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Full Length Research Paper

Evolution of biochemical parameters in Senegalese women using hormonal contraceptive

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This study was conducted to assess the effects of hormonal contraceptives in biochemistry parameters, in two family planning clinics and Medical laboratory of Biochemistry, University Cheikh Anta Diop of Dakar (UCAD). This study has involved159 women of childbearing age in which 106 are hormonal contraception users and 53 women are non users, with the average pregnancy of 3. They had a mean age of 27 +/- 7 years, and a mean weight of 65.25 +/- 10.8. Each participant was submitted to a gynecological examination and blood samples were measured by a biochemistry RA-XT (Technikon ®) autoanalyzer. After six months, we observed in women users a statistically significant increase in uric acid level. We also observed an increase in AST, ALT and PAL levels according to contraceptives used. The significant decrease in urea and lipid such as triglycerides, high density lipoprotein cholesterol (C-HDL) and total cholesterol (CT) was observed within the reference range. Other parameters explored remain unchanged.

Keywords: Contraceptives, biochemistry parameters, Senegal.

INTRODUCTION

Maternal deaths in poor countries represent 25-30% of deaths in women of childbearing age (Bouvier, 2003). In Senegal, studies have revealed alarming maternal morbidity (1,200 deaths per 100,000 live births). In this context, the use of contraceptives in family planning program significantly reduces in the same time mothers and children mortality and the rapid growth of the population. However, if the benefit is enjoyed by some authors, all of them do not agree on the deleterious role of different oral contraceptives. These deleterious effects, including metabolic disorders are detrimental to the health of women using long-term hormonal contraceptives (Agpona, 1998). Despite numerous publications on the subject, contradictions highlighted have shown that it is still necessary to update the data for a more rational approach of contraceptive practices.

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MATERIALS AND METHODS

Materials

This work has involved 159 women of childbearing consulted in the two centers of Family Planning. After informed consent, only women without known risk factors and adopting for the first time hormonal contraception were selected. Women from two centers non users of hormonal contraception have however served as control group. These women have been divided into 106 users of hormonal contraception and 53 controls. They are pauciparous, 3 births on average, 0 to 8 in extreme cases. They had a mean age of 27 +/- 7 years, and a mean weight of 65.25 +/- 10.8. Women users have been divided into 4 groups:

- A group of 32 women taking estrogen-progestin pills (EPP)
- A group of nine women using micro dosed pure progestative pills (PPP)
- Most of women (50) were Ovrette users (micro dosed progesterone injections)
- The remaining 15 women were carrying an

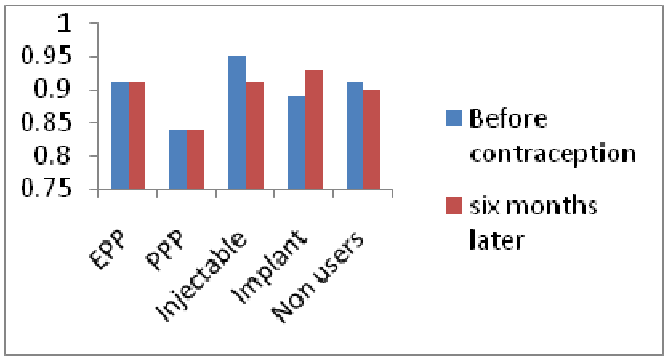

Figure 1. Mean value of glucose (g/l)

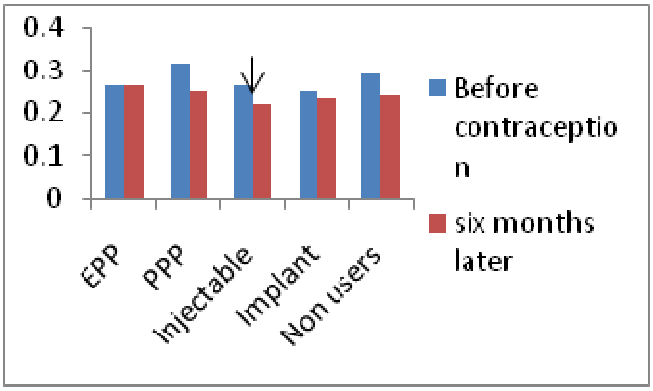

Figure 2. Mean value of urea (g/l)

implant (micro dosed progesterone)

Methods

This work has been done with the same sampling rate. Each patient was submitted a thorough gynecological examination and blood testing. The blood samples were collected in three tubes by venipuncture, after 12 hours these samples were then transported to the Department of Medical Biochemistry, of University where one portion has been treated and the other used as serum bank. Six months after, the same procedure has been used.

Biochemistry parameters were determined by enzymatic method using commercial kits (BIOSYSTEM S.A, Barcelona, Spain). Biochemistry RA-XT (Technikon ®) autoanalyzer and a Biosystems ® 330 spectrophotometer have been used to perform the biochemical tests.

