

Full Length Research Paper

Assessment of Prolactin Level Among Sudanese Psychiatric Subjects

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Abstract

Introduction: Prolactin (PRL) is a polypeptide hormone secreted by the lactotroph cells of the anterior pituitary gland. Prolactin release is pulsatory with approximately 13–14 pulses a day and displays a significant diurnal rhythm. Levels increase shortly after sleep onset, peak during the night, and start to decline shortly after waking, reaching a nadir around noon. Some tricyclic antidepressants cause hyperprolactinemia, as do selective serotonin reuptake inhibitors, due to their increased serotonergic stimulatory effects; increases serotonin activity and can produce elevated prolactin levels. So this study aimed to evaluate the prolactin level among Sudanese psychiatric subjects with different diagnosis and treatment, to ascertain the effect on prolactin and to observe the criterion correlated more with high concentration of prolactin, as according to gender, type of mental disorder, treatment and duration of the disease. **Method:** Enzyme linked immunoassay (ELISA) method used to quantitate prolactin level among 86 Sudanese psychiatric subjects who were diagnosed with bipolar, depression, Schizophrenia and psychosis. Serum concentration of PRL levels measured at Alneelain University, faculty of medical laboratory science. **Result:** Data obtained showed increased level of PRL among both gender, but no significant different obtained, but according to type of mental disorder as p value 0.001 and 0.015 for bipolar and psychosis respectively, and kind of treatment significant different gained as p value 0.000 for Soduim+olanz and 0.012 for tegretol users. **Conclusion:** Clear evidence of hyperprolactinaemia among mentally ill subjects.

Keywords: Prolactin, ELISA, serotonin, bipolar. Depression, schizophrenia, psychosis, sodium and olanz.

INTRODUCTION

Prolactin is a polypeptide hormone secreted by the lactotroph cells of the anterior pituitary gland. Prolactin release is pulsatory with approximately 13–14 pulses a day and displays a significant diurnal rhythm. Levels increase shortly after sleep onset, peak during the night, and start to decline shortly after waking, reaching a nadir around noon, Yen and Jaffe, 1991. The primary physiologic role of prolactin is the induction of lactation.

However, prolactin interacts with other CNS and peripheral processes and its secretion is influenced by both stimulatory and inhibitory endogenous substances, Melmed, 2000. Prolactin release is also indirectly influenced by the effects of exogenous substances on endogenous ones, Melmed, 1995. Prolactin receptors have been identified in several blood cells, notably B-cells, T-cells, and monocytes. Prolactin synthesis by normal lymphocyte cells has also been confirmed. It has been suggested that prolactin is secreted from mononuclear cells and has an autocrine/paracrine effect on immune-cell function, Pellegrini *et al.*, 1992.

Prolactin secretion is under the control of various peptide and steroid hormones and neurotransmitters, Freeman, 1981. Dopamine, however, is the predominant prolactin-inhibiting factor in humans and animals. In the tuberoinfundibular neurons of the hypothalamus, dopamine is produced and released from nerve endings. It is transported by the portal hypophyseal circulation to the pituitary, where it binds to dopamine D2 receptors on the membrane of the lactotroph cells, Gudelsky, 1981.

The presence of dopamine suppresses the release of prolactin to a minimum. Dopamine D2 antagonists, such as most antipsychotics, bind to the D2 receptors and lead to the release of prolactin in the lactotroph cells. Animal and human studies demonstrate that serotonin may stimulate prolactin secretion as well as several peptide neurotransmitters, including thyrotropin releasing hormone and cholecystokinin, Freeman, 1981.

The World Health Organization defined health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity". Mental disorders constitute a major public health problem and contribute to 13% of the global burden of disease measured as disability adjusted life years, Mathers *et al.*, 2004. Low and middle income countries have higher burden of mental disorders than economically developed countries, Bass *et al.*, 2012; Hock *et al.*, 2012. Mental disorders have serious negative effect on survival, and when present with chronic diseases as co-morbid condition, serious mental disorders may reduce life expectancy by about 20 years, Colton and Manderscheid, 2006.

MATERIAL AND METHOD

This study was conducted in Khartoum state –psychiatric hospital, it involved 86 subjects attended to Eltejani Elmahi psychiatric teaching hospital, and some of them were hospitalized while the others were on follow up routine meetings, a formal consent was obtained from the hospital administration and from every co-patient before enrolling in this study. Those subjects were under anti-psychiatric drugs, given according to the diagnosis, 4 groups were enrolled included bipolar, depression, schizophrenia and psychosis (included subjects with un-defined diagnosis yet).

