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Evaluation the effect of amitriptyline and/or ashwagandha on body weight in male rats

Ghada A. Taqa [1]*, Ismail R. Idrees [2]

[1]Department of Dental Basic Sciences, College of Dentistry. University of Mosul, Mosul, Iraq
[2]Ministry of Health, Nineveh Health Directorate, Mosul, Iraq

*Corresponding Author: Ghada A. Taqa

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ABSTRACT: study aims to examine and compare the effects of amitriptyline and ashwagandha on body weight in male rats by measurement weight for 4 weeks after their exposure to these two compound. **Materials and Methods:** This study used twenty healthy adult male albino rats that were 8-10 weeks old and weighed 200-250g. The animals were randomly divided to 4 groups (n= 5 /group), Group 1: were served as a control group received distilled water orally (1.0ml/kg) group 2: were administered amitriptyline (10mg/kg/ orally) group 3: were administered (200mg/kg) of ashwagandha root extract and group 4: were co-administered amitriptyline (10mg/kg) and ashwagandha (200mg/kg). After 30 days of administration, The body weight was measured every week starting from the first day of administration to last week of experimental for all rats. **Results:** According to the one-way analysis of variance(ANOVA) showed significant differences in growth value in the co-administered Amitriptyline and ashwagandha group (1.48±0.09) significantly increased in comparison with control group (1.27 ± 0.04) at week 4, otherwise, there is no significant differences in growth among groups at other periods at p value ≤0.05. **Conclusion:** Amitriptyline induced oxidative stress causing increased in body weight during experimental periods. Administration ashwagandha alone non-significant effect on body weight but when co-administration with amitriptyline significantly increase in body weight.

Keywords: Amitriptyline, Ashwagandha, body weight, Rats

1. INTRODUCTION

Depression is a prevalent mental illness characterized by a loss of interest or enjoyment, unhappiness, a sense of worthlessness, and a propensity to harm oneself. [1, 2]. It is a major contributor to the burden of disease in the globe, and if left untreated, its lingering effects can have a negative impact on one's quality of life and mental health. [3]

The three primary forms of treatment for depression are neuroregulatory approaches, psychosocial therapy, and medication therapy [4]. However, pharmacological therapy can result in dependence and have negative side effects include nausea and abdominal pain [5]. Unfortunately, 30 to 40 percent of patients will not improve after receiving first-line antidepressant treatment. Treatment-resistant depression (TRD) is defined as the inability to react to treatment with two separate antidepressants from two different classes at adequate doses and for the prescribed time periods [6].

Among the side effects that are associated with the use of antidepressants drugs are anticholinergic symptoms including dry mouth, urinary retention constipation, blurred vision, sedation and confusion Weight gain, arrhythmia, nausea, vomiting, abdominal pain, sexual dysfunction, sleep disturbances, Headache dizziness [7].

Some of these antidepressants including tricyclic antidepressants like amitriptyline will cause deficiency in the total antioxidant capacity that will lead to oxidative stress [8,9]. There are finding a complementary therapy with an antidepressant effect is required to address these shortcomings like Ashwagandha [10]. Ashwagandha is cultivated in India, Nepal, China and Yemen. The extract of roots contains steroidal lactones and alkaloids. Ashwagandha modulates the brain oxidative stress makers, such as superoxide dismutase (SOD), catalase, lipid peroxidation (LPO), and non-enzymatic antioxidants like glutathione (GSH), therefore it is effective in neurological disorders like stress, Parkinson and Alzheimer's disease [10].

*Corresponding author: ghadataqa@uomosul.edu.iq

The anti-inflammatory, antioxidant effect of ashwagandha, will prevent cholinergic neuronal cell death and deficit of acetylcholine neurotransmitter which is further increased by dose-dependent acetylcholinesterase inhibition properties of ashwagandha that will strengthen the interest in preventing neuropsychiatric, behavioral symptoms and memory loss [11]. There is no previous study that investigate the effect of Amitriptyline or/and Ashwagandha on body growth in rats .

2. MATERIALS AND METHODS

This study was conducted in the pharmacology laboratory at the Department of Dental Basic Sciences, College of Dentistry/University of Mosul / Mosul, Iraq throughout the period from 4/12/2021 to 4/1/2022.

