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Review of literature

Lithium and suicide prevention in bipolar disorder

Lithium et prévention du suicide dans le trouble bipolaire

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ABSTRACT

Introduction. – Bipolar disorder (BD) is a severe and recurrent psychiatric disorder. The severity of prognosis in BD is mainly linked to the high rate of suicide in this population. Indeed, patients with BD commit suicide 20 to 30 times more frequently than the general population, and half of the BD population with an early age of onset have a history of suicide attempt. International therapeutic guidelines recommend lithium (Li) as the first-line treatment in BD for its prophylactic action on depressive or manic episodes. In addition, Li is the only mood stabilizer that has demonstrated efficacy in suicide prevention. This effect of Li is unfortunately often unknown to psychiatrists. Thus, this review aims to highlight evidence about the preventive action of Li on suicide in BD populations.

Methods. – We conducted a literature search between April 1968 and August 2014 in PubMed database using the following terms: “lithium” AND “suicide” OR “suicidality” OR “suicide attempt”.

Results. – As confirmed by a recent meta-analysis, many studies show that Li has a significant effect on the reduction of suicide attempts and deaths by suicide in comparison to antidepressants or other mood-stabilisers in BD populations. Studies have demonstrated that long-term treatment with Li reduces suicide attempts by about 10% and deaths by suicide by about 20%. The combination of Li and an antidepressant could reduce suicidal behaviours by reducing suicidal ideation prior to depressive symptoms. It appears crucial for Li efficacy in suicide prevention to maintain the Li blood concentrations in the efficient therapeutic zone and to instate long-term Li treatment. The “impulsive-aggressive” endophenotype is associated with suicide in BD. The specific action of Li on the 5-HT serotonergic system could explain the specific anti-suicidal effects of Li via the modulation of impulsiveness and aggressiveness. Furthermore, genetic variants of the glycogen synthase kinase 3 α / β (GSK3 α and β ; proteins inhibited by Li) seem to be associated with more impulsiveness in BD populations.

Conclusion. – The anti-suicidal effect of Li has been very well demonstrated. By its specific action on the serotonergic system, treatment with Li significantly reduces “impulsive-aggressive” behaviour which is a vulnerability factor common to suicide and BD. Long-term appropriately modulated treatment with Li seems to have considerable impact on the reduction of suicidal behaviours, suicidal ideation and death by suicide in the BD population.

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R É S U M É

Introduction. – Le trouble bipolaire (TB) est une maladie psychiatrique sévère et fréquente. La sévérité du pronostic du TB est largement associée au taux élevé de suicides survenant dans cette population. En effet, les suicides sont 20 à 30 fois plus fréquents chez les patients avec TB que dans la population générale, et

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Sels de lithium
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un patient sur deux avec un âge de début précoce du TB présente un antécédent de tentative de suicide. Dans les recommandations thérapeutiques internationales du TB, le lithium (Li) est le traitement de première intention pour son efficacité dans le traitement et la prévention des épisodes maniaques ou dépressifs. De plus, le Li est le seul traitement stabilisateur de l'humeur ayant déjà prouvé son efficacité dans la prévention du suicide. Néanmoins, cet effet du Li est souvent méconnu des psychiatres. Ainsi, cette revue de la littérature a pour objectif la synthèse de l'efficacité du Li dans la prévention des conduites suicidaires chez les patients souffrant de TB.

Méthode. – Nous avons réalisé une recherche bibliographique de la littérature scientifique publiée entre avril 1968 et août 2014 à l'aide de la base de données PubMed, et en utilisant les mots clés suivants : « lithium » AND « suicide » OR « suicidality » OR « suicide attempt ».

