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REVUES GÉNÉRALES ET ANALYSES PROSPECTIVES

TBARs and non-enzymatic antioxidant parameters in Tunisian bipolar I patients

Subtances réactives avec l'acide thiobarbiturique (SRAT) et les paramètres antioxydants non enzymatiques chez des patients bipolaires de type I tunisiens

A. Ezzaher[a,*,b], D. Haj Mouhamed[a,b], A. Mechri[a], F. Neffati[a], W. Douki[a,b], L. Gaha[b], M.F. Najjar[a]

[a] *Biochemistry and Toxicology Laboratory, Monastir University Hospital, Monastir 5000, Tunisia*
[b] *Research Laboratory ''Vulnerability to Psychotic Disorders LR 05 ES 10'', Department of Psychiatry, Monastir University Hospital, Monastir 5000, Tunisia*

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KEYWORDS
Bipolar I disorder;
Oxidative stress biomarkers;
Mood stabilizers

Summary
Aims. — We aim to investigate the variations of some oxidative stress markers (TBARs, uric acid, bilirubin and albumin) in Tunisian bipolar I patients and to explore the association of these parameters to clinical and therapeutic characteristics of this population.
Methods. — Our study included 90 patients with bipolar I disorder and 92 controls. Uric acid, TBARs, bilirubin and albumin concentrations were determined by enzymatic and colorimetric methods.
Results. — Compared with controls, patients had significantly higher values of uric acid and TBARs and significantly lower values of bilirubin. However, no significant change in albumin values was observed. Furthermore, bipolar I disorder was significantly associated with hyperuricemia (OR, 3.64; 95% CI: 1.96—6.75; $P < 10^{-3}$), hyperTBARs (OR, 2.23; 95% CI: 1.23—4.03; $P = 0.008$) and hypobilirubin (OR, 3.09; 95% CI: 1.69—5.66; $P < 10^{-3}$). Our study showed that depressive patients had the highest levels of TBARs. Moreover, both uric acid and TBARs were significantly correlated with the illness duration ($r = 0.221$; $P = 0.03$; $r = 0.356$; $P = 0.001$ respectively) and the total number of illness episodes ($r = 0.213$; $P = 0.05$; $r = 0.247$; $P = 0.02$ respectively). We also showed that uric acid was significantly associated with the treatment. Indeed, patients taking mood stabilizers had higher levels of uric acid than those under antipsychotics.

* Corresponding author.
E-mail address: ezzaherasma@yahoo.fr (A. Ezzaher).

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Conclusion. — Bipolar I disorder was significantly associated with hyperuricemia, hypobilirubin, and hyperTBARs, reflecting the existence of oxidative stress. This risk was significantly associated with treatment by mood stabilizers, the illness episode and duration, and the total number of illness episodes.

MOTS CLÉS
Trouble bipolaire I ;
Biomarqueurs du stress oxydatif ;
Stabilisateurs de l'humeur

Résumé
Objectifs. — Notre objectif est d'étudier les variations de certains marqueurs du stress oxydatif (substances réactives avec l'acide thiobarbiturique [SRAT], l'acide urique, la bilirubine et l'albumine) chez des patients bipolaires de type I tunisiens et d'explorer l'association de ces paramètres aux caractéristiques cliniques et thérapeutiques de cette population.
Méthodes. — Notre étude a porté sur 90 patients atteints de trouble bipolaire I et 92 témoins. L'acide urique, les SRAT, la bilirubine et l'albumine ont été déterminés par des méthodes enzymatiques et colorimétriques.
Résultats. — Comparativement aux témoins, les patients avaient des valeurs significativement plus élevées d'acide urique et de SRAT et des valeurs significativement plus basses de la bilirubine. Toutefois, aucun changement significatif dans les valeurs d'albumine n'a été observé. En outre, le trouble bipolaire I était significativement associé à l'hyperuricémie (OR, 3,64, IC 95 % : 1,96 à 6,75, $p < 0{,}001$), l'hyperSRAT (OR, 2,23, IC 95 % : 1,23 à 4,3, $p = 0{,}008$) et l'hypobilirubinémie (OR, 3,09, IC 95 % : 1,69 à 5,66, $p < 0{,}001$). Notre étude a montré que les patients en phase dépressive avaient les valeurs les plus élevées de SRAT. En outre, l'acide urique et les SRAT étaient significativement corrélés avec la durée de la maladie ($r = 0{,}221$, $p = 0{,}03$; $r = 0{,}356$, $p = 0{,}001$ respectivement) et le nombre total d'épisodes de la maladie ($r = 0{,}213$, $p = 0{,}05$; $r = 0{,}247$, $p = 0{,}02$ respectivement). Nous avons également montré que l'acide urique a été associé de façon significative avec le traitement. En effet, les patients prenant des stabilisateurs de l'humeur avaient des niveaux plus élevés d'acide urique que ceux sous antipsychotiques.
Conclusion. — Le trouble bipolaire I était significativement associé à une hyperuricémie, hypobilirubinémie et hyperSRAT, reflétant l'existence d'un stress oxydatif. Ce risque était significativement associé au traitement par les thymorégulateurs, la durée et le nombre total d'épisodes de la maladie.

Introduction

Oxidative stress is defined as a ''disturbance in prooxidant-antioxidant balance in favor of the former, leading to potential damage''. Free radicals and other so-called ''reactive species'' are constantly produced in vivo by all body tissues, mainly during oxidative phosphorylation in the mitochondrial matrix [1,2].

Under physiological conditions, multiple tiers of defense exist to protect against these free radicals, including the restriction of their production through the maintenance of a high oxygen gradient between the ambient and cellular environments, their removal by non-enzymatic and enzymatic antioxidants, and the reparation of oxidative damages by structural repair and replacement mechanisms [3].

According to some authors [4—6], oxidative stress may be implicated in the pathogenesis of psychiatric disorders particularly bipolar disorder. This hypothesis has theoretical appeal, as the brain is considered particularly vulnerable to oxidative damage for several reasons. The brain consumes large amounts of oxygen and therefore produces a comparatively large amount of free radical by-products, and it has relatively modest antioxidant defenses. In addition, the brain is rich in lipid substrates for oxidation, and iron and copper ions that catalyze free radical reactions are abundant [1,7].

Several recent studies reported that bipolar patients have significant alterations in non-enzymatic mechanism [2,8—11]. However, the findings are not consistent with other studies reporting no change or reductions in various markers [5].

Our study aims to investigate the variations of four oxidative stress markers (thiobarbituric acid reactive substances [TBARs], uric acid, bilirubin and albumin) in Tunisian bipolar I patients and to explore the association of these parameters to clinical and therapeutic characteristics of this population.

Patients and methods

Subjects

Our study included 90 patients with bipolar I disorder from the psychiatry department of the University Hospital of Monastir, Tunisia, aged 37.2 ± 11.8 years, 59 men (37.3 ± 11.2 years) and 31 women (37.1 ± 13.0 years). Consensus on the diagnosis, according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria [12], was made by psychiatrists. The exclusion criteria were age less than 18 years, other psychiatric illnesses, epilepsy or mental retardation. The control group consisted of 92 volunteer subjects without psychiatric pathology, aged 34.1 ± 14 years, 60 men (28.2 ± 11.0 years)