Effect of 5-hydroxytryptophan and melatonin supplementation on mood, sleep and cognition in adult patients with depression

Efecto de la suplementación con 5-hidroxitriptófano y melatonina sobre el estado de ánimo, el sueño y la cognición en pacientes adultos con depresión

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Abstract

5-Hydroxytryptophan (5-HTP) is a precursor to serotonin and has been used as an antidepressant. Its antidepressant potential has been evaluated under different experimental conditions with moderate results. However, it is considered to have poor pharmacokinetics and its use as an alternative treatment for mood disorders has even been questioned. This disadvantage seems to disappear when slow-release 5HTP is used. This study determined whether the combination of slow-release 5-HTP plus the combination with melatonin can reduce symptoms in patients who reported depression. This research consisted of a pre-experimental observational method (qualitative and quantitative). The participants were 20 adults between 25 and 50 years old with a previous diagnosis of depression issued by a mental health professional. Baseline values of depression, sleep quality, and working memory were measured. Subsequently, the participants were randomly assigned to the control group (n = 10) or the experimental group (n = 10). The control group only received information on general aspects of depression, while the experimental group received the combination of 100 mg of 5HTP/10 mg of melatonin for 1 month. The results indicated an improvement in mood, quality of sleep, and both verbal and visual working memory. It is concluded that the tested combination can be an effective alternative to the use of antidepressants.

Keywords: Melatonin, 5-Hydroxytryptophan, depression, sleep quality, working memory

Resumen

El 5-hidroxitriptófano (5-HTP) es un precursor de la serotonina y se ha utilizado como antidepresivo. Su potencial antidepresivo ha sido evaluado bajo diferentes condiciones experimentales con resultados moderados. Sin embargo, se considera que tiene una farmacocinética deficiente e incluso se ha cuestionado su uso como tratamiento alternativo para los trastornos del estado de ánimo. Esta desventaja parece desaparecer cuando se utiliza 5HTP de liberación lenta. Este estudio determinó si la combinación de 5-HTP de liberación lenta más la combinación con melatonina puede reducir los síntomas en pacientes que reportaron depresión. Esta investigación consistió en un método observacional preexperimental (cualitativo y cuantitativo). Los participantes fueron 20 adultos entre 25 y 50 años con diagnóstico previo de depresión emitido por un profesional de salud mental. Se midieron los valores basales de depresión, calidad del sueño y memoria de trabajo. Posteriormente, los participantes fueron asignados aleatoriamente al grupo control (n = 10) o al grupo experimental (n = 10). El grupo control solo recibió información sobre aspectos generales de la depresión, mientras que el grupo experimental recibió la combinación de 100 mg de 5HTP/10 mg de melatonina durante 1 mes. Los resultados indicaron una mejora en el estado de ánimo, la calidad del sueño y la memoria de trabajo tanto verbal como visual. Se concluye que la combinación probada puede ser una alternativa eficaz al uso de antidepresivos.

Palabras clave: melatonina, 5-hidroxitriptófano, depresión, calidad del sueño, memoria de trabajo

Introduction

5-hydroxytryptophan (5-HTP) is a molecule used to produce serotonin (5-HT), an essential neurotransmitter in regulating mood[1]. The conversion to serotonin will depend on the amount of tryptophan available in the body, the level of glucose-insulin, oxidative stress, cortisol levels, the vitamin B6 deficiency, magnesium, and the presence of amino acids that compete with tryptophan to enter the brain[2-5]. Access of exogenous 5-HTP to the brain is easy through the blood-brain barrier without carrier molecules. Once it enters the nervous system, it can increase concentrations of serotonin, melatonin, norepinephrine, dopamine, and beta-endorphins[6-8].

Serotonergic metabolism is known to be decreased in patients who have been diagnosed with depression. The passage of exogenous 5-HTP to the brain is lower in these patients. It has been found that removing tryptophan (a precursor of 5-HTP) from the diet promotes relapses in half of the patients treated with serotonin reuptake inhibitors[9,10]. However, the use of exogenous 5-HTP to treat depression has been effective in doses ranging between 20 and 300 mg per day for periods of 2 to 14 days; the number of patients who have obtained these effects is approximately 60%[11].

The use of some classic drugs to treat depression with exogenous 5HTP has been suggested. Thus, for example, the combination of Fluoxetine with slow-release 5-HTP was more efficient than its individual administration to increase the levels of 5-HTP, serotonin and 5-HT1A receptors in the frontal cortex, hippocampus, and nucleus accumbens of rats[12]. In fact, the combination alone increase the expression of neurotrophic factors in the brain. These results prove that slow-release 5-HTP can be a useful tool to complement the drug therapy.

