

Serum total sialic acids concentrations in hyperprolactinimic infertile women and their relations to some reproductive hormones

مستوى حامض السياليك في مصل النساء العقيمات المصابات بارتفاع مستوى هرمون البرولاكتين وعلاقته ببعض الهرمونات التكاثرية

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Abstract

The study consist of 24 hyperprolactinimic women (patients), age range 17-38 (mean 25.4 ± 1.1) and fifteen healthy women (control), age range 18-36 (mean 28.8 ± 1.1) were included in this study. Prolactin (PRL) and reproductive hormones (FSH and LH) were measured by enzymatic immunoassay (EIA) method, and resorcinol method for serum TSA. Serum PRL, LH and TSA levels in hyperprolactinimic women were significantly elevated in compare to normal women, while FSH was showed no significant different. There is no relationship between TSA and hormones levels, but there is positive relation between PRL and FSH ($r= 0.578$) in control group, FSH and LH ($r=0.419$) in patients. It can be concluded that there is an elevation in TSA levels, but not affected by hormonal levels, and the causes of this elevation may be caused by other reasons.

الخلاصة

لقد تضمنت هذه الدراسة على 24 امرأة عقيمة مصابة بارتفاع نسبة هرمون البرولاكتين أعمارهم تتراوح بين 17-38 سنة و15 امرأة طبيعية أعمارهم تتراوح بين 18-36 سنة. لقد بينت النتائج ان هرمون البرولاكتين والهرمون اللوتيني وحامض السيالك الكلي يرتفع معنوياً لدى مجموعة المرضى مقارنة بمجموعة السيطرة . اما بالنسبة الى الهرمون المحفز للجريبات لم يظهر اي فرق معنوي لدى المرضى مقارنة بالسيطرة. وكذلك بينت النتائج ان مستوى حامض السياليك الكلي ليس له علاقة معنوية مع مستوى الهرمونات التكاثرية . لكن توجد علاقات معنوية بين الهرمونات حيث ان هرمون البرولاكتين ارتبط بعلاقة معنوية مع الهرمون المحفز للجريبات لدى مجموعة السيطرة ($r=0.578$) وكذلك بين الهرمون اللوتيني والمحفز للجريبات لدى المرضى ($r=0.419$). ومن ذلك يمكن ان نستنتج ان ه هناك ارتفاع في نسبة هرمون البرولاكتين ولكن لم يكن سببه الهرمونات التكاثرية فقط بل هناك اسباب اخرى ؟

Introduction

A number of reports described elevated total sialic acids (TSA) levels in various diseases e.g., Tumors, myocardial infarction, diabetes inflammatory disorders and alcoholism. Total sialic acids (TSA) determination during clinical investigation is well established. In view of possible link between TSA and hyperprolactinemia, the present study was designed. Hyperprolactinemia is the presence of abnormally-high levels of prolactin in the blood (1,2). Prolactin (PRL) is agonadotropic hormone, which is synthesized and secreted by specialized cell of the anterior pituitary gland, named lactotrophs (3). Hyperprolactinemia caused by either disinhibition (e.g., compression of the pituitary stalk or reduced dopamine levels) or excess production from a prolactinoma (a pituitary gland adenoma tumor) (4). Pituitary gland also secreted other hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH). (FSH, LH and PRL) are the main regulator of the reproductive axis (5). PRL is a lactogenic hormone ,together with estrogen, progesterone, corticosteroids, growth hormone, thyroxin and insulin initiates and maintains milk secretion by the mammary glands(5). In addition to its action as a hormone it act as growth factor, neurotransmitter,

or immunoregulator (6), it acts directly on tissues (5). FSH controls follicular recruitment, growth, maturation and steroidogenesis. LH acts as a major stimulator for ovulation and progesterone secretion (7,8). The chemical composition of PRL is protein, undergoes several posttranslational modifications that impact its stability, half-life, receptor binding, and biological activity. These include polymerization, proteolytic cleavage, phosphorylation and glycosylation (6). The linkage of the carbohydrate moiety of glycosylated prolactin may be either through nitrogen (N-glycosylation) or oxygen (O-glycosylation). The carbohydrate residues of the oligosaccharide chain may contain varying ratios of sialic acids, fucose, mannose, and galactose (9).

FSH and LH are glycoproteins, also undergoes several posttranslational modifications that modulate their biological properties, (sulfonation and sialylation) (10).

Sialic acids are found in nature in about 40 modifications, the most common in mammalian being N-acetylneuraminic acid (Neu5Ac), and N-glycolylneuraminic acid (Neu5Gc) (11).