The determination of creatinine in the blood was performed using the kinetic method of Jaffe, while searching for various enzymes such as AST, ALT and PAL need the coupling of a product the rate of disappearance or formation of which determines the catalytic concentration.

Statistical analyses

Data were computed on Excel and were analyzed using EPI INFO 2000, Version 3.3.2 and SPSS. The means and standard deviations were calculated for each biochemical parameter. Student's test was used to compare means in the different groups and the differences were considered to be statistically significant with values of $P < 0.05$.

RESULTS

The comparison of biochemical tests between users hormonal contraceptive and nonusers before and six months after use showed variations according to different parameters (Figure 1 -9, Table 1 and 2). Almost all biochemical parameters proved to be in the normal physiological range. However, results have shown uric acid values significantly higher in users than in nonusers ($p < 0.05$).

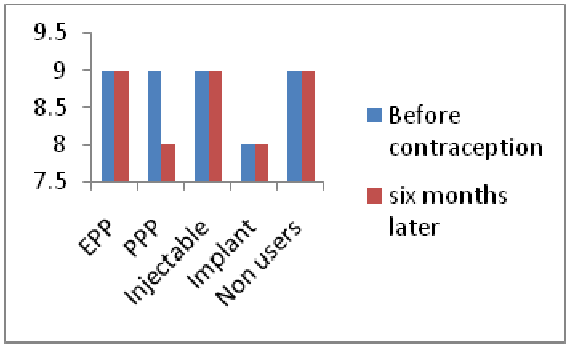

Figure 3. Mean value of creatinine (g/l)

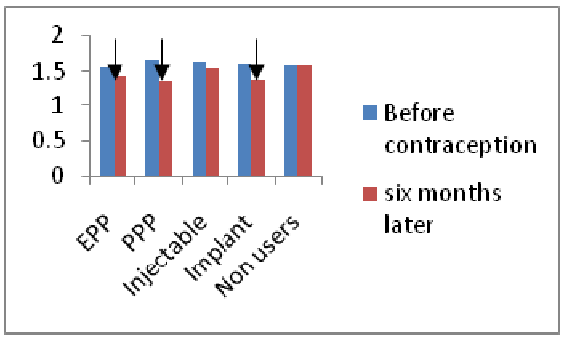

Figure 4. Mean value of cholesterol (g/l)

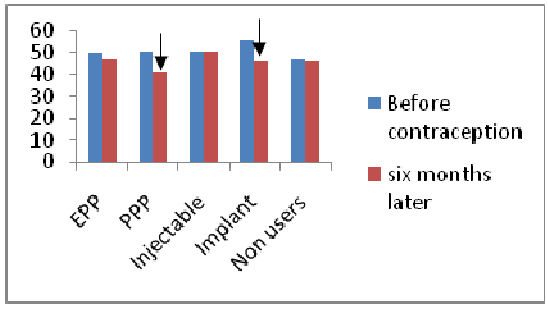

Figure 5. Mean value of HDL cholesterol (mg/l)

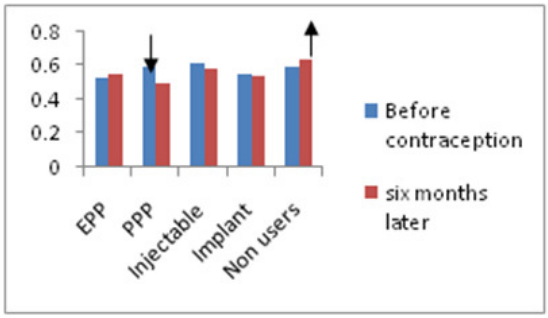

Figure 6. Mean value of triglycerides (g/l)

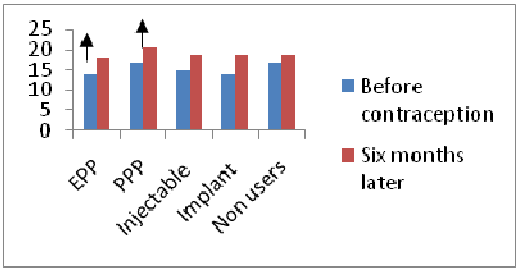

Figure 7. Mean value of AST (UI/l)

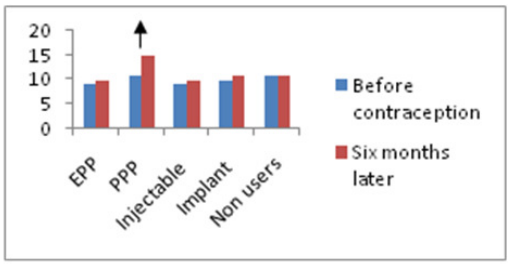

Figure 8. Mean value of ALT (UI/l)