In the same way that the combined treatment of slow-release 5-HTP with an antidepressant was tested, it is necessary to evaluate whether such effects could be efficient with the combination of another supplement such as melatonin, which has been used to treat mood disorders. mood and has a favorable interaction on brain serotonin[13,14]. The objective of this research was to determine the effect of daily consumption of 100 mg of slow-release 5-HTP and 10 mg of melatonin on working memory, mood, and sleep quality.

Method

Participants. This research consisted of an observational pre-experimental method (qualitative and quantitative). The participants were 20 adults between 25 and 50 years with a previous diagnosis of depression issued by a mental health professional. These patients were invited to participate in the experiment in a medical consulting-room, explaining the objectives of the study and giving them informed consent. The project was reviewed and endorsed by the ethics committee of the Universidad Autónoma de Hidalgo.

In the inclusion criteria, patients considered were between 25 and 50 years of age, indistinct sex with a diagnosis of depression, patients with pathologies related to depression with sleep disorders or memory disorders. The exclusion criteria was: patients who were already treated with controlled medication for depression patients who are not in a position to take the supplement on their own, patients who do not have at least three consultations prior the treatment, patients who were in psychological therapy or meditation programs.

Instruments

Depression

The Beck Depression Inventory-II is a pencil and paper self-report composed of 21 Likert-type items. Its items describe the most frequent clinical symptoms of psychiatric patients with depression. It has four ordered response categories that are coded from 0 to 3, the range of scores goes from 0 to 63 points, the higher the score, the greater the severity of the depressive symptoms. Four groups are established based on the total score: 0-13 without depression; 14-19 mild depression; 20-28 moderate depression and 29-63 severe depression. The test should preferably be intended for clinical use, as a mean to assess the severity of depression in adult and adolescent (13 or older) patients with a psychiatric diagnosis[15].

Sleep quality

The Pittsburgh Sleep Quality Index (PSQI) is a simple and accessible instrument in terms of filling and obtaining the score, reliable for measuring the quality of sleep in the Mexican population both in the clinical field and in that of research. This instrument has 19 items that aim to assess the quality of sleep. The items analyze different determining factors of sleep quality: latency, duration, efficiency, disturbances, use of sleep medication, and daytime dysfunction[16].

Working memory

For memory evaluation, the computerized tests of continuous execution Memory Span and Digit Span were applied using the platform Psychology Experimental Building Language PEBL-2[17]. Memory span is a test where visual stimuli are presented in series and, later, they should be selected in order. The selection is made on a screen where there are nine images. The participant must press the mouse selecting the images recognized on the screen and then press the “DONE” button. After pressing that button, a caption appears that may say “Correct” or “incorrect”. The completion time is variable since it depends on the time each participant uses to make the choice, although it does not usually exceed 5 minutes.

The digit span test (dspan) consists of the presentation of a numerical series that gradually increases (initially there are three and gradually increases depending on the performance of the participant; the better the performance, the greater the length of the series presented and the duration of the test). After the presentation of the number series, the participant writes the sequence that he considers correct and presses the “ENTER” button.

5-HTP/melatonin combination

Participants receiving the treatment took 1 capsule of exogenous slow-release 5-HTP 100 mg orally along with 1 capsule of melatonin 10 mg every 24 hours before bedtime for 30 days. They were asked to inform the doctor daily if they had side effects or discomfort.

Process

The first part of the study consisted of submitting the project to an ethics committee. Once approved, the patients attending the medical consulting-room, who reported having symptoms of depression, were personally invited. Initial stage (pre-test): Baseline values for depression, sleep quality, and working memory were measured. Experimental stage: subsequently, the participants were randomly assigned to the control group (n=10) or the experimental group (n=10). The control group only received information on general aspects of depression while the experimental group received the combination of 5HTP/melatonin in the concentrations and duration mentioned above. Participants were also asked to report their sensations to the treatment to the physician who was supervising. Final stage (post-test): the same tests used before the intervention were applied to all participants after 4 weeks of treatment (see table 1). Finally, the control group also received the experimental treatment (data not shown). At all stages, each patient had supervision and medical support.

Table 1. The rows show a summary of the stages the participants went through, while the columns differ in the treatment to which they were subjected to.

Stage/ Experimental condition	Control group (n=10)	Experimental group (n=10)
Initial stage (pre-test)	Beck's Inventory Pittsburgh Sleep Quality Index Mspan, Dspan	
Experimental stage	Informative talks on depression	5-HTP 100 mg-melatonin 10 mg/daily/30 days
Final stage (post-test)	Beck's Inventory Pittsburgh Sleep Quality Index Mspan, Dspan	

