

Correlation between Levels of Serum Prolactin and Total Sialic Acids Concentrations in Fertile and Infertile Women

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Abstract

The aim of this study was investigating the correlation between elevation of Prolactin levels and the increase of the concentrations of total sialic acids. The study was performed on 149 women consisted of 93 infertile hyperprolactinimic women (patients), age ranged 16-38 years old, and 56 normoprolactinemic women as a control group, 18-37 years old. Serum prolactin (PRL) and gonadotroph hormones (Follicle stimulating hormone FSH and Luteinizing hormone LH) were measured using enzymatic immunoassay (EIA) method, resorcinol method for serum total sialic acids (SIA). Patients were divided into four groups, each group represented the level of prolactin of infertile women as follow: G1= (21-30), G2= (31-40), G3= (41-50), and G4= (51-60) ng/mL. Serum PRL levels in the patients groups were significantly ($P \leq 0.05$) elevated compared to the normal women. Serum SIA, FSH and LH levels showed no significant differences ($P \leq 0.05$) in the groups 1, 2, 3, and 4 when compared to healthy women (control). There was no correlation between serum prolactin hormone levels and SIA levels in the control and patients women. In conclusion there was an elevation in PRL levels, not combined with elevation in SIA, FSH, and LH levels. There was no correlation between elevation of PRL levels and total sialic acids concentrations in control and patients women. Thus, sialic acid has no correlation with the fertility or infertility in the women.

Keywords: Prolactin, Sialic acid level, FSH, LH.

Introduction

PRL is gonadotropic hormone, which is synthesized and secreted by specialized acidophilic staining cells of the anterior pituitary gland, named lactotropes or mammotropes constitute 15% to 20% of the parenchymal cells in the anterior lobe of the pituitary gland (1). PRL is a lactogenic hormone, and there are major functions for PRL: it promotes mammary gland development; initiates milk formation and maintains milk secretion by the mammary glands; stimulates and maintains secretion of casein lactalbumin, lipids, and carbohydrate in to the milk (2). Pituitary gland also secreted FSH and LH by basophilic staining cells, named gonadotropes constitute about 10% of the parenchymal cells in the anterior lobe of the pituitary gland, the release of FSH and LH is regulated by gonadotropin-releasing hormone (GnRH) produced by hypothalamus. Both FSH and LH play an important role in male and female reproduction (3). In addition to the pituitary gland secretion, PRL may produced and released from the non pituitary tissues in such sites: it releases from the deciduas (4) and myometrium (5); it releases

also from lymphocytes (T-lymphocyte) (6) and human adipose tissues (7). Since, there is no uniform mechanism for the control of PRL release in the various sites, with each cell type utilizing a different set of regulators.

Sialic acids, are one of the most important molecules of life, since they occupy the terminal position on macromolecules and cell membranes and modification of glycoproteins and glycolipids (8). Sialic acids are more than 40 natural forms existing in nature and they can be attached in a variety of linkages to other sugars (including themselves) (9). It makes up a family of over 50 related sugars derived from neuraminic acid, the most common in mammalian being N-acetylnuraminic acid and N-glycolylneuraminic acid. In vertebrates (11), sialylated glycans are abundantly present on cell surfaces and in the extracellular milieu (12); they are involved in cell adhesion and cell communication (13), participating in a variety of crucial biological processes; recognition (14), regulates neuronal excitability and affects the function of a voltage-gated sodium channel in *Drosophila* (15), regulation of cell proliferation and cell

differentiation (16). Sialic acids themselves (17) or abnormal sialylation has been implicated in a number of pathobiological conditions, including neurological diseases, immunodeficiency, liver disease (18), cancer (19), bacterial (20) and protozoa infection (21). Glycoprotein sialylation has been extensively studied in mammals and some roles of this posttranslational modification have been determined. These roles often depend on the nature of acceptors, as well as on the linkage of sialylation (22), both determined by properties of sialyltransferases, enzymes that attach sialic acid to specific acceptors (23).

The attachment of carbohydrate to PRL may be play an important role in this hormone. Thus, the aim of this study is to measure the concentration of the total sialic acids with hyperprolactinemic women and if there is correlation between them [if the increasing in PRL levels combined with increasing the total sialic acids in the serum].