Five ml of venous blood withdrawn under hygienic condition from each subject, blood allowed to clot formation then separation of serum which preserved frozen till analytical part which performed at Alneelain University, faculty of medical laboratory science, depart of clinical chemistry by means of ELISA device (Maplab trade mark, Italy version 2006). A Germany made ELISA kit was used. Prolactin KIT is a solid phase immunoassay based on sandwich principle for the quantitative detection of the hormone in human serum. ELISA kits typically

include: Antibody-coated 96-well plate Standards; Primary detection antibody (typically biotinylated); Secondary detection reagent (usually streptavidin-HRP); Diluent buffers; Wash buffers; Substrate and stop solutions; Plate covers

RESULT

This study involved 86 subjects, who professionally diagnosed with psychiatric issues, 52 (60.5%) were males and 34 (39.5%) were females, their age mean was 32.6 years and mean of disease duration was 4.6 years. The prolactin level for both genders as in table 1, mean+SD, for male 21.5+17.3 and for females 27.3+23.6. Comparison of levels of two genders did not bring a significant difference.

DISCUSSION

Understanding of the definitions of wellness and illness has changed from the mid-20th century to modern times, moving from a diagnosis-focused to a person-focused definition of mental illnesses, and from an "absence of disease" model to one that stresses positive psychological function for mental health.

Currently, wellness refers to the degree to which one feels positive and enthusiastic about oneself and life, whereas illness refers to the presence of disease. These definitions apply to physical as well as mental illness and wellness.

All conventional antipsychotic drugs block D₂ receptors on lactotroph cells and thus remove the main inhibitory influence on prolactin secretion. Normal serum concentration of PRL varies with sex, Hamner, 2002; Byerly *et al.*, 2007; Zhang-Wong and Seeman, 2002. Elevation of prolactin levels occurs within a few hours of treatment initiation, and the use of high doses of depot antipsychotics.

In this study increased level of prolactin among mentally ill subject observed, it agrees with many studies interested on the same manners, one of them conducted among females under antipsychiatry drugs, it revealed that prolactin concentrations can rise to ten times normal levels or above, and existing data indicate that 17-78% of female patients have amenorrhea with or without galactorrhea, Wieck and Haddad, 2003.

Another study demonstrated the high concentration of prolactin among both genders as this study, Nakamura and Nagamine, 2012. According to the type of mental illness prolactin evaluated in this study, among bipolar one it found elevated with highly significant difference from the normal range, this in agreement with a study conducted among out patients with severe depression, Papakostas *et al.*, 2006.

Table 1. Prolactin levels in male and females

| | Gender | Mean | Std. Deviation | P-value |
|-----------|--------|-------------|----------------|---------|
| Prolactin | Male | 21.50±17.31 | 17.31 | 0.197 |
| | Female | 27.25±23.59 | 23.59 | |

Prolactin reference range accompanied with ELISA kit was 1.0-16ng/ml, used to compare the level of hormone among each group of subjects, which divided according the diagnosis, bipolar, depression, schizophrenia and psychosis which comprised subjects with undefined diagnosis yet.

Mean±SD of prolactin of each sub class of diagnosis showed in table 2, significant difference obtained among bipolar and psychosis ones as p value 0.001 and 0.015 respectively, while no significant difference with the other two diagnostic disorders.

Table 2: Shows comparison between normal range of prolactin and mean±SD of prolactin levels of different diagnosis types involved

| | Mean±SD ng/ml | P-value |
|---------------|---------------|---------|
| Normal Range | 1.0-16 | |
| Bipolar | 36.04±22.84 | 0.001 |
| Depression | 27.70±22.84 | 0.392 |
| Schizophrenia | 24.82±22.84 | 0.334 |
| Psychosis | 21.93±22.84 | 0.015 |

Significant difference obtained as p value <0.05

Considering type of treatment taken by subjects, the group who was under sodium accompanied with Olanzapine brought a high significant difference as p value 0.000 as well as the Tegretol drug users as p value 0.012, while other drugs did give significant difference when compared with the reference range of the prolactin, as in table 3.

Table 3. Mean±SD and p value of prolactin among each drug users

| | Mean±SD ng/ml | P-value |
|-------------------|---------------|---------|
| Normal Range | 1.0-16 ng/ml | |
| Drug groups | | |
| sodium+olanzapine | 46.36±22.67 | 0.000 |
| olanzapine | 17.90±9.89 | 0.977 |
| residone | 25.43±20.46 | 0.470 |
| resipal | 19.67±18.68 | 0.841 |
| Tegretol | 22.49±19.66 | 0.012 |

Significant difference obtained as p value <0.05

Considering duration of the disease effect on prolactin level, correlation between both brought a negative correlation factor (R), indicator of inversion relationship, as prolactin level decrease with the increasing of disease duration bringing a significant difference as p value 0.000, as in figure 1.

For schizophrenia, our finding did not show significant difference and that disagrees with many studies, as prolactin measured levels were highly concentrations among those subjects, Haddad and Weick, 2003; Wu *et al.*, 2013. About psychosis in general we did find increase level of prolactin, which agrees with certain study suggested that prolactin measurement should be considered for monitoring psychosis, Citrome, 2012, and other study found prolactin elevated among subject with early stage of psychosis, Montalvo *et al.*, 2014.