Résultats. – De nombreuses études, et une méta-analyse récente, confirment l'efficacité du Li sur la réduction des tentatives de suicide et la réduction des suicides chez des patients avec TB, en comparaison aux autres stabilisateurs de l'humeur ou aux antidépresseurs. Il est démontré que l'utilisation au long cours du Li permet de réduire de 10 % les tentatives de suicide et de 20 % le taux de suicide dans cette population. L'adjonction du Li à un traitement antidépresseur en cours permettrait de réduire les comportements suicidaires et ceci en diminuant les idées suicidaires avant que n'apparaisse la réduction des symptômes dépressifs. Pour obtenir une efficacité dans la prévention du suicide, il apparaît indispensable de maintenir le traitement par Li au long cours et à des doses efficaces, permettant une lithiémie dans la zone thérapeutique. De manière intéressante, il a été démontré que l'endophénotype « impulsif-agressif » est largement associé au suicide dans les TB. L'action spécifique du Li sur le système sérotoninergique 5-HT pourrait expliquer l'effet spécifique du Li dans la réduction des conduites suicidaires, ceci via la régulation de l'impulsivité et de l'agressivité. Enfin, des variants génétiques de la glycogène synthase kinase $3\alpha/\beta$ (GSK3 α et β , protéines inhibées par le Li) semblent être associés à une augmentation de l'impulsivité chez les patients souffrant de TB.

Conclusion. – L'effet anti-suicidaire du Li est largement démontré par la littérature scientifique. Par son action spécifique sur le système sérotoninergique, le traitement par Li permet de réduire significativement les comportements « agressifs-impulsifs », qui sont des facteurs de vulnérabilité communs entre le suicide et le TB. Le traitement par Li, au long cours et en zone thérapeutique efficace, semble avoir un impact considérable dans la réduction des conduites suicidaires, des idées suicidaires et des suicides chez les patients souffrant de TB.

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1. Introduction

Bipolar disorder (BD) is a severe, cyclic, psychiatric illness entailing recurrences of mood episodes referred to as “manic” or depressive“. BD is a frequent illness, affecting 1% of the general population if Types I and II BD are considered, with a prevalence reaching 4.4% if wider spectrum BD is considered [1]. It is a severe pathology, to the extent that it is the fourth-ranking contributor to the general morbidity burden worldwide (whatever the age) among mental, neurological and substance use disorders [2]. Unlike the general population, BD patients have not seen an increase in life expectancy over recent decades. It is indeed on average 20 years below that of the general population [3]. The poor prognosis for this illness is partly linked to high suicide levels, with half the subjects with an early onset of the illness attempting suicide [4]. This high prevalence of suicide attempt, which remains the strongest predictive factor for actual suicide, contributes to placing BD patients among those with the highest suicide risk. Indeed, their suicide rate is 20 to 30 times that of the general population [5]. According to WHO data, more than 800,000 individuals die from suicide every year in the world, amounting to one every forty seconds [6]. Although 75% of suicides occur in countries with low to medium income, in Europe the suicide rate was 11.4/100,000 in 2012, that is to say slightly above the world average [6]. Suicide is the main cause of death in the 15–29 age group, and the evaluation of suicide risk thus appears as a major challenge for prevention, and all the more so in case of BD [7].

Lithium (Li) has for decades been considered as the first-line reference treatment for BD, and is included in all international recommendations [8]. It is the first mood-stabiliser treatment with efficient therapeutic and preventive action in both manic and depressive recurrent episodes [9], unlike the majority of treatments that act on only one pole of bipolar disturbances [10]. Li also has an effect on deaths from suicide among patients with a mood disorder

[11]. Thus Li remains the first-line treatment in BD, and appears to be the only treatment to date that decreases suicide attempts and suicide in these patients [8]. This emblematic anti-suicide effect of Li is however not well known by psychiatric physicians. We therefore set out to perform a synthesis of the scientific data in the international literature on the prevention of suicide by Li among BD patients. It can indeed be thought that enhanced awareness of the anti-suicidal effect of this mood-stabiliser treatment could improve care and also prognosis among our patients, reducing deaths from suicide.

2. Methods

2.1. Definitions

Suicide can be described as intentionally causing one's own death, an act that is initiated and accomplished by a person who has awareness of the fatal outcome and intends to succeed [12]. Self-harm acts with suicidal intent include intentional intake of substances or medications, self-mutilation, scarification, independently from motivation, from which the intention and desire to live are either completely absent, or present only to varying degrees [13,14].

2.2. Scientific literature search strategy

We conducted a bibliographic search between April 1968 and August 2014 in the PubMed database for international scientific publications on the medications for preventing suicide and assessing the efficacy of Li in the reduction of suicidal behaviours. We used the following MeSh terms: “lithium” AND “suicide” OR “suicidality” OR “suicide attempt”. We chose to include only clinical trials and the most recent literature reviews. Scientific articles in English and French were included.

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