Subjects and Methods

The study was conducted on a total number of 93 infertile hyperprolactinemic women who attended to Fertility and IVF center, Kamal AL-Samarai Hospital, Baghdad, Iraq. Control group consisted of 56 healthy women. The diagnosis of patients was established by hormonal tests (serum PRL, FSH and LH tests).

Venous blood sample (5ml) was collected from fertile and infertile women at 2th-4th day of menstrual cycle. Each sample centrifuged for serum separation (4000 r.p.m./10 mins.). The serum was isolated equally into two parts: one of them for PRL, FSH and LH tests, which performed by enzyme immunoassay method using commercial kit (Biomerk, USA). The second part was kept at -25°C until use for sialic acids measurements, which performed according to resorcinol method described by Svennerholm (24). The patients were divided into 4 groups according to their prolactin results tests as the follow ranges to: group 1(21-30ng/mL), group2 (30-40ng/mL), group 3(40-50ng/mL), and group 4 (50-60ng/mL) respectively. The correlations between variables were studied using standard correlation methods. The comparison between

patients and control using student's test, P values ≤ 0.05 was considered (25).

Results and Discussion

Table (1) shows selected parameters PRL, FSH and LH hormones and sialic acids for control and patients women. The results showed that there was a significant increase in PRL levels ($P \leq 0.05$) in the subgroups 1, 2, 3, and 4 (93 infertile women) in comparison with 56 normal women. Total sialic acids appeared with variant levels but without significant difference ($P \leq 0.05$) in all the subgroups (1, 2, 3, and 4) of the patients in comparing with the control whereas the levels of the FSH and LH was not changed in the infertile women in comparing with the levels of the same hormones in normal women (control).

The normal range values for serum prolactin was 1.2-19.5 ng/mL from the kit, and the range values in the global laboratories was about 1.5-20 ng/mL (1.5- 20 mcg/L SI units) as the global normal value (26), The results in current study clearly indicated that prolactin levels elevated, although that there are no relation with SIA and reproductive hormones levels (FSH and LH). PRL levels elevation is the main sign for hyperprolactinemia, which is one of the most common endocrinological disorders affecting the hypothalamic – pituitary axis.

Hyperprolactinemia is one of a major causes of infertility, brought about by inhibition of gonadotropin-releasing hormone (GnRH) or pulsatile GnRH secretion from the hypothalamus and impairment of LH output from the pituitary gland (27).

Table (1)
Serum levels of sialic acids and reproductive hormones in normal and patients women.

	No	Mean \pm S.E.			
		PRL ng/ml	FSH mIU/ml	LH mIU/ml	SIA μ g/ml
\boxtimes St. Val		1.2-19.5	2 - 12	0.5 -10.5	46 - 71
Con.	56	13 \pm 0.62	5.39 \pm 0.5	3.88 \pm 0.40	70.75 \pm 3.50
G 1	38	24.48 \pm 0.47*	5.61 \pm 0.63	3.81 \pm 0.32	80.6 \pm 5
G 2	31	33.95 \pm 0.48*	5.26 \pm 0.72	4.03 \pm 0.50	67.33 \pm 6.99
G 3	12	43.16 \pm 0.59*	5.10 \pm 0.57	3.82 \pm 0.65	65.79 \pm 5
G 4	12	55.7 \pm 1.18*	5.79 \pm 0.25	3.87 \pm 0.36	68.85 \pm 5.40

S.E.=standard error, \boxtimes ST. Val.=standard values from the kits, but only SIA value from Svennerholm (24).
*P \leq 0.05 significantly different from control group.

PRL within gonadotroph cells are controlled by dopamine, the main hypothalamic inhibitory regulator of PRL release *in vivo*, this specific actions of PRL within the gonadotroph and the cell signaling interactions that ultimately underlie hyperprolactinemia-induced infertility (27); hyperprolactinemia can occur in physiological and pathological conditions (28) such as psychotic stress, severe mental illness or other causes, and the reproductive dysfunction affecting about one third of infertile women (29).