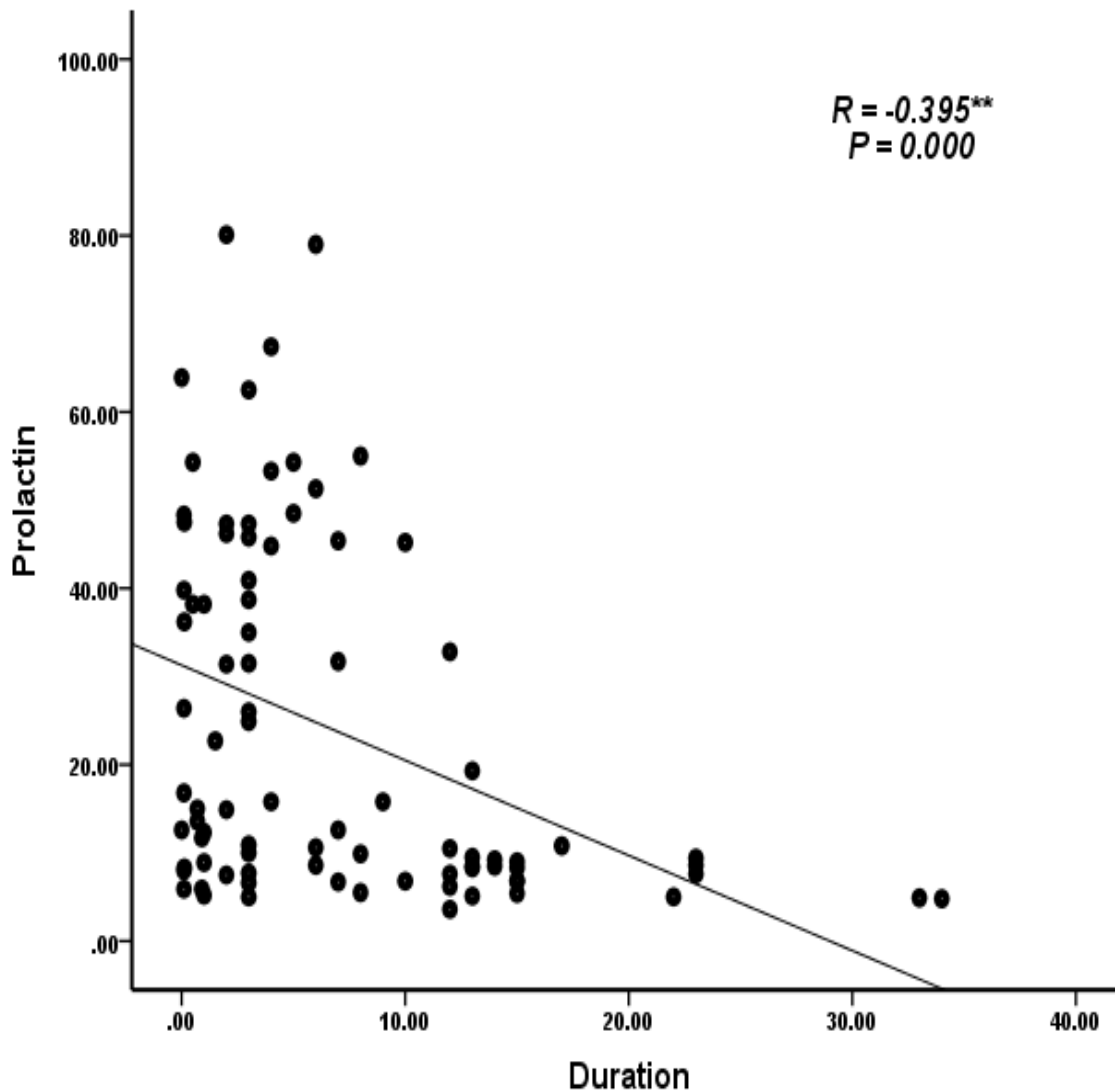


Figure 1. Correlation between duration of psychiatric disorders and prolactin level

Considering antipsychotic drugs used, this study showed that treatment used for bipolar (sodium + olanz) and psychosis (tegreto) brought significant difference in prolactin level, while other drugs involved did not (risperidone, olanz and resibal) which opposite to findings observed that risperidone contributes predominantly to hyperprolactinaemia. While other study reviewed of effects on prolactin levels due to certain types of drugs suggested that a clear relationship between changes in prolactin level and the response to certain antipsychotics. The equivocal results obtained with other drugs may be related to the observation that prolactin has little predictive value beyond a certain level and may also reflect variables such as the effects of gender, the use of drugs with low dopamine antagonist activity, short treatment durations, small sample sizes.

CONCLUSION

Prolactin level among psychiatric subject has been affected regardless type of sub-diagnosis of mental issue and with certain drugs on treatment of psychotic symptoms and episodes.

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