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Concentrations of Some Biochemical Parameters in Breast Milk of a Population of Nigerian Nursing Mothers Using Hormonal Contraceptives

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Abstract: Breast milk contains the entire essential nutrients needed by neonates for growth, development and maintenance of healthy tissue. However, previous reports suggest that several classes of contraceptives induce changes in the concentrations of protein, carbohydrate and lipid macromolecules to varying degrees thus raising serious concerns on the safety and possible detrimental consequences on neonatal well-being. Breast milk obtained from eighty-two (82) lactating mothers using hormonal contraceptives (test) and one hundred (100) lactating mothers not using any hormonal contraceptive devices (control) aged 26-46yrs in two selected facilities in Ibadan, South West, Nigeria were analyzed for glucose, phosphate, Triglyceride (TG), Zinc (Zn), Copper (Cu), Lead (Pb), Cadmium (Cd), Chromium (Cr), Iron (Fe), Manganese (Mn) and Selenium (Se) concentrations using standard methods. Results obtained from this study showed significant decrease in means of glucose ($p<0.01$) and phosphate ($p<0.01$) content of breast milk obtained from of mothers in the test group was observed when compared with values from the corresponding controls. Significant increase in means of calcium and albumin were observed in the breast milk of lactating mothers using hormonal contraceptives when compared with the respective means of corresponding control. However, no significant changes in means of TG, Zn, Cu, Pb, Cd, Cr, Fe, Mn and Se in the breast milk samples of test subjects were seen when values were compared with respective corresponding control. Significant reduction in breast milk glucose in lactating mothers using hormonal contraceptives could negatively impact infants thriving on exclusive breast feeding.

Key words: Lactating mothers, breast milk, hormonal contraceptives

INTRODUCTION

In both the developed and developing countries, women use contraceptive primarily for child-spacing and prevention of unwanted pregnancy, even during breast feeding period (Fathalla, 1993) Hormonal contraceptives are steroidal drugs containing either estrogen and/or progestin and are generally of five types namely; oral contraceptives, injectable, insertions, barrier contraceptives and spermicidal agents. Some studies (Robert, 1986; Obisesan *et al*., 2002) indicate that the intake of oral contraceptives could cause metabolic changes in carbohydrate, protein and lipid macro molecules. Contraceptives may induce carbohydrate intolerance in some women (Ludicke *et al*., 2002). Adequate glucose content in breast milk is important for infant well-being especially in infants thriving on exclusive breast feeding. Infants fed with breast milk low in glucose level manifest a broad spectrum of clinical symptoms of central nervous system dysfunction such as headache, convulsion, blurred vision, dizziness, seizures, loss of consciousness and death (David, 1999).

Previous reports showed that colostrum protein contains cellular and humoral immuno-competent components, which confer passive immunity to the neonates. Colostrum contains high concentration of immunoglobulin that are responsible for the passive immunity in the newborn babies (Abraham *et al*., 1978). Immunoglobulin A (IgA) secreted in ductules of a lactating breast protects neonates from intestinal infections (Correa *et al*., 2006). A study by Lonnerdal *et al*., reported a significant increase in the concentration of total protein as well as in different milk protein fractions such as lactoferrin and alpha-lactalbumin in breast milk samples of lactating women using oral contraceptives when compared with controls (Lonnerdal *et al*., 1980).

The use of estrogen-containing oral contraceptives has been associated with increases in plasma triglycerides and Very Low Density Lipoprotein (VLDL), but a decreased level of plasma High Density Lipoprotein (HDL) cholesterol (Duvillard *et al*., 2010). Reports from Tangney and Driskell (1977) indicate elevated plasma triglycerides in women taking combined oral contraceptives with two different estrogen

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concentrations. In another study, O'Connor *et al*. (2001) reported that high levels of long chain n-3 and n-6 PUFA in human milk increase the synthesis of Docosahexaenoic Acid (DHA) and Arachidonic Acid (AA) which are required for rapid brain maturation in the first year of life.

The specific distribution of fatty acids in triglycerides plays a key role in lipid digestion and absorption (Lopez-Lopez *et al*., 2001). Triglycerides (Sn-2 Palmitate) in breast fed infants and structural palmitate in infants' formula is also associated with enhanced intestinal calcium absorption (Kennedy *et al*., 1999). Low calcium and phosphorus have been observed in infants receiving breast milk from hypocalcaemic lactating mothers (Greer *et al*., 1982).