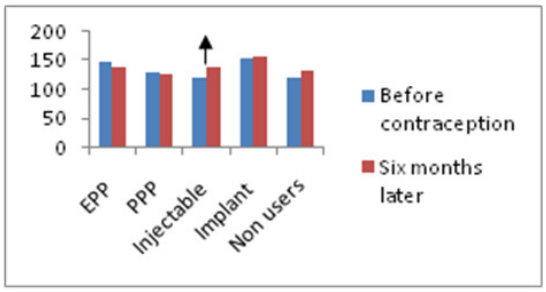

Figure 9. Mean value of PAL (UI/l)

Table 1. Evolution of biochemical parameters six months after hormonal contraceptives use

	Biochemical parameters									
Hormonal Contraceptives	**Glucose**	**Urea**	**Uric Acid**	**Créatinine**	**Trigycerides**	**Total cholesterol**	**HDL-cholesterol**	**AST**	**ALT**	**PAL**
estrogen-progestin pills	0	0	↗	0	0	↘	0	↗	0	0
Pure progestative pills	0	0	↗	0	↘	↘	↘	↗	↗	0
Injectable	0	↘	↗	0	0	0	0	0	0	↗
Implant	0	0	↗	0	0	↘	↘	0	0	0
Non users	0	0	0	0	↗	0	0	0	0	0

0 : no variation

↘ : significantly decrease

↗ : significantly increase

Table 2. Mean value of uric acid (mg/l)

	Mean value of Uric Acid (mg/l)		
Hormonal contraceptives	**Before use hormonal contraceptives**	**Six months later**	**P -value**
EPP (n = 32)	37 ± 13	46 ± 12	0,001*
PPP (n = 9)	43 ± 13	53 ± 13	0,035*
Injectable (n = 50)	39 ± 10	49 ± 9	0,001*
Implant (n = 15)	39 ± 8	49 ± 11	0,001*
Non users (n = 53)	42 ± 11	38 ± 12	0,253

*Significant difference $p < 0.05$

DISCUSSION

Our study shows that the evolution of different biochemistry parameters remains within the normal limits six months after hormonal contraception. However, the results suggest a specific variability of each parameter according to the nature of the contraceptive molecule.

- For glycemic control: the administration of different hormonal contraceptives does not cause significant variation. This effect has also reported by (Stephan et al., 1977) and (Colau et al., 2002) with the same conclusion. However, (Cathelineau et al., 1986, Vexiau et al., 2000) demonstrated that the effect has been dose-dependence, since a decrease in glucose tolerance, of fasting blood glucose level, and even an increase as have been reported with hormonal low-dose and normal dose, and to high dose micro progestin.

In the present study, the absence of disturbances may even result from the low dose of contraceptives used. Such outcome suggests that the diabetogenic effect of hormonal contraceptives is highest in the ethinyl-estrogen - norsteroid progestin association than with non-androgenic progestin at low dose (Schlienger et al., 1992).

- In addition, the evaluation of cardiovascular risk factors showed a significant decrease in total cholesterol, in HDL cholesterol and in triglycerides during the use of progestogen-only pills. This decrease has been observed with the implant in accordance with the triglycerides. However, only total cholesterol is affected with estrogen plus progestin ($p = 0.019$) and less so with the injection method ($p = 0.054$). This confirms the detrimental effect of androgenic progestin in the decrease of HDL cholesterol (Belaisch, 2000; Chemama, 1986; Donnay et al., 1991, Akpona, 1998) even if we consider the low level of serum cholesterol in Senegalese Black population (Sow, 1989). It should be noted that this decrease in the fraction of HDL cholesterol results from the inhibitory effect of progesterone on the production of HDL regulated by Apo AI (Kazuhisa et al., 2001), which hinders the elimination of cellular cholesterol. (Johnson, 1991; Oram, 1996). This disruption of cellular homeostasis leads to the loss of the beneficial effect of HDL cholesterol and increases the risk of cardiovascular morbidity and mortality (Samsioe, 1994). Yet, a significant increase in triglycerides observed in women controls (figure 6) ($p = 0.001$) reported that eating habits are often very high in fat (Touré, 1982).

- Analysis of constant occurrence of hyperuricemia (Table 2) in all women undergoing contraceptives blames strong hormonal impregnation. Indeed, the occurrence of hyperuricemia in this context is poorly documented because no pathophysiological explanation has been selected. If (Sow, 1989) in his approach had put this under the account of the terrain itself, further analysis of the present study criminalizes the use of contraceptives at the origin of the disturbance. The occurrence of this hyperuricemia seems to be a complex mechanism which would involve the inactivation of cytochrome P450 1A2, an enzyme involved in the metabolism of many nutrients, as was also reported by some authors (Hasler, 1999). Others like (Kelley, 1981) have shown that this increase is due to a decrease in renal clearance of uric acid. Monitoring these patients over a long period would support these assumptions because hyperuricemia is a predictive marker for cardiovascular and renal risk (Brand et al., 1985).