2.1 EXPRIMENTAL ANIMALS

This research used forty healthy albino rats that were 8-10 weeks old and weighed 200-250g.They were obtained from the Faculty of Veterinary Animal House at Mosul University, Iraq. They were kept in rodent plastic cages with wire mesh covers as shown in Figure 1. The animals were kept at a room temperature of 22±2C° with12 hours of light and darkness, unrestricted access to food and water *add. libitum*. All procedures followed the guidelines of the Faculty of Dentistry's institutional animal research ethics committee in the College of Dentistry, University of Mosul, Iraq (UOM. Dent/A.L.56/22).

FIGURE 1. - A photograph of rats were used in this study

2.2 MEDICATION

1- Amitriptyline was available in the form of a tablet(10mg) from accord company, United Kingdom (accord ,U.K.) **(**Figure2 **).**

FIGURE 2. - Amitriptyline tablet used in this study

2-Ashwagandha root extract powder (Roya pharma, Turkey) **(Figure 3)**

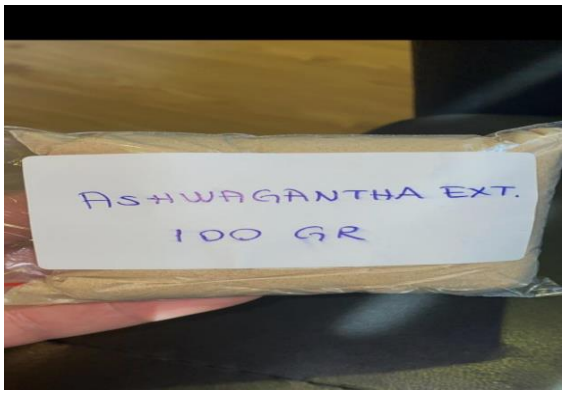

FIGURE 3. - Ashwagandha root extract powder used in this study

2.3 PREPARING DRUG SOLUTION

Ashwagandha powder is given according to weights of rats (200mg/kg) [12]. Rats treated orally by oral gavage needle with 0.5 ml aqueous of Ashwagandha root extract (100 ml water +5000mg plant) at dose of 200 mg \ kg body weight (50 mg/rats) for 30 days) (Mahmoud et al 2022). and preparing amitriptyline solution after milling amitriptyline tablet**s** taking in consideration amitriptyline dose is 10mg/kg [13].

Experimental groups:

A twenty rats were divided into four groups as following:

group 1:(n=5) were served as a control group received distilled water orally for 4 weeks using gavage needle at (1.0ml/kg)

group 2 (n=5) were administered amitriptyline using gavage needle at (10mg/kg) for 4 weeks

group 3 (n=5) were administered (200mg/kg) of ashwagandha root extract using gavage needle at for 4 weeks (Khane *et al.*,2015)

group 4 :(n=5) were co-administered of amitriptyline(10mg/kg) and ashwagandha (200mg/kg).

2.4 ROUTE OF DRUG ADMINISTRATION NTRODUCTION:

Both amitriptyline and ashwagandha root extract were diluted with distilled water and injected orally in 10mg/kg ,200mg/kg respectively. The gavage needle was properly attached to the mantoux syringe and then injected into esophagus toward the stomach as shown in figure 4. [14] .

FIGURE 4. - Amitriptyline and ashwagandha administration

After 30 days of administration, study the development of animals by measuring the weighed at day 0, (1st,2nd,3rd,and 4thweek)of experiment. The growth or actual change of body weight could be calculated by dividing

body weight of each rat at different periods on mean of rats in the day 0 of the same group to evaluate effect of amitriptyline or/and ashwagandha on growth of animals .

2.5 STATISTICAL ANALYSIS

Software called SPSS program version 21 for Windows was used to do the statistical analysis. Mean and standard deviation are two ways to express descriptive statistics of data (SD). Statistical tests such one-way analysis of variance (ANOVA) followed by (Duncan's post-hock) were used to compare the differences between the four study groups. P≤0.05 was the significance level.

