Serum Ferritin Correlation Study in Idiopathic Parkinson's Disease Severity

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ABSTRACT

Background: Iron and the extrapyramidal system may be strongly related. The diversity of response to this element may cast light on the possible mechanisms of idiopathic Parkinson's disease and the complex extrapyramidal system dynamics. Objectives: To evaluate the possible correlation of serum ferritin, and the severity of Parkinson's disease. Methods: Twenty five male idiopathic Parkinson patients were included. Full exclusion of secondary etiology was achieved. Clinical assessment was done using the Hoehn Yahr scale. Serum ferritin level was assessed and repeated one month later. Results: The serum ferritin level varied in Parkinson according to severity and duration of disease; it was high in 72% (328 ng/ml mean); normal in 20% (112 ng/ml mean) and low in 8% (23 ng/ml mean). Three Parkinson patients gave history of RLS before, and symptoms disappeared one year prior to their Parkinson features. Conclusion: Serum ferritin may correlate with the severity of idiopathic Parkinson disease. The diverse response of the extrapyramidal system to this element with the few studies performed requires more active and further investigations. (Egypt J. Neurol. Psychiat. Neurosurg. 2009, 46(2): 463-466)

Key Words: Serum Ferritin, Idiopathic Parkinson's Disease

INTRODUCTION

Evidence suggests that abnormal iron metabolism is associated with Parkinson disease (PD), with raised iron levels found in pathologically affected areas in PD.¹ It is unclear why such dysmetabolism should lead to preferential substantia nigra (SN) zona compacta (SNzc) neuron death.² The SN is known to be iron-rich, and iron is extensively used by neurons for mitochondrial oxidative metabolism³, with dopaminergic neurons having an additional requirement in the synthesis of dopamine.⁴ Previous Studies have shown elevated iron in PD SN using in vivo imaging where T2-weighted MRI scans indicate raised nigral iron.⁵ Bulk analysis of postmortem PD SN reveals raised non-heme iron, though this is associated almost exclusively with glia, it would be expected that iron levels might be raised within the neuron.⁶ This was confirmed by Oakley et al⁷ who identified raised intraneuronal iron in single defined SN neurons in postpartum tissues of PD patients using sensitive and specific wavelength microanalysis coupled with cathodoluminrscence spectroscpe. If iron plays a primary role in PD, We have therefore tried to evaluate the possible correlation of serum ferritin level and the severity of Parkinson's disease.

METHODS

The study included 25 idiopathic Parkinson patients. They were recruited from the movement disorders clinic, neurology department, faculty of medicine, Alexandria University, Egypt. All subjects provided written informed consent to participate in this research protocol.

Patients were subjected to clinical evaluation which included detailed history and complete neurological examination. The Parkinson's disease diagnosis was carried out using UK Parkinson's disease severity society brain bank (PDSBB)⁷ clinical diagnostic criteria of idiopathic Parkinson's disease. Full exclusion of secondary etiology was achieved. The clinical motor staging of the 25 Parkinson patients was done using Hoehn Yahr motor scale⁸ which consists of 5 stages to assess the
disease severity. Serum ferritin level was assessed in Parkinson patients and repeated one month later. Other causes of iron disturbances were excluded.

Statistical analysis:
The statistical package of social science (spss / version 11.0) software was used to analyze the obtained data. Descriptive data were expressed as mean ± standard deviation SD or frequencies. Correlation study was performed using Pearson’s correlation coefficient.

RESULTS

The present study included 25 Parkinson patients. All patients were males. Their mean age was 52 years. The disease duration ranged from 1 to 10 years with a mean 5.6 years. All patients were receiving carbidopa (25 mg)/l-dopa (250 mg) at 750-1000 mg/day orally.

According to Hoehn Yahr scale, the clinical patients stages of the Parkinson's disease severity were as follow: 10 patients were on stage 2, 12 patients were on stage 3 and 3 patients were on stage 4. The serum ferritin level varies in Parkinson according to duration and severity of disease, it was high in 72%(18 patients), ranged from 220 to 410 with a mean of 328 ng/ml. It was normal in 20%(5 patients), ranged from 88 to 170 with a mean of 112 ng/ml. it was low in 8%(2 patients), ranged from 21 to 69 with a mean of 23 ng/ml. Three Parkinson patients gave history of Restless legs syndrome (RLS) before, and symptoms disappeared one year prior to their Parkinson features. There were positive correlation (r=0.799, p=<0.001; r=0.768, p=<0.001) between the serum ferritin level and duration of disease and clinical severity using Hoehn Yahr motor scale in Parkinson patients respectively (Figs. 1 and 2).

