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The Effects of Levodopa on Albinism

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Abstract: Albinism, a refractory disease with reduced pigmentation. And it has caused great distress to the patient's body and mind. How to treat the disease is a troubling problem in history. Levodopa, a medicine is used when needed to treat the return of Parkinson's symptoms. However, since the last century, some doctors have proposed using levodopa to treat albinism. The results of the experiment were not very significant. We research the effects of levodopa on albinism from mechanism of action, clinical trial, molecular mechanism and clinical studies. We find that levodopa has only a weak or no effect on fetuses with albinism.

Keywords: Levodopa; Albinism; GRP143; Pigmentation

Introduction

Albinism, a group of inherited disorders where there is little or no production of the pigment melanin. The common clinical symptoms are apparent in patient's skin, hair and eye color, but sometimes are slight. Albinism is a genetic disorder, as a result that it can't be cured at present. Levodopa and nitisinone have been confirmed with limited success in improving albinism. Meanwhile, the treatment thoughts also bring lights for the patients and researchers. Experimental gene-based strategies for editing the genetic errors in albinism have also met early success in animal models. The emergence of these new therapeutic modalities represents a new era in the management of albinism^[1]. Nevertheless, when we are gathering information about how levodopa acts on albinism, we find that the effects of levodopa on albinism are rife with controversies. Here we display and summarize some information of "levodopa on albinism".

1. Explore the effects of levodopa on albinism in clinical trial

In the C Gail Summers' study, a randomized, controlled clinical trial was done. It conducted that 45 subjects with albinism were randomly assigned to one of three treatment arms: levodopa 0.76 mg/kg, levodopa 0.51 mg/kg, placebo. The conclusion was levodopa, in the doses used in this trial and for the time course of administration, did not improve visual acuity in subjects with albinism^[2]. In other words, patients who take levodopa can't alleviate the symptoms of albinism in this clinical trial. This is the only trial we find about the effects of levodopa on albinism at present.

2. Levodopa does work on rescuing retinal morphology and visual function in a murine model of human albinism

In the study, the authors demonstrate for the first time that post-natal L-DOPA supplementation can rescue retinal development, morphology and visual function in a murine model of human albinism, but only if administered from birth or 15 days post-natal age^[3].

One of the albinism's symptoms is ophthalmic diseases—the damage of retinal morphology and visual function. By extrapolating from the thesis, we can draw the conclusions that maybe levodopa has an efficient action on albinism when the patients are child and even, they get this treatment since they are infants. Coincidentally, in the C Gail Summers' study, he

mentioned that there is a possibility of guessing of a link between curative effect and the age of patients. We could retain a guessing: the effects of levodopa are related with the treatment age of patients.

3.GPR143 ligands and L-DOPA stimulation

Tyrosinase controls melanocytes and RPE. It catalyzes tyrosine hydroxylation to L-DOPA and L-DOPAs oxidation to dopaquinone. To date, only L-DOPA has been proposed to be a GPR143 endogenous agonist activating the Gq/11 protein associated pathway^[4]. Furthermore, L-DOPA stimulation promotes GPR143-Gq/11 protein coupling, although GPR143 also coprecipitates with G α , G β , and G γ subunits of heterotrimeric G proteins in melanocyte extracts^[5]. The decreased levodopa level caused by the disruption of melanin synthesis may be the basis of the developmental disorder of optic nerve tract. Thus, developmental eye defects are present in all forms of albinism, regardless of the mutated gene^[6]. Production of dopamine from L-DOPA in immature retina cells induces activation of dopamine receptors and plays a role in retinal differentiation from early development stages^[7]. Therefore, we mention “immature” once again. L-DOPA acts on immature cells to play a role in enhancing the synthesis of the melanin. According to this calculation, L-DOPA should be given to patients whose systems are immature. The effects of L-DOPA relate to age of patients. However, L-DOPA is unlikely to be effective in ocular albinism, as it requires an intact OA1 effective^[8].

4.Does levodopa have effects only on fetus?

In 1983, Eady completed the first prenatal diagnosis of albinism in a pregnant woman from the Middle East who had given birth to a child with albinism through fetal biopsy and electron microscopy. At 20 weeks gestation, the fetus was shown to have pink skin, thin hair, and no pigmentation. The stage I and II melanosomes were observed in the melanocytes under electron microscope, but no stage III and IV were observed. In 1994, Shimizu incubated skin hair follicle melanocytes of normal fetus at 20 weeks of gestation with levodopa. Under electron microscopy, early (stage I-III) melanocytes developed and matured into late (stage IV) melanocytes, but this situation did not exist in albino patients. He successfully diagnosed an albino fetus at 20 weeks gestation with an ultrasound-guided fetal skin biopsy. It follows that probably levodopa has no effect on babies' skins as well.

Conclusion

Synthesize our above analysis, levodopa has effects only on immature tissues. On the contrary, in the mature tissues, they may can't accept the effects of levodopa. The available evidence suggests that levodopa has weak effects on infants with ocular albinism and no effects on children or infants with cutaneous albinism. Few clinical studies have been conducted on the use of levodopa in the treatment of albinism. The effect of levodopa on the treatment of albinism has not been fully established. Treatment for albinism is currently a problem around the world. We hope that more and more drugs are being found to treat albinism and fewer and fewer people with albinism get relief in the future.

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