- Assessment of renal function by determining creatinine and blood urea shows no disturbance outside a significant decrease in uremia with the administration of progestin-only pills, while (Inal, 2008) a decrease in creatinine with the implant has noted. Besides, the impact of hormonal contraceptives on liver risk showed a significant increase in AST and ALT with pure progestin, respectively ($p = 0.014$ and $p = 0.046$), increase in AST with the combined form ($p = 0.001$), and PAL ($p = 0.001$) with the injection method (figure 7-9). The same result was observed for the implant with authors like (Mohsen, 2005). Despite this significant increase, all values are within the reference range.

CONCLUSION

Our study shows biochemical disturbances in some constants using contraceptives. There is particularly a

significant increase in uric acid. Despite the absence of a clinical picture, a long-term monitoring of these patients is necessary to search for renal and cardiovascular complications.

REFERENCES

Akpona SA, Nendjul Pongoue ER, Iwole S, Ribas A, Sawadogo M, Parra HJ (1998). Etude du bilan lipdique de la femme sous contraceptive au long cours à Cotonou, Bénin. Biochimica Clinica : 22 :11-12

Belaisch J (2000). Les pilules à 15 mg d'éthinyl estradiol. La Lettre du Gynécologue : 253:45-47.

Bouvier MH (2003). Mortalité maternelle dans les pays en voie de développement : données et améliorations statistiques des soins obstétricaux. Rev. Méd. Trop. 63 (5):358-365.

Brand FN, McGee DL, Kannel WB, Stokes J, Castelli WP (1985). Hyperuricemia as a risk factor of coronary heart disease: the Framinghan study. Am. J. Epidemiol.: 121:11-18.

Cathelineau G, Hilal M (1986). Action de la contraception orale chimique sur la tolérance au glucose et l'insulinosécrétion. Doins éd., Paris, pp. 241-257.

Chemama DE (1986).Foie et pilule. Doins éd., Paris, pp.319-322.

Colau JC, MadelenaTP, Serfaty D (2002). Implant sous-cutané à l'étonogestrel : une nouvelle méthode de contraception. La Lettre du Gynécologue : 268 : 49-54.

Donnay F, Jourdan A (1991). Controlling fertility. Child Trop. 194:1-80.

Hasler JA (1999). Estabrook R, Murray M et al, Human cytochromes Pp. 450. Mol. Aspects Med. 20:1-137, hémoglobines glycosylées chez le Noir Sénégalais sain.

Inal MM, Yildirim Y, Ertopcu K, Avci ME, Oezlmas I, Tinar S (2008). Effect of the subdermal contraceptive etonogestrel implant (Implanon) on biochemical and hormonal parameters (three years follow- up). Eur J Contracept Reprod Health Care. 13(3):238-242

Johnson WJ, Mahlberg FH, Rothblat GH, Phillips MC (1991). Cholesterol transport between cells and high density lipoproteins. Biochim. Biophys.Acta : 1085: 273 -298

Kazuhisa K, Sumiko AD, Reijiro A, Isamu M, Kaoru S, Shinji Y (2001). Biochimica et Biophysica Acta: 1532: 173 - 184

Kelley WN (1981). Approach to the patient with hyperuricemia, in Kelly WN, Harris E D, Ruddy S, et al (eds):Texbook of Rheumatology. Philadelphia, W B Saunders, pp. 494- 500

Moshen T, Majid R, Mohammad N, Provide other author name(s) (2005). Effects of a subdermal levonorgestrel contraceptive implant (Norplant) on serum cholesterol, triglycerides, ALT and AST in Iranian women. Contraception: 73:56 -58.

Oram JF, Yokoyama S (1996). Apolipoprotein-mediated removal of cellular cholesterol and phospholipids. J. Lipid. Res. 37: 2473- 249

Samsoie G (1994). Cardioprotection by estrogens: mechanisms of action-the lipids. Int. J. fertile Menopausal Stud. 39 Suppl1: 43-49

Schlienger JL, Pradignac A, Dreval A, Schlaeder G (1992). Contraception hormonale : risques métaboliques et vasculaires. Journal de Médecine : 23(10):577-581

Sow A (1989). Profil biochimique de la femme sous contraceptifs oraux : (Etude préliminaire). Thèse Médecine, Dakar, n°94.

Stephan F, Reville P (1977). Diabetes and estro-progestins. Minerva Med : 68(35):2461-2472.

Thèse Méd, Dakar, n°103.

Touré M (1982). Détermination des valeurs de référence du cholestérol des HDL et des

Vexiau P, Cathelineau G (2000). Métabolisme glucidique et contraception orale. Masson éd., Paris, pp.110-113.