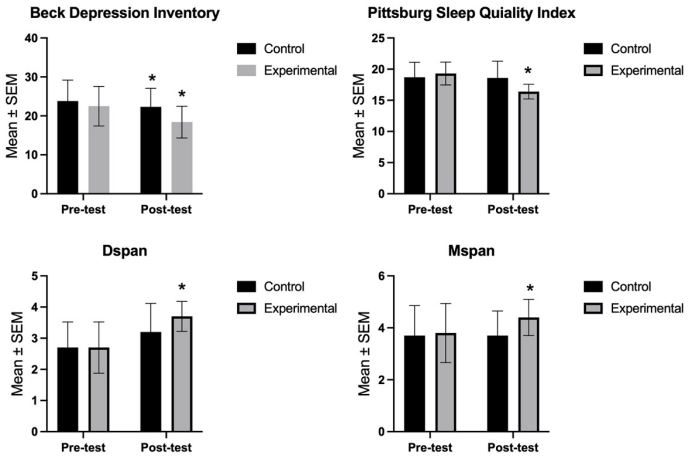
Statistical analysis

Once the averages of sleep quality, hours of sleep, depression, dspan and mspan in the participants were determined, it was analyzed whether the data had a normal distribution through the Kolmogorov-Smirnov test ($p > .05$) and equality of the variances using Levene's test ($p \geq .05$). Data that had a normal distribution were analyzed with the related samples t test. The effect size was also determined using d of Cohen. The program used was Graphpad prism 9.

Results

The initial values of depression in the control and experimental groups were 23.8 and 22.5, respectively. In this test, such scores correspond to a level of moderate depression. The evaluation carried out 1 month later showed that the average values in the Beck test were 22.3 and 18.4, respectively (figure 1). In the control group, the level of depression remained at the moderate level, while in the experimental group it was downgraded to mild depression. Statistical analysis revealed that there was a significant reduction in the experimental group [$t(9)=7.8$, $p<.01$, $d=2.5$], although such an effect was also found in the control group [$t(9)=2.8$, $p<.05$, $d=.87$].

Figure 1. Shows the averages and standard errors of the variables of depression, sleep quality and working memory evaluated in the control and experimental groups, before and after the intervention. * Versus Pre-test. Indicates that significant differences were found with p <0.05



The sleep quality index showed that the participants in the experimental group showed a significant reduction in the index (indicating an improvement in sleep quality) [$t(9)=6.1$, $p<.01$, $d=1.9$], (figure 1). In the control group, no significant change was observed in the post-test phase [$t(9)=.36$, $p=.73$]. Similarly, in the Dspan test this trend was observed since the experimental group improved in its performance after one month of treatment [$t(9)=3.9$, $p<.01$, $d=1.2$], It should be mentioned that an improvement trend was also observed in the control group, although it is not significant [$t(9)=1.9$, $p=1$]. Finally, in the mspan test, a significant increase was observed in the performance of the experimental group [$t(9)=2.3$, $p<.05$, $d=.71$].

In this way, most participants who received the treatment reported an improvement in energy levels after 24 hours of treatment, as well as greater tranquility during their daily activities.

Discussion

Reports of perceived improvement in energy levels as well as in mood were reported by most patients who took 5-HTP / melatonin combination. These results are consistent with reports where 5-HTP supplementation can produce favorable responses in mood in 48 hours[10-11]. The mood improvement that was found here can be comparable to an experiment where the combination of 100 mg of 5-HTP with creatine monohydrate was effective in reducing 60% of depressive symptoms in women with major depressive disorder who had not responded to selective 5-HTP inhibitors[18]. It has also been found that depressive symptoms reported in patients with Parkinson's disease have been reversed after the daily intake of 50 mg of 5HTP during 4 weeks[19]. Additionally, they are consistent with the fact that melatonin has been used as an anxiolytic before surgery to calm patients and agomelatine (melatonin receptor agonist) has also been shown to have antidepressant properties[14].

Regarding the sleep quality, our findings are compatible with reports where the individual use of these supplements are effective and safe for the treatment of insomnia[20]. In animal models where treatment with 5-HTP and quality of sleep has been positively associated with an increase in the transcription of the 5-HT1A receptor, as well as in the brain concentrations of 5-HTP, so these changes could be behind the chronic consumption of these supplements[21].

Working memory was a function in which an improvement was also observed. This coincides with experiments where 5-HTP and melatonin were able to promote such improvement by having a favorable effect on areas of the prefrontal cortex, limbic system and basal ganglia[12,22-23]. Increased serotonergic activity from 5-HTP supplementation has been suggested to have a positive effect on the hippocampus and memory. This idea arises from the fact that parenteral administration of 5-HTP in rodent models improves performance in maze tests and induces postsynaptic electrical changes in the hippocampus[24].

It can be concluded that the combination of 5-HTP and melatonin could be auxiliary to the treatment of common antidepressants in a safe and accessible way for the adult population; the benefits can be found in the affective and cognitive domain. However, to reinforce this conclusion it will be necessary to evaluate the effect of this treatment for a longer time and, if it is terminated, to measure the duration of the positive effects.

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