

Assessment of Some Coagulation Parameters among Clients on Hormonal Contraceptive in a Tertiary Health Facility in Sokoto, North Western, Nigeria

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Abstract

Background: Hormonal contraceptives are widely used, and contain different doses of estrogen and types of progestogen. However, these hormonal contraceptives may potentially be associated with some side effects of coagulopathy.

Objective: The aim of this study was to evaluate the Prothrombin Time (PT) and Partial Thromboplastin Time with Kaolin (PTTK) among clients on hormonal contraceptives.

Method: This descriptive case-control study was conducted among clients on hormonal contraceptives. A total of 43 clients on hormonal contraceptives constituted the subjects. Twenty non-hormonal contraceptive users were monitored as controls. PTTK and PT was carried out on citrated samples from subjects and control participants using the Diagen kit for PTTK and PT.

Results: The mean values for PT and PTTK of the contraceptive users was 15.6 ± 1.5 s and 36.4 ± 2.7 s respectively, while the mean value for the control group was 16.0 ± 1.2 s and 38.6 ± 3.9 s respectively. The PT and PTTK mean values of the contraceptives users although marginally lower among subjects compared to the control group (0.4 and 2.2 seconds) respectively. The bivariate analysis did not demonstrate any significant difference between the coagulation parameters of contraceptive users and control group ($t = 0.702$, $p = 0.491$ for PT; $t = 1.732$, $p = 0.100$ for PTTK). There was significant differences in the in the PT and PTTK values of hormonal contraceptive users based on age. There was a negative correlation between PT and duration of contraceptive use.

Conclusion: There was no clinically significant differences between the values of coagulation parameters of contraceptives users and non-users. However, it is not conclusive whether long term use of modern hormonal contraceptives increases the risk of thrombosis. There is need for more studies to investigate the effect of long-term hormonal contraceptive use on the PT and PTTK.

Keywords: Coagulopathy; Family planning; Hormonal contraceptive; Sokoto

Introduction

Contraception is the use of various devices, drug agents, sexual practices or surgical procedures to prevent conception or impregnation (pregnancy). This process help couples plan when they want to have a child. The first available preparation of hormonal contraceptives contained a high dose of the estrogen EE2 which was linked to increased risk of thrombosis. Estrogen containing contraceptives particularly at a reduced dose can lead to an additional risk reduction of venous thrombosis [1]. Hormonal contraceptives are often associated with side effects commonly; nausea, headache, breast tenderness, weight gain, irregular bleeding, and mood changes [2]. Oral pills are the most frequently used hormonal contraceptives and commonly contribute to increased blood pressure, blood clots, heart attack and stroke [3,4]. In Europe and North America studies have demonstrated that estrogen/progestogen oral contraceptives are

associated with myocardial infarction, thromboembolism and stroke commonly among women over the age of 35 and smokers [5].

The lowering of the estrogen dose from $>50 \mu\text{g}$ to $30 \mu\text{g}$ has been shown to be associated with a significant decrease in the risk of venous thrombosis [6]. The cause of differences in the coagulation and haemostatic status between women using hormonal contraceptives from widely diverse geographical areas is not clearly understood. WHO recommended that studies should be conducted in different settings to bring about a clearer picture [7].

The most drastic adverse effect associated with hormonal contraceptive use is predisposition to higher risk of thromboembolic phenomena. Progestins have antiplasmin and antithrombin activity [8]. Its use increase platelet count and aggregability, thus predisposing to hypercoagulability. A previous study reported an increased rate of thrombosis of 1-3 per 100,000 individuals per year [9-11]. There is increasing use of oral contraceptives in Nigeria. There is paucity of data on the effect of hormonal contraceptive use on the indices of coagulation of Nigerian women. The aim of this present study is to

assess some coagulation parameters (PT and PTTK) among clients on hormonal contraceptives in Sokoto, North Western Nigeria.

Materials and Methods

Background information of study area

The study was conducted in Family Health Clinic (FHC) of the Department of Community Medicine, Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto. The clinic runs every Wednesday on appointment receiving on the average about 60 clients on a weekly basis.

Study design

This is a comparative descriptive case-control study carried among clients on hormonal contraceptives attending FHC. Women who have never used any family planning method and or hormonal contraceptives constituted the control participants.

Inclusion and exclusion criteria

Subject for this study were randomly selected from among clients attending FHC in Usmanu Danfodiyo University Teaching Hospital. Inclusion criteria included; age (≥ 18 years), hormonal contraceptives use for a period of three months and above and willingness to give a written informed consent to participate in the study. Exclusion criteria included; age (<18 years), non- hormonal contraceptive use and contraceptives use of <3 months, presence of underlying disease condition that could affect their clotting system and failure to offer a written informed consent to partake in the study.

Data analysis

Data obtained was analysed using Statistical Package for Social Science (SPSS) version 15.0. The data was tested for normal distribution. The mean and standard deviation was determined for the continuous normally distributed variables. Bivariate analysis of mean using student t-test was carried out to compare the mean difference between the PT and PTTK of the subjects and control individuals. A p-value of <0.05 was considered significant in all statistical comparisons.

Ethical consideration

As part of the requirements for conducting surveys on human subjects in Usmanu Danfodiyo University Teaching Hospital Sokoto, the study was approved by the Research Ethics Committee of the hospital. In addition, all study participants gave a written informed consent before they were enrolled in this study and samples taken.