Zinc, copper, manganese, molybdenum, selenium and chromium are considered to be essential nutrients in infants. Copper and zinc deficiency develops in early life between 3-6 months of age when the concentration in breast milk is falling and dietary supplementation of dietary trace elements has not been introduced (Shaw, 1982). One study reported that colostrum obtained from lactating mothers had higher zinc concentrations which declined significantly by 4-6 months of lactation, corresponding to the age when the breast-fed infants had lower zinc levels (Hemalatha *et al*., 1997). Breast milk from mothers who gave birth to preterm babies contained significantly higher levels of copper, zinc and iron during the early lactation period when compared with values obtained from mothers who delivered at term in a study population in Nigeria (Atinmo and Omololu, 1982). However, Okolo and coworkers (2000) showed that mean zinc concentration in breast milk obtained from lactating women in Jos, Northern Nigeria appeared to contain adequate levels of magnesium, manganese, sodium, potassium, phosphorus and iron, but a relatively low concentration of zinc. This low level of zinc in their breast milk did not affect the serum zinc level in their exclusively breastfed infants.

MATERIALS AND METHODS

Selection of subjects: Breast milk expressed by eighty-two (82) lactating mothers using hormonal contraceptives which comprised of oral (progestin-only) and injectable (depo-medroxy progesterone acetate, noristerat and norigynon) served as test group while one hundred (100) lactating mothers without contraceptives served as control. The age range for participating lactating mothers was between 26-45 years. Subjects in both test and control groups were attending the Parenthood Planning Federation of Nigeria, Liberty Road, Oke-Ado and Maternal and Child Heath Hospital, Moor Plantation, Apata, Ibadan, South West, Nigeria. Ethical approval (Reference No: AD. 13/262/11) was obtained for the study from the Ministry of Health, Department of Planning, Research and Statistics, Oyo State, Ibadan, Nigeria.

Lactating mothers who made use of intrauterine contraceptive devices such as copper T, barrier method such as diaphragm, cervical cap as well as hormonal implantation and suppositories were excluded from the study.

Sample collection and preservation: 2-5 ml of breast milk sample was obtained via self-manual expression by lactating mothers in both the test and control groups. A portion was dispensed into a tube containing fluoride oxalate anticoagulant, while the remaining aliquot was dispensed into a plain tube. Breast milk samples were preserved at -20^{0}C until analysis was carried out.

Estimation of triglyceride level was by an enzymatic colorimetric method (Bucollo and David, 1973). Bromocresol Green (BCG) indicator method was used for the estimation of albumin (Doumas *et al*., 1971) while glucose concentration was measured by the, glucose oxidase/peroxidase colorimetric (Thomas, 1998). Zinc, copper, iron, manganese, selenium, chromium, lead and cadmium concentrations were determined directly with Atomic Absorption Spectrophotometer (AAS) method described by Kaneko (1999). Breast milk calcium and phosphate concentrations were determined using the Spectrophotometric methods of Bauer (1981) and Tauskky and Shorr (1953) respectively.

Statistical analysis: The results were expressed as mean (±SD). Means obtained from the results were analyzed using the Student's t-test. The relationships between variables were determined with the Pearson's correlation coefficient (r). Results were regarded as significant at $p<0.05$.

RESULTS

The mean age, periods of Lactation (LP) and Contraception Period (CP) of lactating mothers during the study is shown in Fig. 1. The mean breast milk glucose concentration in lactating women using contraceptives decreased significantly (48.8±16.3 mg/dl) when compared with corresponding control (34.4±14.6 mg/dl). Significant increases in mean albumin (0.13-0.17 g/dl) and calcium (7.9-9.0 mg/dl) was seen when values from test subjects were compared with corresponding controls. No change in breast milk triglyceride level was however observed when mean value in test was compared with corresponding control (Table 1). As shown in Table 2, there were also insignificant changes in means of zinc, copper, lead, cadmium, chromium, iron, manganese and selenium concentrations in breast milk of mothers on contraceptives when compared with corresponding means of control in the study.

Table 1: Mean concentrations of glucose, albumin, calcium, phosphate and triglyceride concentrations in breast milk of control lactating mothers and those on hormonal contraceptives

Parameters	Control (n = 100)	Test (n = 80)	t-value	p-value
Glucose (mg/dl)	48.75 (16.27)	34.39 (14.59)	-6.2	0.01
Albumin (g/dl)	0.13 (0.13)	0.17 (0.10)	2.33	0.01
Calcium (mg/dl)	7.89 (1.87)	9.04 (1.85)	4.11	0.01
Phosphate (mg/dl)	7.62 (2.68)	5.13 (1.88)	-7.12	ns
Triglyceride (mg/dl)	131.00 (75)	130.00 (72)	-0.133	ns

Table 2: Mean concentrations of zinc, copper, lead, cadmium, chromium, iron, manganese and selenium concentrations in breast milk of control lactating mothers and lactating mothers on hormonal contraceptives

