independent risk factor for impaired sexual desire in women in reproductive age.

A recent study by Yaylali et al[35] found a significant negative correlation between BMI and the orgasm domain. The study demonstrated that the satisfaction domain was negatively correlated with weight. After six cycles of the COC treatment, our findings did not demonstrate a correlation between weight, abdominal circumference and BMI and the sexual function domains and the total FSFI scores. However, the present study found a significant positive correlation between HDL cholesterol levels and the lubrication domain ($r = 0.255$, $p = 0.038$), the orgasm domain ($r = 0.299$, $p = 0.018$) and the total FSFI score ($r = 0.267$, $p = 0.031$). These findings support the hypothesis that obesity is not a major contributor to sexual dysfunction; however, this condition affects several aspects of sexuality.[35]

A study by Kadioglu et al[36] indicated that obese patients are more depressed than their age-matched normal counterparts, and obesity may not be a risk factor for female sexual dysfunction. Esposito et al[22] demonstrated for the first time that women with hyperlipidemia have significantly lower FSFI domain scores when compared with age-matched women without hyperlipidemia. They believe that hyperlipidemia affects specific domains of the female sexual function, including desire, arousal, lubrication and orgasm. However, a reduction in serum lipid levels, increased physical activity and the prevention of hyperlipidemia could be potential therapeutic strategies to improve and preserve sexual function in women.[22]

Additionally, the COC formulation that was used in this study affected the HDL levels, the sexual function domains and the total FSFI scores. There was a significant correlation between these variables, which was unrelated to the HDL levels at baseline.

The strengths of this study include the enrollment of women who previously presented normal sexual function; therefore, the prevalence of sexual dysfunction in women with and without dyslipidemia could be assessed. An additional strength was that the patients answered the questionnaire by themselves, without interference from the investigators.

One limitation of our study was the open, single blind design, because the COC formulation is commercially used more than other formulations in Brazil; however, we believe that this limitation did not influence the results. Although the sample calculation has been performed, a more robust sample of participants could have presented different results. The weakness of this study was the small number of women with dyslipidemia, which may have been due to the lower prevalence of this condition in women in reproductive age who were selected for this study.

In conclusion, this study showed that the EE30/LNG150 formulation decreased the total cholesterol and LDL cholesterol levels, especially when these levels were higher at baseline. This composition increased the sexual function, and there was a positive correlation only with the HDL cholesterol level after six cycles of treatment. Overall, these data indicated a low correlation between sexual function and the changes in the lipid and lipoprotein metabolism.

The present study provides important and new information as well as some insight into the influence of lipid and lipoprotein metabolism on female sexual function; however, the findings also suggest avenues for future research with larger numbers of participants.

Declaration of Conflicts of Interest

The authors report no conflicts of interest in this work.

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