Method

4.5 ml of the participants' blood samples were collected by a venepuncture in to a test tube containing 0.5 ml of 3.1% trisodium citrate. The sample was thoroughly mixed by gently inversion and centrifuged at 3000 rpm for 5 min to separate the plasma which was then used to determine the PTTK and PT manually using the Diagen PTTK and PT Kit (Diagen Diagnostics UK). Testing was carried out following the manufacturers' standard operating procedures.

Results

Participants on hormonal contraceptives aged between 20 to 40 years constituted the subjects. Age-matched women who were not on any hormonal contraceptives were monitored as controls. Table 1 shows the age distribution of subjects. The mean value of PT for the study and control groups were 15.6 ± 1.5 s and 16.0 ± 1.2 s respectively. There was no statistically significant difference between the mean values of PT for the two groups ($t= 0.702$, $p= 0.49$). The PTTK values of the subjects and control groups were 36.4 ± 2.8 s and 38.6 ± 4.9 s respectively. There was no statistically significant difference between the mean values of PTTK for the two groups ($t= 1.732$, $p= 0.10$) as shown in Table 2.

Participants on hormonal contraceptives	
Age groups (Years)	Frequencies (%)
20 – 24	8 (18.6)
25 – 29	22 (51.2)
30 – 34	9 (20.9)
35 – 40	4 (9.3)

Table 1: Age distribution of subjects on hormonal contraceptives

Variables	Subjects	Controls	t –Value	p – value
P T	15.6 ± 1.5 s	16.0 ± 1.2 s	0.702	0.49
PTTK	36.4 ± 2.8 s	38.6 ± 4.9 s	1.732	0.10

Table 2: Comparison of mean value of PT, PTTK for study and control groups

Table 3 showed that all the participants that were not exposed to hormonal contraceptives had normal prothrombin time. Eleven percent of study participants who were on hormonal contraceptives for less than a year was found to have abnormal prothrombin time while the participants exposed to hormonal contraceptives for ≥ 1 year have prothrombin time within normal range. Table 3 show the prothrombin time in relation to the duration of exposure to hormonal contraceptives.

Prothrombin time			
Duration(years) result	Normal result	Abnormal	Total
Control	20 (100%)	0 (0.0%)	20 (100%)
< 1year	29 (67.4%)	5 (11.6%)	34 (79.1%)
>1year	9 (20.9%)	0 (0.0%)	9 (20.9%)

Table 3: Prothrombin time and duration of exposure to hormonal contraceptives

Discussion

The PTTK is a performance indicator measuring the efficacy of both the intrinsic and the common coagulation pathways. Apart from detecting abnormalities in blood clotting, it can be used to monitor the treatment effects in patient at risk of thrombosis on heparin therapy. It is used in conjunction with PT which measures the extrinsic pathway. Shortening of the PT and PTTK predisposes patients to an increased risk of thrombosis [12,13].

In this study we found no statistical significant association between coagulation parameters of PT and PTTK of hormonal contraceptives users and that of the control group. There was however a decrease of 0.4 seconds in the mean PT values of the subjects compared to the control group. This finding is in agreement with previous report by Abdalla et al. [14] who reported 0.4 seconds decrease in the mean value of the PT between subjects on hormonal contraceptives and controls. Our finding is however at variance with report by Roshida et al. [15] who reported 0.4 decrease in the PT values of subjects on hormonal contraceptives compared to controls.

Our overall values of the PT for the subjects and controls were found to be higher compared with previous reports [14,15]. This difference may indicate possible differences in the normal ranges among different races and across geographical regions. This re-affirms the need for the determination of normal ranges for coagulation parameter among African subjects instead of the erroneous use of cutoff values derived from the West as diagnostic indices for Africans.

We observed a non-statistically significant difference between the mean PTTK values of the subjects and controls. This finding is in agreement with findings by Abdalla et al. [14] and Roshida et al. [15]. In the past, studies have demonstrated that high doses of estrogen/progestogen containing oral contraceptives are associated with myocardial infarction, thromboembolism and stroke commonly among women over the age of 35 and smokers [5]. Most modern oral contraceptives are now associated with the lowering of the estrogen dose from >50 µg to 30 µg. This dose reduction has been shown to be associated with a significant decrease in the risk of venous thrombosis [6].

We observed the mean value of PT and PTTK although marginally higher among subjects in the 25-29 years group and lowest in the 35-39 age groups, this difference in the PT and PTTK did not seem to differ significantly based on age. This mean values of the coagulation parameters were within the normal range across the different age groups. Our finding is consistent with previous report by Joseph et al. [16] who observed that the mean values of the haemostatic parameters did not vary significantly based on age.

Our work showed a negative correlation between PT and duration of contraceptive use. We used the Odds ratio and found out that less than 1 year use has odd ratio of 0.172 while those above 1 year use has odd ratio of 0. These findings indicate that early introduction of hormonal contraceptive have an insignificant effect on PT. This finding is in agreement with work of Ahmad and Kashmoola [17], who reported a negative correlation between PT and the duration of oral contraceptives use. It is also in conformity with the finding of Li [18], who stated that, long-term use of Chinese low-dose combined oral contraceptives (COCs) had a slight negative influence on haemostatics. Our finding is in agreement with previous report that the risk of venous thrombosis is unrelated to the duration of hormonal contraceptives [19].

Conclusion

This study indicated that there was no clinically significant differences between the values of coagulation parameters (PT and PTTK) of contraceptives users and non-users. However, it is not conclusive whether long-term use of modern hormonal contraceptives increases the risk of thrombosis. There is need for more studies to investigate the effect of long-term hormonal contraceptive use on the PT and PTTK.

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