



CASE REPORT

Tactile Hallucinations in Rheumatoid Arthritis Patient in Use of Agomelatine, Painkiller and Methotrexate, Case Report and Possible Mechanisms

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Abstract

Rheumatoid arthritis (RA) is an autoimmune disease. RA patients may undertake traditional therapy with antidepressants to control the depressive symptoms and to reduce their pain levels. This is the case of a patient with RA who presented with tactile hallucinations. On the second day of the pain crisis, the RA patient used agomelatine and a painkiller and showed symptoms of tactile hallucination. This is the first report of tactile hallucinations in this context. There isn't any other scientific communication about this resultant side effect, suggesting a new and urgent area of research.

of the disease [4]. The treatment includes analgesics, Nonsteroidal Anti-inflammatory Drug (NSAIDs), corticosteroids and drugs known as disease-modifying drugs (DMDs), this last is responsible for 20 to 25% of remissions achieved [5].

RA Patients can have associated with traditional therapy to some antidepressants control the depressive symptoms and reduced pain levels as the selective serotonin reuptake inhibitor (SSRIs). These drugs are conventionally used in the treatment of depressive states, even in patients with comorbid medical illness. Despite its common and traditional use, studies have indicated that agomelatine, an antidepressant with action on melatonin receptors and shows antagonistic effect of serotonin receptors may be effective in treating anxiety disorders and depression [6].

Agomelatine is a specific agonist at MT1 and MT2 receptors and antagonist 5HT2C and 5HT2B which has antidepressant properties with apparent resynchronization capacity of the circadian cycle. The receptorial peculiar profile of the compound involves the same neurotransmitter systems engaged in the mechanism of action of melatonin, and also acts on serotonin and norepinephrine reuptake; This latter mechanism is pointed out by the authors as responsible for a supposed inhibitory effect on sensitivity to pain [7].

Usually the treatment for RA is with the combination of painkillers and anti-inflammatory non-steroidal, which often does not reduce as expected pain in pa-

Introduction

Rheumatoid arthritis (RA) is an autoimmune, chronic, progressive and incapacitate disease [1] that affects about 1% of the world population [2], causing intense pain, stiffness, joint deformity, movement restrictions and reduced quality of life [3]. There are common symptoms of depression, anxiety and suicidal ideation in patients with this disease, and this is because of RA control therapy, the progressive and deforming characteristics action or because of most striking symptom of the disease: the chronic pain condition.

The current treatment for this disease is directed to alleviate the symptoms (inflammation, swelling and pain), minimize joint damage, maintain the functions and quality of life and reduce premature mortality associated with the condition, but the main goal is the suppression of inflammation, which means the remission

tients, although nowadays there are new possibilities; For example it is known that overall antidepressants have a satisfactory response that the symptom of fibromyalgia patients and agomelatine had already been experimentally used in research in a group of people with fibromyalgia [7] with success in suppress the pain and reduce the depression levels. Because of that, agomelatine can be considered an excellent option to RA population because it has antidepressant properties and also by the resynchronization of the circadian cycle.

Case Report

A 42-year-old female, diagnosed when she was 17-years-old, with severe RA evolved without remission to the present progressively. Patient bedridden with severe deformities in the joints of the ankles, knees and hips, preventing her from sitting, getting around and change her position in bed alone; Patient also has serious and significant changes in the joints of all the fingers, wrists, elbows and shoulders, which prevent it from having any autonomy to eat or pick up objects, non-smoking. Patient was referred for psychotherapy after detection of major depression symptoms by her rheumatologist although she had no psychiatry history of any other pathology.

The patient was being treated with 50 Mg of agomelatine per day, 20 Mg per week of methotrexate in combination with 40 Mg of Adalimumab biweekly, and had as SOS medicine for pain crisis which was an association of 30 Mg of codeine phosphate and 500 mg of paracetamol. The patient followed the scratching antidepressant treatment for four weeks and did counseling 2 times a week for the same period, when she had a crisis of disease with very severe pain and inflammatory symptoms having to resort to SOS prescribed medicine.

At the end of the second day of the RA crisis the patient had taken four tablets of the painkiller (two on the first day and three in the second day). In this second day also, the patient started to present hallucination tactile, she began to complain of heat, and sensations that something was under her skin. Some hours after, the patient began screaming and thrashing her body in the bed complaining that there were bugs coming out of her entrails, and eating her body beneath the skin. With screaming and restlessness, the patient scratching and rubbing the skin to cut it so that "the animals could get out," and also happened to bump his head on the headboard and bed rail screaming that did not want to see or feel that anymore. The patient was sedated with a home care service and after past the sedative drug effect, she said she does not remember anything about her crisis. Agomelatine and the painkiller were removed, and she continued her treatment with drugs of her disease. We performed examinations and assessments all inconclusive, thus suggesting some drug interactions between prescribed dose of agomelatine and the dosage of analgesic association (codeine phosphate and

paracetamol).

Discussion

The patient had been evaluated previously by the beginning of your calls in psychology with the assessment tool and diagnostic Mini International Neuropsychiatric Interview (MINI) and the Hospital Anxiety and Depression Scale (HADS). After the evaluation, it was found that the patient had only depressive episode, excluding any possibility of psychotic disorders except induced substances. The prevalence of psychotic disorders induced by substances varies in general in the world population, but it is estimated that 7-25% of individuals who have a first episode of psychosis, have psychotic disorder induced by substance [8]. The main features of this disorder are delusions and/or prominent hallucinations, which can be strongly associated with the physiological effects of a substance/medicament [8].

Tactile hallucinations presented by the patient can be classified according to secondary criteria and these clinical or other order as subjective, phenomenological or circumstantial. This kind of dysfunction can be easily explained by psychotic syndromes, acute clinical and / or chemical poisoning as in delirium tremens [9].

Conclusion

There are no studies in the literature to explain the phenomenon suffered by the patient, generating only speculative ideas about the cause. There is knowing that agomelatine can cause hallucinatory symptoms (rarely), but there's no evidence literary about it. In relation to the medicine that makes the association of codeine and paracetamol, there is no reports in the literature even in the own label that makes reference to cases of hallucination, even in over dosage or as drug interaction.

It is also possible that the situation could be occurred can be allocated for drug interactions. There are in the literature any study so far to talk about this. This interaction may have occurred between the by-products of such substances or one of them. However, we ran into each other in the absence of information from these, since the technical document provided by the laboratory only cites as agomelatine of metabolites hydroxylated and demethylated agomelatine, which according to it, are not active and are rapidly excreted in the urine.

It is necessary clinical trials testing the association of this common drug interaction (antidepressant agomelatine X codeine painkiller) to prove the safety in order to avoid exposure of this group that makes use of these medications and which is already considered weakened by their major disease to induce chemically hallucination crisis.

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