Changes in body weight and blood pressure in women using Depo-Provera in Northwest Ethiopia

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Abstract
Objectives: Depo-Provera is a widely known brand name for medroxyprogesterone acetate. It has some adverse effects which is reversible after discontinuation include changes in bleeding patterns and bone mineral density loss risk of weight gain in obese adolescents. The study aims to investigate the effects of Depo-Provera on body weight and blood pressure of Ethiopian women. Institutional based cross-sectional study design was conducted. The data was analyzed using SPSS version 21 software packages. Paired t-test, independent t-test and ANOVA were used to evaluate the presence of mean difference and relationship between changes in variables and duration of use of Depo-Provera. The p-values less than 0.05 were considered as statistically significant. Results The mean weight and body mass index (BMI) of Depo-Provera users were increased significantly (p-value-0.02 and p-value-0.019 respectively). There was no significant difference in mean arterial blood pressure (MAP) of Depo-Provera users compared to controls or their respective pretreatment value (p-value-0.85, p-value-0.67, respectively). Depo-Provera users showed weight gain and an increased BMI, which requires attention of stake holders.

Introduction
Worldwide average fertility rate is 1.7 in developed countries compared to 4.6 children per woman in least developed countries [1]. In Ethiopia average total fertility rate is 4.1, which is among the highest in the word. [2,3]. Increased use of family planning methods helps to bring these figures down to low levels.

In Ethiopia, the family planning service which is subsidized of cost is provided in both governmental and NGO health facilities, including hospitals, clinics, health centers, and health stations [4]. Among the different methods of family planning, injectable hormonal contraceptives; Depo-Provera (Depo-medroxyprogesterone acetate) is the most popular contraceptive method in Sub-Saharan Africa including Ethiopia, contributing to about 40% of total method mix in the region [5]. Depo-Provera is among a highly effective, convenient non-daily injectable hormonal contraceptive option with a very low failure rate that has been available worldwide for many years. The recommended dose of this contraceptive is 150 mg, administered by deep intramuscular (IM) injection using strict aseptic
technique in the gluteal or deltoid muscle [6, 7]. Side effects of this contraceptive include changes in bleeding patterns, bone mineral density loss and risk of weight gain in obese adolescents.

Prior studies have demonstrated the association between Depo-Provera with both weight gain [8, 9] and blood pressure [10]. On the other hand, another study reported that Depo-Provera injections didn't cause a significant increase in body weight and blood pressure [6]. Since previous studies performed among different ethnic groups showed diverse results and available data on this topic are mostly from developed countries, this study was aimed to investigate the effects of Depo-Provera on body weight and blood pressure among Ethiopian women.

Methods

Study area and period

This study was conducted at Azezo Health Center, Gondar, Northwest Ethiopia. It serves for a total population of more than 25000 individuals per year. The study was conducted from January 2017 to April 2017.

Study design: Institution-based comparative cross-sectional study design was employed.

Source population

All Depo-Provera user women between 18-45 years of ages and age matched non Depo Provera user women

Study population

All Depo-Provera user women between 18-45 years of ages and age matched non Depo Provera user women who were present in the study period

Eligibility criteria:

Inclusion criteria: All Depo-Provera user women between 18-45 years of ages and age matched non Depo Provera user women who were present in the study period

Exclusion criteria: women who had concomitant disease during the study period were excluded
Sample size determination

The sample size for this study was determined by double-population formula assuming 95% confidence interval, 80% power and using the highest standard deviation. Systematic random sampling technique was used to select 50 healthy women who had been using Depo-Provera for at least six months and convenient sampling technique were used to recruit 50 healthy age-matched (±2 years) non-users of hormonal contraceptive who visited the health centers accompanying the patients during the study period (controls).