Hyperprolactinemia is often associated with amenorrhea, anovulation, reduced libido, and orgasmic dysfunction in women, up to 20% of secondary amenorrhea in women is attributed to elevated PRL, PRL elevation lead to hypogonadism this in turn impaired gonad steroid secretion, which alters positive feedback effects at the hypothalamic and pituitary levels, lead to lack of gonadotropin cyclicity (FSH and LH levels decline) and to infertility (30). Thus, the elevation of PRL in our study consisted with these evidences, whereas no significant changes in the normal levels of LH and FSH hormones with high levels in prolactin.

The relationships among PRL levels and SIA concentrations were measured and illustrated in Table (2), the results showed no significant (P \leq 0.05) correlation between PRL levels and SIA concentrations in normoprolactinemic (control) and hyper-

prolactinemic women (the groups of patients women 1, 2, 3, and 4. The results clearly indicated that SIA levels not elevated, in spite of elevation of PRL levels. There were no significant correlation between PRL and SIA in normoprolactinemic and hyperprolactinemic infertile women, these results may demonstrate that sialylated glycoprotein (an operation took place within PRL biosynthesis) in PRL was not predominant at follicular phase and may be other glycoform can be contribute in the structure of this hormone at that phase of menstrual cycle in normal and hyperprolactinemic women. Thus, there was no correlation between total sialic acids with FSH and LH levels, as we thought because their concentrations in patients and control women was not changed.

Table (2)
Pearson correlation between serum levels of sialic acids and prolactin hormone levels in patients and control.

<i>Varia</i>	<i>PRL Mean ± S.E.</i>	<i>SIA Mean ± S.E.</i>	<i>Corr. Sign.</i>	<i>P ≤ 0.05</i>
Con.	13 ± 0.62	70.75 ± 3.50	0.134	N.S
G 1	24.48 ± 0.47	80.6 ± 5	0.930	N.S
G 2	33.95 ± 0.48	67.33± 6.99	0.487	N.S
G 3	43.16 ± 0.59	65.79 ± 5	0.529	N.S
G 4	55.70 ± 1.18	68.85 ± 5.40	0.46	N.S

Varia = Variables, N.S : Not significant.

There is no correlations between SIA concentrations and elevations of PRL levels, but only that sialic acid participates with glycosylation (31) as the one of steps of prolactin biosynthesis (32).

The causes of hyperprolactinemia may be due to dysfunction of regulation of prolactin in the pituitary gland which alters the feedback mechanism, or there is no balances in the regulation in the non pituitary tissues, Since, there is no uniform mechanism for the control of PRL release in the various sites, but surly sialic acid has no relation with the elevation of PRL.

Conclusion

There was no correlation between SIA concentration and elevation of PRL levels in normoprolactinemic and hyperprolactinimic infertile women. Thus, the total sialic acids have no correlation with the fertility or infertility in the women.

Acknowledgments

So thankful to Dr. Hussein Hassan and Miss Rasha Ali form Arabian Gulf Laboratory for their invaluable cooperation.

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الخلاصة

تضمنت هذه الدراسة مشاركة ١٤٩ امرأة ، منهن ٩٣ امرأة مصابة بمرض ارتفاع نسبة هرمون البرولاكتين ويعانين من حالة العقم ، تراوحت أعمارهن بين ١٦-٣٨ سنة و ٥٦ امرأة طبيعية تراوحت أعمارهن بين ١٨-٣٧ سنة. بينت نتائج الدراسة إن هرمون البرولاكتين ارتفع معنويا لدى مجاميع المرضى اللواتي تم تقسيمهن إلى ٤ مجاميع اعتمادا على نسب هرمون البرولاكتين المحسوبة أثناء فترة الدراسة والتي كانت مجموعة ١ (٢١-٣٠) ومجموعة ٢ (٣١-٤٠) و مجموعة ٣ (٤١-٥٠) ومجموعة ٤ (٥١-٦٠) نانوغرام / مللتر على التوالي مقارنة بمجموعة السيطرة. أما بالنسبة إلى مستوى تراكيز حامض السياليك ومستويات الهرمون المحفز للجريبات والهرمون اللوتيني لم يظهر أي فرق معنوي لدى المريضا وفي كل المجاميع مقارنة بالسيطرة. وقد بينت النتائج إن مستوى حامض السياليك الكلي ليس له علاقة معنوية مع ارتفاع مستوى هرمون البرولاكتين وبالتالي ليس له علاقة لا بخصوصية ولا بعقم النساء.