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Lipid Profile as a Biomarker of Atherogenicity in Subfertile client with Hyperprolactinemia: A North- Central Nigerian University Teaching Hospital Experience.

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Abstract

Hyperprolactinaemia is associated with amenorrhoea and decreased estrogen concentration which may lead to the elevation in total cholesterol and low density lipoprotein cholesterol (LDL-C) and decrease in high density lipoprotein cholesterol (HDL-C). The aim of this present study was to evaluate lipid profile as an atherogenic biomarker in hyperprolactinaemic sub-set of subfertile individuals. This cross-sectional study was carried among clients with hyperprolactinaemia at the Assisted Reproductive Unit of University of Ilorin Teaching Hospital, Ilorin between January and June 2015. Serum fasting total cholesterol (TC), triglycerides (TGs), high density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were measured in 51 women with hyperprolactinaemia who were non-pregnant and not breastfeeding and 40 age-matched non-pregnant and non-breastfeeding women of child bearing age. Comparisons between serum hormonal profiles as well as lipids profiles as biomarkers of atherogenic index were assessed. Women with hyperprolactinaemia present with significantly lower serum level of FSH, progesterone and oestradiol than those of controls, while there was insignificant elevation in mean LH. There was a significant elevation in the levels of prolactin, testosterone, total cholesterol, triglycerides, HDL-C, LDL-C, mean coronary heart disease risk ratio and Castelli ratio II

in hyperprolactinaemic subjects when compared with controls. In contrast, there was no significant difference when mean values of atherogenic index and Castelli II in hyperprolactinaemic subjects were compared with those of controls. This study revealed an association between hyperprolactinaemia and dyslipidaemia with higher atherogenicity than the controls. We concluded that dyslipidaemia is common in hyperprolactinaemia and as such early lipid profile is advised as well as holistic interpretation of lipid profile as prompt treatment may prevent cardiovascular events in hyperprolactinaemic patients.

Keywords: Biochemical, Atherogenicity, Hyperprolactinaemia, Subfertile client, North-Central Nigerian.

Introduction

Subfertility generally describes any form of reduced fertility with prolonged time of unwanted non-conception and have been reported to be associated with hyperprolactinaemia (Gnoth *et al.*, 2005). Hyperprolactinaemia is defined as circulating prolactin levels above normal range, which occurs in conditions other than pregnancy and lactation, when physiological hyperprolactinaemia occurs (Bernichein *et al.*, 2010). It is one of the most common endocrine disorders of the hypothalamic-

pituitary ovarian axis affecting the reproductive functions (Prabhakar and Davis, 2008). It is present in as high as 9 to 17% in women with reproductive disorders (Biller et al., 1999).

Prolactin is defined as a pituitary-secreted polypeptide hormone which acts primarily to stimulate lactation during pregnancy as well as post-delivery (Kars et al., 2010). Hyperprolactinaemia has been shown to be associated with abnormalities of carbohydrate and lipid metabolism as well as obesity, the mechanism is not well known but prolactin may have a direct effect on adipose tissue (Doknic et al., 2002 and Ben Jonathan et al., 2006). It has been demonstrated that, prolactin increase triglyceride (TG) levels by reducing the lipoprotein lipase activity in adipose tissue (Ling et al., 2003). Hyperprolactinaemia is associated with amenorrhoea and decreased estrogen concentration which may lead to the elevation in total cholesterol and low density lipoprotein cholesterol (LDL-C) and decrease in high density lipoprotein cholesterol (HDL-C) (Hesmati et al., 1987). The aim of our present study was to evaluate lipid profile as an atherogenic biomarker in hyperprolactinaemic subset of subfertile clients.

Materials and Methods

The study was a cross-sectional one performed among subjects with hyperprolactinaemia at the Assisted Reproductive Unit of University of Ilorin Teaching Hospital, Ilorin between January and June 2015. A total of 51 female clients with hyperprolactinaemia constituting a subset of sub-fertile patients attending the facility were recruited for the study. The subjects were aged 22 and 45 years, while 40 healthy age and gender- matched non-pregnant women were monitored as control. The serum hormonal profile (LH, FSH, prolactin, Progesterone, Estradiol, which was analyzed using Accubind (USA) ELISA kits. Serum total cholesterol was estimated by cholesterol Oxidase method (Flegg, 1973). HDL-c and LDL-c were also estimated by enzymatic method while triglycerides were estimated using glycerol-3 phosphate oxidase method as described by Jacobs and Van Demark (1960) using commercially prepared kit by Agappe Diagnostics Ltd (India). The absorbance of samples

and standards were measured against reagent blank using Jenway 6300 spectrophotometer at 505nm. Atherogenic index (Log TG/HDL-C), Castelli risk index I and II (T. Chol/HDL-c and LDL-C/HDL-C) respectively. Coronary heart disease risk ratio was calculated as described by Bhardwaj *et al* (2013). Other descriptive parameters and information were extracted from their hospital folders. Ethical approval was gotten from the Ethical committee of the hospital.