Parameters	Control (n = 100)	Test (n = 80)	t-value	p-value
Zinc (mg/dl)	7.04 (1.31)	6.74 (2.19)	-1.14	ns
Copper (µg/dl)	82.68 (15.10)	82.80 (26.04)	0.04	ns
Lead (µg/dl)	87.13 (25.06)	83.10 (30.48)	-0.98	ns
Cadmium (µg/dl)	97.79 (21.73)	94.78 (29.42)	0.79	ns
Chromium (µg/dl)	95.79 (21.78)	92.78 (29.42)	-0.79	ns
Iron (µg/dl)	94.82 (18.25)	93.07 (24.47)	0.55	ns
Manganese (µg/dl)	93.19 (21.24)	88.38 (26.91)	-1.35	ns
Selenium (µg/dl)	91.95 (20.65)	90.90 (24.61)	1.35	ns

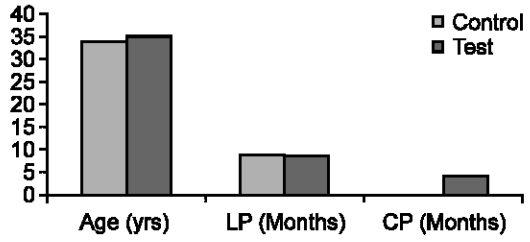

Fig. 1: Bar chart showing the age, periods of lactation (LP) and Contraception Period (CP) of lactating mothers in control and those on hormonal contraceptives

DISCUSSION

The result of this study showed a significant decrease in mean breast milk glucose level of samples collected from lactating women taking hormonal contraceptives when compared with corresponding control. Previous reports (Ludicke *et al*., 2002; Lopez *et al*., 2009) showed that most contraceptive pills significantly decreased the fasting plasma glucose levels and glucose tolerance. Contraceptive pills high in estrogen contents produced maximum decreasing effects. Several possible mechanisms for the altered glucose level in breast milk have been proposed. Alan (1998) suggested that progesterone could increase the basal insulin level and promotes glycogen storage in the liver. Oral contraceptive intake appears to diminish the insulin-secretory capabilities of the Islets of Langerhans (Cagnacci *et al*., 2003), cause a slight deterioration in insulin sensitivity (Monier, 1988) and increase insulin resistance (Kahn *et al*., 2003).

Therefore, decreased glucose level seen in this present work study might be due to the ability of synthetic progestin contents of the contraceptives to stimulate the β-cell of the Islet of Langerhans causing a rise in insulin secretion resulting in low breast milk glucose level. On the other hand, significant increases in the mean albumin level in breast milk of lactating women taking hormonal contraceptives was observed when compared with corresponding control values in this present study. These observed increases were similar to the findings of Toddywalla *et al*. (1977) who in their study showed that the use of conventional contraceptives such as a low-dose combination pill or a low-dose progestational compound caused a significant increase in the protein content of breast milk. Truittt *et al*. (2003) however suggested that injectable contraceptives have a beneficial effect on the quality of breast milk in terms of its fat concentration, calories, minerals and protein composition.

Decreased mean total protein content of breast milk lower than published reports were observed in lactating women without hormonal contraceptives in a study carried out in lactating the Igbo ethnic group in Nigeria (Ogbu, 2003). Hambraeus *et al*. (1978) also reported remarkably low levels (0.8-1.0 g/100 ml) of protein with no significant difference between well-nourished and malnourished lactating women. The significant elevation of albumin in the present study might primarily be due to the stimulatory effect of estrogen content of the contraceptives on the liver cells and its metabolic role in the production of insulin, cortisol, thyroxin, growth hormone and their protein carriers.

A significant increase in mean calcium content of breast milk of test subjects was observed when compared with control. Paul *et al*. (1998) suggested that oral contraceptives containing estrogen could increase gastrointestinal absorption of calcium and may lead to a concomitant rise of calcium level breast milk. However, Dorea and Myazaki (1998) indicate that the use of hormonal contraceptives did not seem to affect the secretion of both calcium and phosphorus in breast milk

of lactating mothers. On the other hand, mean breast milk phosphate concentration decreased significantly in test subjects when compared with mean value of the controls.

In this study, the mean TG concentration of breast milk of mothers on hormonal contraceptives was not significantly different from the control values. Some studies however, suggested that progesterone containing contraceptives elevates plasma progesterone level which has antagonistic effect on the synthesis of TG resulting in decreased triglyceride level during exclusive breast-feeding (Wynn and Doar, 1960; Truittt *et al*., 2003).

No significant change in means of Zn, Cu, Pb, Cr, Cd, Fe, Se and Mn in breast milk of lactating mothers on contraceptives and controls was observed. Presently, it appears there is no consensus on the implications of varying amounts of trace metals in breast milk with regards to the use of contraceptives.

In conclusion, the observed significant reduction in breast milk glucose in lactating mothers using hormonal contraceptives means that this could negatively impact infants thriving on exclusive breast feeding.

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