They are one of the most important molecules of life, since they occupy the terminal position on macromolecules and cell membranes and are involved in many biological and pathological phenomena (12). Sialic acids commonly have the terminal position and appear in coating cell surfaces or in secretions (13). The wide occurrence of sialic acids in exposed positions of molecules and cells, their negative charge, the existence of multiple tissues suggests their involvement in cellular functions. In fact, enzymatic removal of sialic acids leads to marked differences in the biological behavior of cells, five main functions for these sugars can be distinguished: 1-Negatively charge 2-masking 3-recognition 4-they are essential components of receptor 5-prevent recognition of receptors by the corresponding ligands, or vice versa (14). The relationships among reproductive hormones concentrations in addition to their relations to sialic acids levels in hyperprolactinemic women was not searched before, so our study interested with it.

Subjects and Methods

This study was conducted on total number of 24 infertile hyperprolactinemic women whom attended to Kamal Al-samaray hospital for infertility. Control group consist of 15 healthy women. The diagnosis of patients was established by hormonal tests (serum prolactin, follicle stimulating hormone and luteinizing hormone tests).

Venous blood sample (5ml) was collected from control and patients at 2-4 days (follicle phase) of menstrual cycle. Each sample centrifuged for serum separation.

The serum divided into two tubes one of them for hormonal test (serum prolactin, FSH and LH) which performed by enzyme immunoassay method using commercial kit (biomerix), and the second tube was kept at 25°C until use for sialic acids measurements, which performed according to resorcinol method described by Sphenerholm (15).

The relationships between variables were studied using standard correlation methods. P values ≤ 0.005 . The comparison between patients and control using student's (t-test). P values ≤ 0.005 , and P value ≤ 0.001 (16).

Results

Analysis of the data obtained from the women included in this study showed the following: Significant elevation in TSA levels in 24 women (patients), age range 17-38 yrs, in comparison with 15 normal women, age range 18-36 yrs P ≤ 0.05 . Prolactin level and luteinizing hormone level also elevated significantly P < 0.001, P ≤ 0.05 , respectively. While follicle stimulating hormone not significantly elevated, as shown in table 1.

Table1: Serum level of sialic acid and reproductive hormones (prolactin, FSH and LH) in patients and controls.

Parameter	Mean \pm S.E.		P \leq
	Patients(No.=24)	Controls(No.=15)	
Total sialic acids μ g/ml	74.00 \pm 3.09	65.13 \pm 2.69	0.05
Prolactin(ng/ml)	37.45 \pm 2.82	17.37 \pm 0.91	0.001
FSH(mIU/ml)	6.64 \pm 0.87	5.12 \pm 0.34	N.S.
LH(mIU/ml)	8.41 \pm 1.99	4.22 \pm 0.53	0.05

N.S.: Not significant

These results were shown graphically in Figure (1, 2, 3, and 4).

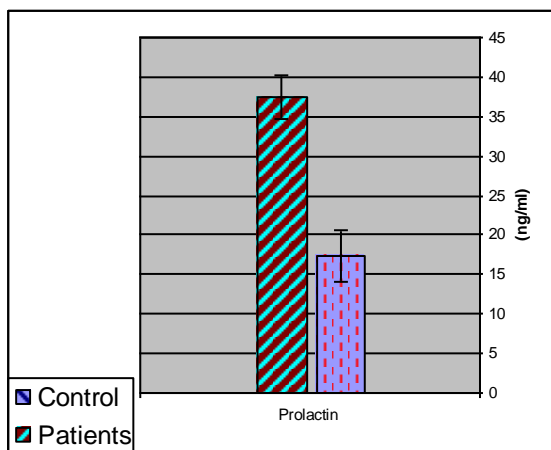


Fig1: Prolactin concentration in normal and infertile hyperprolactinemic women.

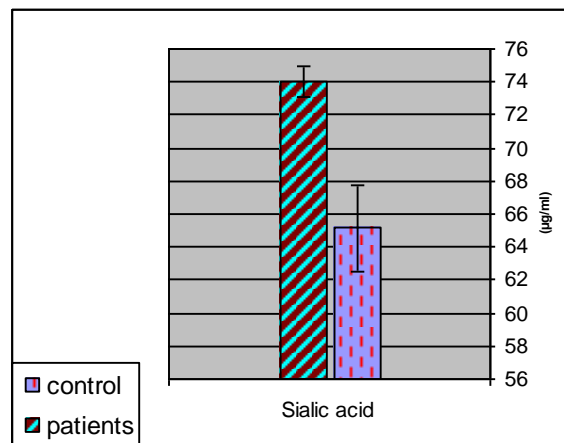


Fig2: Total sialic acids concentrations in normal and infertile hyperprolactinemic women.

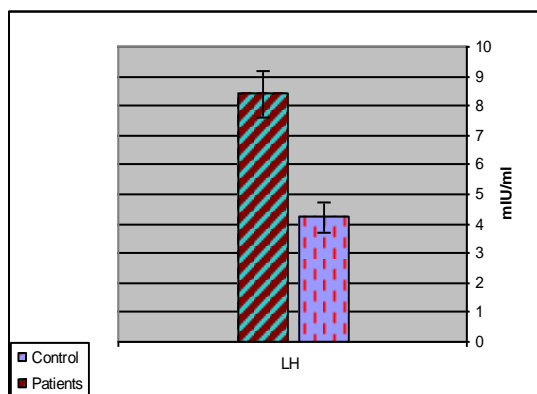


Fig3: Luteinizing hormone concentration in normal and infertile hyperprolactinemic women.