Statistical analysis

Statistical analysis was done using Statistical Package for Social Science (SPSS version 20.0). Results were expressed as means $\pm$ SD. Paired sample t-test was used to compare means of results where appropriate. A p-value ≥ 0.05 was considered significant.

Results

This cross-sectional study was carried among clients with hyperprolactinaemia at the Assisted Reproductive Unit of University of Ilorin Teaching Hospital, Ilorin between January and June 2015. Serum fasting total cholesterol (TC), triglycerides (TGs), high density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were measured in 51 women with hyperprolactinaemia who were non-pregnant and not breastfeeding and 40 age-matched non- pregnant and non-breastfeeding women of child bearing age. Comparisons between serum hormonal profiles as well as lipids profiles as biomarkers of atherogenic index were assessed.

There was no statistically significant difference when the mean age and plasma level of LH in hyperprolactinemic subjects were compared with that of controls (Table1). There was a statistically significant elevation in mean level prolactin and testosterone levels in hyperprolactinemic subjects when compared with controls. Plasma levels of FSH, progesterone and estrogen were significantly reduced in hyperprolactinemic subjects when compared with controls.

Significant elevations were observed in the mean values of total cholesterol, triglycerides, HDL-C and



LDL-C, in hyperprolactinaemic clients when compared with controls (Table 2).

There was a statistically significant elevation in the mean value in CHD-RR and Castelli ratio II in

hyperprolactinemic subjects when compared with controls. On the other hand, there was no significant difference in mean atherogenic index and Castelli ratio I between the groups.

Table 1: Comparing Mean Values of Fertility Profile in Hyperprolactinaemic Clients with the Controls.

Variables	Subjects	Control	p-value
Mean Age (Years)	30.0± 5.0	26.6± 5.6	0.421
Mean FSH (mIU/ml)	5.5± 1.9	7.3± 7.6	0.000*
Mean LH (mIU/ml)	5.0± 1.9	4.9± 1.8	0.691
Mean Prolactin (ng/ml)	56.7± 35.8	14.3± 2.5	0.000*
Mean Progesterone (ng/ml)	1.9 ± 3.7	5.1± 5.4	0.000*
Mean Oestrogen (pg/ml)	54.4± 50.0	103.3± 42.4	0.000*
Mean Testosterone (ng/ml)	0.4±0.3	0.31± 0.07	0.000*

Table 2: Comparing Mean Values of Lipid Profile in Hyperprolactinaemic Clients to That of Controls.

Variables	Subjects	Control	p-value
Mean T-C(mmo1/L)	4.1± 1.5	3.5± 0.5	0.000*
Mean Trig (mmo1/L)	1.3± 0.7	1.0± 0.2	0.000*
Mean HDL-C (mmo1/L)	1.6 ± 0.7	1.3± 0.3	0.001*
Mean LDL-C (mmo1/L)	1.5± 0.7	1.3± 0.2	0.000*

Table 3: Comparing Mean Values of Biomarkers of Atherogenicity in Hyperprolactinaemic Clients and the Controls.

Variables	Subjects	control	P-value
Mean CHD-RR	0.40± 0.10	0.36± 0.08	0.000*
Mean atherogenic index	- 0.103± 0.162	-0.108± 0.072	0.152
Mean Castelli ratio I	2.66 ± 0.07	2.39± 0.53	0.202
Mean Castelli ratio II	0.73± 0.17	1.69± 0.44	0.000*

Discussion

Hyperprolactinaemia is the most common endocrine disorder of the hypothalamic-pituitary axis (Doknic *et al.*,2002). Hyperprolactinaemia has long been associated with oligoamenorrhoea, galactorrhoea

and impaired reproductive function (Berinder *et al.*, 2005). Metabolic abnormalities such as obesity, dyslipidaemia and insulin resistance, which was shown to be associated with hyperprolactinaemia, are mostly not given the utmost attention it deserves

as it has been shown that hyperprolactinaemia may leads to weight gain in human studies (Shibli and Schlechte, 2009; Doknic *et al.*, 2002 and Delgrange *et al.*,1999).

Many studies have reported adverse lipid profile such as hypercholesterolemia, hypertriglyceridaemia while others reported no alteration in hyperprolactinaemia (Berider *et al.*,2011; Serri *et al.*,2006 and Yavuz *et al.*, 2003). In this study, elevated levels of total cholesterol, triglycerides and low density lipoprotein cholesterol was observed. The mechanism associating disorder of lipid metabolism in hyperprolactinaemia is poorly understood. Some reports associated this to a decrease in lipoprotein lipase activity in individuals with elevated prolactin level. In addition, hyperprolactinaemia leads to a reduction in estrogen levels by inhibiting the gonadotropin releasing hormone secretion, which may lead to an elevation in total and LDL-C as reported in this study (Jellinger *et al.*, 2012). Elevated coronary heart disease risk ratio and LDL_C/HDL-C ratio as seen in this study has been reported to be associated with six times higher rate of atherosclerosis and other coronary events (Jellinger *et al.*, 2012; Ramah *et al.*, 2007 and Assman *et al.*, 1998). In conclusion, our study revealed a possible association between hyperprolactinaemia and dyslipidaemia with higher atherogenicity than the controls.