Variables of the study

Dependent variable: Body weight, BMI and blood pressure
Independent variables: Age, duration of use of Depo Provera

Data collection instrument and procedure

Structured pretested interviewer administered questionnaire was used. The questionnaire was prepared in English first and translated to Amharic and then, retranslated back to English by another person to check its consistency. Written informed consent was taken from the participants. Blood pressure was measured using recently calibrated standardized sphygmomanometer. The height measurement was taken using stadiometer on flooring that is not carpeted and against a flat surface such as a wall with no molding and by remove the child or teen's shoes, bulky clothing, hair ornaments, and unbraid hair that interferes with the measurement. The weight (Kg) of study participants was taken using a mechanical scale or balance.

The MAP was calculated by using the formula $\text{MAP} = \text{Pd} + \frac{1}{3}(\text{Ps}-\text{Pd})$. BMI was computed by dividing weight (Kg) to the square of height (M). The change in body weight, BMI and MAP of Depo-Provera users were calculated as the difference between initial body weight, BMI and MAP on the first day of injection, recorded by the health care providers and the final weight, BMI and MAP taken at their visit during study period.

Data quality control

Training was given for data collectors. Pretest was also done. During data collection, data collectors
were closely supervised by the supervisor and principal investigator on daily basis. Then after appropriate data clean up and correction was done just before analysis.

Data processing and analysis

Data were entered into Epi Data version 3.1 and exported to Statistical package for Social Sciences (SPSS) version 21 for analysis. Descriptive statistics such as mean, standard deviation (SD) and range were calculated. Paired t-test was used to evaluate change in body weight, BMI and blood pressure of Depo-Provera users. Independent t-test was also used to compare the results of blood pressure of Depo-Provera users and their age-matched control group. One-way ANOVA was used to identify the variation of variables in relation to the duration of use of Depo-Provera. Pearson’s correlation-test was used to evaluate the association between the variables. All values were quoted as the means ± SD, p-values of ≤0.05 were considered to be statistically significant.

Results

Description of study participants

A total of 100 study participants (50 Depo-Provera users and 50 controls) were included in the study. The mean age (years) of Depo-Provera users was 27.54±5.63 and 27.44±5.02 for control group. The mean BMI (Kg/m$^2$) was 22.05±3.10 and 21.55±3.05 in Depo-Provera users and controls, respectively.

Magnitude and determinants of change in body weight and Body Mass Index

This study indicates that Depo-Provera caused a significant weight gain. Weight gain varies from 1 to 14 Kg. Excessive weight gain (≥10%) was observed in 9 (18%) of Depo-Provera users. Moreover, Depo-Provera users showed significant increase (p-value-0.02) in BMI compared to their respective pretreatment value (Table 2). The mean change in BMI (Kg/m$^2$) among Depo-Provera users was 0.67 (+3.13%). The maximum increment of BMI among Depo-Provera users was 5.9 Kg/m$^2$. However, student’s paired t-test showed significant changes in mean weight and BMI among Depo-Provera users, the one-way ANOVA didn’t show significant (p>0.05) changes in mean weight and BMI between groups of Depo-Provera users in relation to duration of use (6-24, 27-48 and 51-96 months) (Table 3).
Magnitude and determinants of change in mean arterial pressure among study participants

Table 1 revealed a non-significant difference (p=0.85) in the MAP between Depo-Provera users and control group. There were no significant difference in systolic blood pressure (SBP) and diastolic blood pressure (DBP) between Depo-Provera user (108.4 ±12.47; 70.7±7.82) and controls (108.2±11.00; 72.8±7.83). Furthermore, the change in MAP of Depo-Provera users and control group was not statistically significant (p=0.67). The mean SBP and DBP were 107 ±8.86; 70.6 ±8.18 before and 108.4 ±12.47; 70.7±7.82 after they had been using Depo-Provera. This difference was not significant (p=0.41 and p=0.94, respectively). The present study found no association between the variables, weight (BMI) and blood pressure of Depo-Provera users (Table 2).