DISCUSSION

The present study showed variable levels of serum ferritin level in Parkinson patients. They varied according to severity and duration of disease, suggesting that these changes may be later or secondary changes. Also, this may reflect the diversity of role of iron level in Parkinson patients especially those three Parkinson patients gave history of RLS before, and symptoms disappeared one year prior to their Parkinson feature. Is there is relation between the low ferritin level found and the history of RLS, as the serum ferritin level is known to be low in RLS patients. Although this was not enough evidence pointing to the presence of a possible link between Parkinson and restless legs syndrome. It is clear that most of the iron measured in the adult brain is in the form of nonheme iron, we didn't measure nonheme iron in glial ferritin as
well as neuronal iron. Further advanced analytical techniques will need to be used.

It was found that elevated neuropil iron may indicate a disturbance in the glial handling of iron and ferritin in PD, which is known to occur in other iron associated neurodegenerative diseases. Previous results have shown that ferritin is the only detectable iron storage unit in control subjects and PD patients, and the number of ferritin cores increases along with heavier ferritin iron loading in PD, although this in the presence of reduced ferritin L-chain content. Any problem with iron handling by neurons may therefore be exacerbated by defects in glial iron and ferritin metabolism.

Also the study of the role of iron in Parkinson’s disease using transcranial sonography has recently been reviewed by Berg. The development of PD is associated with a loss of neuromelanin and increase of iron in the (SN). The increase of iron leads to hyperechogenicity. The SN which appears as small patchy areas of slightly increased echogenicity in healthy controls, becomes clearly visible and more delineated. Several neurodegenerative disorders caused by abnormal iron metabolism show alpha synuclein aggregates, suggesting iron dysmetabolism is a principal cause of degeneration. Raised neuronal iron in PD suggests the possibility that this may be a primary event leading to alpha synuclein aggregation via ferric iron by the generation of hydrogen peroxide and hydroxyl radicals through direct interaction with alpha synuclein. So elevation of iron levels detected in the pars compacta of the substantia nigra in patients with Parkinson’s disease is believed to be an important factor in causing oxidative stress. Interestingly, increased iron and reduced complex I activity are not found in the brains of patients with incidental Lewy body disease, suggesting that these may be later or secondary changes. However, a reduction in the level of reduced glutathione is evident even at the early stage. This coincidence with our results as the presence of variable levels of ferritin and its correlation to the duration and severity of disease.

We concluded that serum ferritin may correlate with the severity of idiopathic Parkinson disease. Abnormalities of neuronal and also glial may provide some insights into disease process, and the study of iron metabolism may provide one possible avenue of therapeutic intervention. The diverse response of the extrapyramidal system to this element with the few studies performed requires more active and further investigation.

REFERENCES


الملخص العربي

دراسة مقارنة لمستوى الفريتيه في المصل مع شدة مرض الباركيينوس الأولي

المقدمة: يہ ساہم فی تطور مرض باركیئنوس والتنافس فی داؤر هیذا العنصر يساعد فی مزیج من الفم ألائی عمل الجهاز خارج النعر.

الهدف: من هذة الدراسة هو تقييم احتلال وجود علاقة بين مستوى الفريتيه في الدم مع شدة مرض باركیئنوس الأولي.

طرق البحث: تم دراسة 25 مريضًا يعانون من مرض باركیئنوس ثم قياس مستوى الفريتيه في مصل المرضى مع استخدام قياسات لتقدير شدة مرض باركیئنوس، وتم استعداد الأسباب الأخرى لاضطراب تمتيل الحديد.

النتائج: أظهر البحث تنوء في مستوى الفريتيه في حالات الباركیئنوس حسب شدة الحالة ودرجة المرض حيث كان مرتفعًا (328 نانوجرام لكل مللي في المتوسط) 72% وطبيعي (112 نانوجرام لكل مللي في المتوسط) في 20% وانخفاضًا في (23 نانوجرام لكل مللي في المتوسط) 8% من حالات الباركیئنوس كما كان هناك ثلاث حالات من الباركیئنوس يعانون من متلازمة الأقدام الحركية وقد أخليت أعراضهم قبل ظهور المرض.

الخلاصة: تستخلص من هذا إلى أن مستوى الفريتيه في الدم قد يتناسب مع شدة مرض الباركیئنوس الأولي وأن اختلاف استجابة الجهاز خارج النعر لهذا العنصر مع ندرة الدارسات في حالات المتلازمة، يحتاج لمزيد من الفم ومثقو الوضوء على آلية العمل في هذا الجهاز العصبي المعقّد.