

Treatment with the Harmala Alkaloid “Harmine” During Pregnancy and Foot Shockstress between Accepted and Declined

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Harmine recently known by its multi-beneficial effects like neuroprotection, anti-diabetic and antitumor effect, but its impact upon animals and human during pregnancy remain pre-estimated with undesirable effects of *Peganum harmala*, as the plant usually used as an abortifacient by Middle Eastern population, morocco and many other countries. It took place an in depth debate due to its multiple uses and importance, the most abundant alkaloid in the parts of the plant is harmine that concentrated most in dry seeds and roots, but miss in flowers.

Specificity of their structures gives them a large spectrum of interactions. Works by many teams confirmed its inhibition of MAO-A in one hand, and its inhibition of postsynaptic currents confers them more interest, in addition harmine transformed to more than 20 analogues, which helped in extending of its actions in animal and human bodies.

The dramatic change of hormones participate in the smooth progress of pregnancy, like estrogen interactions with glucocorticoids, megakaryocyte and proplatelet, and normal estrogen levels during pregnancy adjust the myelinisation and ameliorated secretion of anti-inflammatory cytokines. Psychobiological response to stress as may be associated with depression symptoms it aggravates life stress. There were about 15% cases of anxiety and depression among pregnant women [1]. That is attract more attention to prevent increase of this amount of stressed women during pregnancy, especially when they combined with rare syndromes, because rare syndromes with dereliction of studies caring about pregnancy exacerbated the possibility of success of recovery attempts right on time. The second annoying point, is that stress during pregnancy disturb immune cell levels and alter the foetus.

Immune responses have a large set of cell type, and any change occurs in one type increased the frequency of the total cells interacted, as the case of immunological perturbations during pregnancy. Decidualization due immunological metabolic and biochemical perturbations threaten maternal-fetal attachment and finalising with failure of implantation and pregnancy loss, generally reduction in reproductive outcome are associated with endometrium diseases.

In the current study, female rats revealed the effect of the β -carboline alkaloid harmine during pregnancy, as they could show a trustworthy behavior.

Materials and Methods

Female rats had been divided into three groups according to pregnancy stages, and each group had sub-divided into seven groups as follows: control group, two treated groups at different doses of harmine (ip), two groups stressed with footshock (FS), psychological stressed group, and a group treated-stressed with FS. Pregnant rat has logged lonely to avoid social interactions and competition that misrepresent behavior during tests as open field (OFT), plus maze (PMT), forced swimming test (FST), and light/dark box test that have carried at the last two days of the stage.

At the end of each stage rats has decapitated, and the blood has analysed for complete blood count.

Results

Response of treated rats during behavioral tests:

During FST, immobility time of treated rats decreased significantly, and the time of climbing increased significantly during three phases of pregnancy.

In the OFT, time of immobility spent in the corner decreased, but the number and time of rearing increased during the second and third stage of pregnancy.

During PMT, time spent in open arms increased compared to control group.

Psychological stress during the first week appeared more effective “the organs had formed during this stage” as number of entries and time spent in open arms decreased significantly, and immobility time during FST increased significantly, and distance travelled in OFT increased significantly.

In the other stages, psychological stressed group showed an increase of immobility time in FST, but a decrease in time spent in the corner of OFT, and an increase in time spent in open arms.

FS stress affected behavior of rats as it decreased swim time and increased immobility during FST, increased time spent in the corner and decreased the number of rearing in OFT, and increased time spent in light box.

Harmine increased the red blood cells and haemoglobin so that correction of anemia during pregnancy and FS stress.

In the current study, we marked a decrease in monocytes of pregnant rats, while treatment with harmine.

Discussion

The immobility time of open field test could not reflect the psychological state of rats, as the psychological stressed group showed a low time of immobility during the open field test but a high time of immobility during FST.

The increase in time spent in open arms has attributed to the anxiolytic-like effect of harmine on benzodiazepine receptors, this indicated that whether the degree of stress of pregnant rats, it could be attenuated with harmine treatment.

Locomotion activity of treated group enhanced, due an increase in the dopamine in ventral pallidum, but the increase in locomotor activity of stressed group has referred to lesion of medial rugh nuclei.

As harmine exerted its antidepressant-effect via inhibition of MAO-A, and increased noradrenaline it attenuates stress that was obvious in FST.

Amelioration in behaviors of FS group, was more likely due regulation of fear-circuitry disorders and anti-nociceptive effect of harmine.

The increase of neutrophils from the second stage to last pregnancy, due harmine treatment, considered useful as their clustering in placental blood vessels, at sites of necrotic areas facilitates decidua. Recently, the increased level of neutrophils correlated with lack in vitamin D and identified as inducer of cerebral fetuses diseases, which contradict with its beneficial effect.

The attenuation of placental and foetus numbers and weights of stressed rats was due deterioration of placental vascularization and decline in blood flow of the umbilical cord.

Obesity is associated with high amounts of food intake and lack of cognition. In our case decreased in food intake of treated rats was associated with high cognition.

The importance of harmine was evident in enhancing number of implantations even in case of stress, relieving stress disorders occurred during pregnancy and amelioration of activity, but its decrease effect on food intake, as known could induce ovarian oxidative stress.

The increase in platelets has referred to high levels of serotonin due MAO-A inhibitor effect of harmine.

Conclusion

Our study carried on pregnant rats revealed that harmine significantly alleviated anxiety of pregnant rats even if it escalated with stress [2].

The hopeless side of the treatment of footshock stress that increasing dopamine levels in the brain with an inhibitor of MAO-A "Harmine", is not inevitable as harmine increased dopamine efflux in striatum "nucleus accumbens shell" and footshock enhance dopamine in prefrontal cortex, the sites were different. The likely mechanism by which harmine increased dopamine efflux in striatum shell was presynaptic 5-HT_{2A}, and exerted an agonist therapy, in other hand the both sites encoded reward information in beta band (25-29Hz), which indicate the lower flows between the both brain regions.

The antioxidant effect of harmine exerted on kidney damaged cells, liver, and regulation of inflammatory mediators with beneficial effects on nervous system accelerating neurodegenerative diseases that has revealed on male animals in previous studies has established in the same way in pregnant rats.

Harmine is not responsible for neuro-inflammation, hallucination and abortion induced by the plant *Pharmala*, the high level of neutrophils remains the only annoying result that needs further studies on progenitor of treated rats with harmine.

The activation of rootstocks during summer lead to the transformation of harmaline to harmine on the leaves of the plant, during dry years lower levels of potassium conduct to accumulation of inactivated enzymes and harmaline in combination with harmalol and vasicine that were estimated responsible of abortion in animals consumed the plant [3].

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