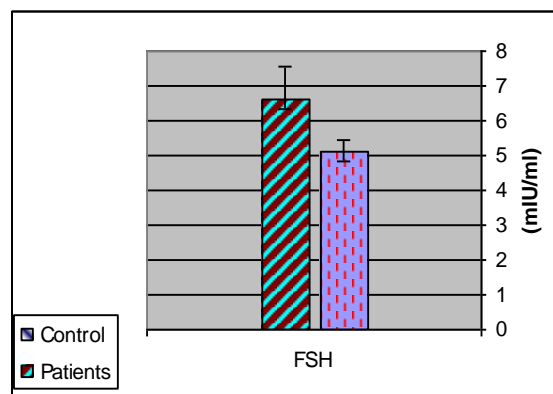


Fig 4: Follicle stimulating hormone concentration in normal and infertile hyperprolactinemic women.

Table 2 illustrated the relationships among hormones which showed positive relation between prolactin and FSH in control group $P \leq 0.05$, but not significantly related in patients. Prolactin and LH relation was not significant in patients and controls, while FSH and LH positively related in patients $P \leq 0.05$ and not significantly related in controls.

Table2: Pearson correlation between serum levels of reproductive hormones (prolactin, FSH and LH) in patients and controls.

Reproductive hormone	Patients(No.=24)		Controls(No.=15)	
	Correlation	P value	Correlation	P value
Prolactin vs. FSH	-0.085	N.S.	0.578	0.05
Prolactin vs. LH	-0.030	N.S.	-0.186	N.S.
FSH vs. LH	0.419	0.05	0.173	N.S.

N.S.: Not significant

The relationships of reproductive hormones with TSA were measured, and resulted in no significant relation between TSA and prolactin in control and patients. TSA and there relations to FSH was not significant in the two groups, in addition to no significant relation between TSA and LH (Table 3).

Table3: Pearson correlation between serum levels of sialic acids and reproduct -ve hormones (prolactin, FSH and LH) in patients and controls.

Reproductive hormone	Patients(No.=24)		Controls(No.=15)	
	Correlation	P value	Correlation	P value
Prolactin	0.211	N.S.	0.042	N.S.
FSH	-0.324	N.S.	-0.252	N.S.
LH	-0.005	N.S.	-0.199	N.S.

N.S.: Not significant

Discussion

The results summarized in this study clearly indicated that TSA levels elevated, in spite of there are no relation with reproductive hormones levels (PRL, FSH and LH). PRL level elevation is the-main sign for hyperprolactinemia which is a common problem in reproductive dysfunction affecting about one third of infertile women (17).PRL elevation lead to hypogonadism this in turn impaired gonad steroid secretion, which alters positive feed back effects at the hypothalamic and pituitary levels. This lead to lack of gonadotropin cyclicity (FSH and LH decline) and to infertility (18,19), another cause of infertility is the low esteradiol (E_2) production caused by PRL elevation (19,20).The results controversies with these evidences, whereas, revealed LH elevation and no significant elevation in FSH levels associated with PRL elevation.This may be due to one of these states:-

Hyperprolactinemia associated with polycystic ovary syndrome (PCOS),and increased rate of anovulatory cycles (21,22).Reduction in the inhibitory influence of hypothalamic dopamine might be a cause of in appropriately elevated LH and PRL levels (23).

The results showed significant positive relation between PRL and FSH levels in normoprolactinimic women .PRL have many changes through out the normal menstrual cycle; it was increase significantly in follicular and luteal phase and the higher one was recorded in the preovulatory period (24). Follicular phase is dominated by FSH and rising estrogen (25).These evidences may be explaining the positive relationships between PRL and FSH .FSH and LH was positively correlated, these results consisted with Anne Klibanski (26). FSH and LH belong to family of glycoproteins (10) and have a heterodimeric structure in which a α subunit, common to FSH and LH, and non-covalently joined to hormone specific unique β subunit. Each hormone exists as a family of glycoforms which differ in their oligosaccharide structures, including the extent of terminal sialylated and / or sulfunated. Deleeuw (27) and Burgon (28) showed that biological activity was positively correlated with sialic acid content .There are changes in the glycoforms observed at different menstrual cycle stages appear to be attributed to alterations in the hormones secreted from pituitary .

The results revealed that there were no significant correlation between TSA and reproductive hormone in normoprolactinimic and hyperprolactinimic women, these results can demonstrate that sialylated glycoprotein in PRL, FSH and LH were not predominant at follicular phase and other glycoform may be contribute in structure of these hormones at this phase of menstrual cycle in normal and hyperprolactinimic patients.The elevation of TSA can be caused by other effects.

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