Conclusion

We concluded that dyslipidaemia is common in hyperprolactinaemia and as such early lipid profile monitoring is advised as well as holistic interpretation of lipid profile as prompt treatment may prevent cardiovascular events in hyperprolactinaemic patients.

References

- Assman, G., Gallen, P. and Schule, H. (1998). The heart study (PROCAM). Results of follow up at 8years. *European Heart Journal*; **19**: 196-205
- Ben-Jonathan, N., Hugo, E.R., Brandebourg, T.D. and LaPensee. C.R (2006). Focus on prolactin as a metabolic hormone. *Trends in Endocrinology and Metabolism*; **17 (3)**:110-116.
- Berinder, K., Nyström, T., Höybye, C., Hall, K. and Hulting, A. L (2011). Insulin sensitivity and lipid profile in prolactinoma patients before and after normalization of prolactin by dopamine agonist therapy. *Pituitary*; **14(3)**:199-207.
- Berinder, K, Stackenäs, I., Akre, O., Hirschberg, A.L. and Hulting, A. L (2005). Hyperprolactinaemia in 271 women: up to three decades of clinical follow-up. *Clinical Endocrinology*; **63 (4)**: 450-455.
- Bernichtein S., Touraine P. and Goffin V (2010). New concepts in prolactin biology. *Journal of Endocrinology*; **206**:1–11.
- Biller, B.M., Luciano A. et al (1999). Guidelines for the diagnosis and treatment of hyperprolactinaemia. *Journal of Reproductive Medicine*; **44**:12.
- Delgrange, E., Donckier, J. and Maiter. D. (1999). Hyperprolactinaemia as a reversible cause of weight gain in male patients? *Clinical Endocrinology*; **50 (2)**: 271.
- Doknic, M., Pekic, S., Zarkovic, M., Medic Stojanoska, M., Dieguez, C., Casanueva, F, and Popovic, V (2002). Dopaminergic tone and obesity: an insight from prolactinomas treated with bromocriptine. *European Journal of Endocrinology*; **147 (1)**: 77- 84.
- Flegg. H. M. (1973). An investigation of the determination of serum cholesterol by an enzymatic method. *Annals of Clinical Biochemistry*; **10**: 79-84.
- Gnoth., C., Godehardt, E., Friol, K. and Freundl, G. (2005). Definition and prevalence of subfertility and infertility. *European Journal of Human reproduction and Embryology*; **20(5)**: 1144-1147.
- Hesmati, H. M., Turpin, G. and de Gennes, J.L (1987). Chronic hyperprolactinaemia and plasma lipids in women. *Klin Wochenschr*; **65 (11)** :516-519.
- Jacobs, N.J. and Van Demark, P.J (1960). Enzymatic determination of serum triglyceride cholesterol. *Biochemistry and Biophysics*; **88**: 250-255.
- Jellinger, P.S., Smith, D.A., Mehta, A.E., Ganda. O., Handelsman, Y., Rodbard, H.W., Shepherd, M.D. and Seibel, J.A. (2012). AACE Task Force for Management of Dyslipidemia and



- Prevention of Atherosclerosis. American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. *Endocrine Practice*; **18 (1)** :1- 78.
- Kars M, Dekkers, O.M., Pereira, A.M. and Romijn, J.A (2010). Update in prolactinomas. *Netherlands Journal of Medicine*; **68 (3)**:104-112.
- Ling. C., Svensson, L., Odén, B., Weijdegård, B., Edén, B., Edén, S. and Billig H (2003). Identification of functional prolactin (PRL) receptor gene expression: PRL inhibits lipoprotein lipase activity in human white adipose tissue. *Journal of Clinical Endocrinology and Metabolism*; **88 (4)**:1804-1808.
- Prabhakar, V. K. and Davis, J.R. (2008). Hyperprolactinaemia. *Best Practice in Research in Clinical Obstetrics and Gynaecology*; **22 (2)**: 341-353.
- Rahma, S., Rashid, J.A. and Farase, A.H. (2007). The significance of lipid abnormalities in children with insulin dependent diabetes mellitus. *The Iraqi Postgraduate Medical Journal*; **5**:281-294.
- Serri, O., Li, L, Mamputu, J.C., Beauchamp, M.C., Maingrette, F. and Renier, G. (2006). The influences of hyperprolactinemia and obesity on cardiovascular risk markers: effects of cabergoline therapy. *Clinical Endocrinology*; **64 (4)**:366-370.
- Shibli, R. A. and Schlechte, J (2009). The effects of hyperprolactinemia on bone and fat. *Pituitary*; **12 (2)**: 96-104.
- Yavuz, D., Deyneli, O., Akpınar, I., Yildiz, E., Gozu, H., Sezgin, O., Haklar, G. and Akalin S (2003). Endothelial function, insulin sensitivity and inflammatory markers in hyperprolactinaemic premenopausal women. *European Journal of Endocrinology*; **149 (3)**:187-193.