3. RESULTS

Developmental study: ΔΔ value of Body weight assessment

Body weight at day 0,(week1,2,3and4) was estimated for all rats and data were enrolled in this work in Figure(5),Table (1) as following:

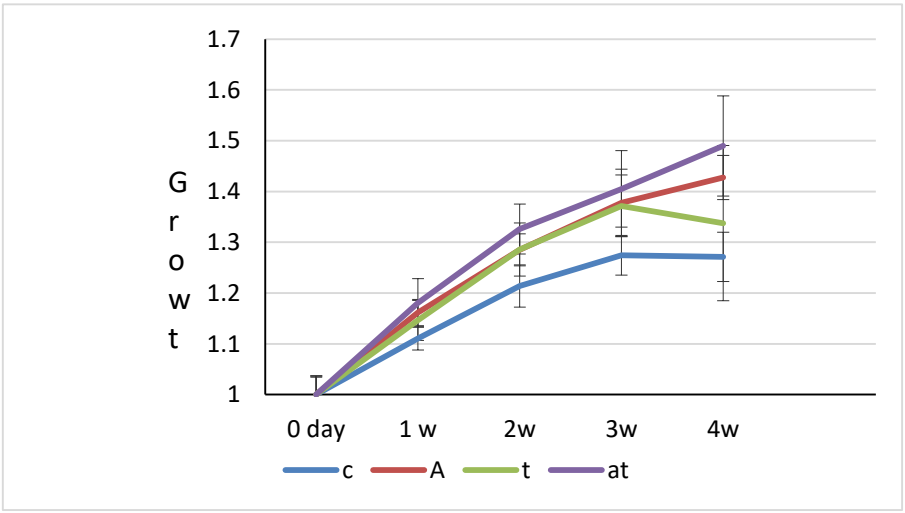

FIGURE 5. - A normalized histogram representing the effect of amitriptyline or/and ashwagandha on Δ value of body weight in different groups and weeks

The results showed growth in the combination group (1.48 ± 0.09) significantly increased Δ value of growth in comparison with control group (1.27 ± 0.04) at week 4, otherwise, there is no significant differences in growth among groups at other periods.

Table 1. - Mean and standard deviation of Δ value growth rats in all groups on different periods of time

	Control	Amitriptyline	Ashwagandha	Combination	p value
Day 0	1 ± 0.03	1 ±0.03	1±0.03	1±0.03	
Week 1	1.11 ± 0.02	1.14±0.03	1.16 ±0.02	1.18 ±0.04	0.09
Week 2	1.21 ± 0.04	1.28±0.05	1.28± 0.03	1.32±0.04	0.06
Week 3	1.27±0.03	1.37±0.06	1.37±0.07	1.40 ± 0.07	0.09
Week 4	1.27 ± 0.04	1.33±0.15	1.42±0.04	1.48 ± 0.09	*0.02

4. DISCUSSION

Depression has long been successfully treated with amitriptyline. Due to it's wide side-effect profile, which includes oxidative stress and anticholinergic side effects that cause decrease in salivary glands secretion and other side effects on oral health limiting usage of this drug [16]. Therefore, this study used alternative therapy that has antidepressant effect like ashwagandha and evaluation effect on body weight. In this study after administration of amitriptyline or /and ashwagandha for 30 days, the body weight that is increased during experimental periods measured at day 0 (week 1,2,3 and 4) for all groups. In amitriptyline group, the oxidative stress induced by amitriptyline is responsible for increment in growth since there is a relationship between oxidative stress and body weight therefore, the oxidative stress that is also result from genetic susceptibility, sedentary life style, poor quality diet Will lead to increase lipogenesis and increase food intake and consequent obesity Also oxidative stress may cause hyperglycemia ,hyperlipidemia, hyperleptinemia and adipose and endothelial tissue dysfunctions and consequently increase inflammation and free radicals production and decrease antioxidant defense coming back to oxidative stress [17] .

In ashwagandha group, the body and muscle growth is increased that is attributed to two effects: (i) increase in testosterone, which leads to muscle growth and (ii) decrease in the levels of cortisol, which act as catabolic agent. In terms of energy production, ashwagandha (i) can have beneficial effects on mitochondrial energy levels and functioning and reduce the activity of the Mg^{+2} dependent ATPase enzyme responsible for the breakdown of ATP, and (ii) can increase creatine levels that can, in turn, lead to ATP generation. Finally, the effects of ashwagandha on the nervous system as an anti-anxiety agent and in promoting focus and concentration may translate to better coordination and recruitment of muscles [18].

In combination group at the end of experiment, the growth is higher than other groups that is attributed to all mentioned above. moreover, oxidative stress induced by amitriptyline is exacerbated by iron in ashwagandha through Fenton reaction [19].

5. CONCLUSION

In this study after oral administration of amitriptyline in a dose 10mg/kg or /and ashwagandha in a dose 10mg/kg for 30 days, the body weight is increased during experimental periods for all groups due to the oxidative stress and free radicals generation induced by amitriptyline which responsible for increment in growth since there is a relationship between oxidative stress.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

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