Discussion

Findings of this study demonstrated that Depo-Provera users had significant weight gain and increased BMI as compared to their respective pretreatment value. This is in agreement with a prospective cohort study performed on 97 Brazilian women, aimed to compare body weight and body composition in Depo-Provera and copper IUD users at baseline and after 1 year of use [11]. Other study, done to assess the association between progestin-only contraceptive use and changes in body weight, revealed that weight gain was greater in Depo-Provera group than the group using a non-hormonal IUCD which is in agreement with findings of the present study [12]. Another similar study showed that use of Depo-Provera was associated with weight gain compared to the copper IUCD [9]. They also suggested that only black race was associated with significant weight gain. The present study also supports finding of other studies where the BMI of the Depo-Provera users was increased significantly than the control group and were in the overweight range [13]. Moreover, a recent study conducted to assess dietary intake and weight gain among adolescents on Depo-Provera, demonstrated that mean BMI increased significantly from 23.7 ±5.3 at the baseline to 25.3 ±5.7 after 12 months of use of Depo-Provera with increased mean percentage body fat significantly [14]. While other study indicated Depo-Provera users poses increased body weight in comparison to their
controls, however, changes were not statistically significant [6]. This could be due to the difference in race/ethnicity which is associated with weight gain, where black women had a greater mean weight gain compared to white, Bushmen, oriental and Papuan with continued Depo-Provera use [16, 9]. It can also be due to practicing physical exercise following good counseling of study participants in the previous study.

Increment of weight is a common phenomenon for women initiating hormonal contraceptives, especially Depo-Provera. However, the existing literature does not provide a clear-cut picture of the mechanism of Depo-Provera-related weight gain. The previous authors were tried to report the reasons why the use Depo-Provera can lead to weight increase. Self-reported increase of appetite after six months of Depo-Provera use was investigated by Le et al, (2009) [17]. This supports Leiman who reported weight gain among Depo-Provera users was related to their higher appetite and subsequently higher dietary ingestion as a result of modifications of the hypothalamic appetite control center by Depo-Provera. Contrary to the prior studies, findings of Lange et al, (2015) suggested that Depo-Provera associated weight gain cannot be explained by a simple, direct relationship to increased food consumption [14,18]. Therefore, the role of appetite and dietary intake for Depo-Provera-associated weight gain remains to be clarified.

The result obtained from the present study indicates Depo-Provera does not have unfavorable effect on blood pressure. The MAP, SBP and DBP between Depo-Provera users and control group were not significantly different. Changes in MAP, SBP and DBP before and after they had been using Depo-Provera were not statistically significant. This finding was similar with the findings of another studies [6,15]. This study needs to be extended on wider population so as to generalize the effects of Depo-Provera on health of Ethiopian women and further studies required to elucidate the molecular mechanism, if any which contribute the change in body weight among women using Depo-Provera.

Conclusion

In conclusion, Depo-Provera users had significant weight gain and significant increase in BMI compared with their respective pretreatment value, although, these effects appeared to be independent of the duration of use of Depo-Provera. Women taking Depo-Provera didn’t show
significant change in MAP compared to controls or to their respective pretreatment value, which indicates Depo-Provera use does not have unfavorable effects on blood pressure.

Limitations
The limitation in the present study may be the smaller number of participants recruited in comparison with the other trials. The other limitation lies in the fact that potential confounders including total daily caloric intake, physical activity and intake of cholesterol rich diets were not considered. This study was conducted only in one district, which makes generalization to the wider population difficult.

Declarations

Abbreviations
MAP: Mean Arterial Pressure, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, IUCD: Intrauterine Contraceptive Device, BMI Body Mass Index

Consent to publication

Note applicable

Ethics approval and consent to participate
Ethical clearance of this study was obtained from Ethical Review Board of University of Gondar with a protocol number of GCMH71/2017.

Availability of data and materials
The data could be accessed by a requesting the corresponding author.

Consent for publication
Not applicable

Competing interest
Authors declare that they have no any conflict of interest

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There was no specific funding for the research.

Authors’ contributions
MF collected data, designed the study, performed analysis and interpretation of data. YY supervised the data collection, analysis, interpretation of data. TM, YMF, TB drafted the manuscript. All authors
read and approved the final Manuscript.

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