Toxicity effect of vincristine on mice fetus cerebellum

Sajjad Hejazi¹, Sina Yaghoubi², Mohamadreza Delghandi² (Corresponding author)¹

1 - Department of Anatomy, Faculty of Veterinary Medicine, Tabriz branch, Islamic Azad University, Tabriz, Iran
2 - Graduated of Veterinary Medicine, Tabriz branch, Islamic Azad University, Tabriz, Iran

Sajjad.hejazi@yahoo.com
Corresponding author: dr.mohamadreza.delghandi@gmail.com

Abstract: Vinncristine Alkaloid originates from vina-rosa and its mechanism includes the depolarization of microtubals that take part in the process of mitotic divisions (17,2). This drug stops the chain of cell mitotic so that its usage in the halting of divisions in malignant cancers with high proliferation has been suggested (2,17). Cerebellum, with respect to the formation and appearance of fetus, is originated from metasfal. The shape of cerebellar neurons and the order of their interstitial space during their development in central nervous system are the same in all vertebrates and abnormal growth of this area causes disturbances in the movement of the given animals. [Hejazi S, Yaghoubi S, Delghandi MR. Toxicity effect of vincristine on mice fetus cerebellum. Life Sci J 2013;10(6s):287-291] (ISSN:1097-8135).

Key Words: Vincristine, Mice, fetus, cerebellum

Introduction

In the previous studies, it has been mentioned that the initial appearance of cerebellum is in the from of a mass which is traceable during the pragnency. Days of 14-17, and the initial shape of cerebellum is recognizable from the 17th day of pragnency onward and it is in a foliated shape (3). In a study on the development of mice fetus cerebellum it has been observed that X ray and drugs with anti-mitotic activity effects (cytotoxics) have destructive impacts on the regulation (uniformity) of cell development, migration, and the segregation of 3-layer segment of cerebellar cortex (10). In another study which was on the migration of neural telyal cells, followings were reported. when mice were poisoned with the vincristine during the pragnency period, this drug caused disturbance in chin cephalic and optic cup, and condition of non-growth to asymmetrical-growth were also observable(16). Moreover, damage to purkinje cells has some relationship with most of illnesses which appear after the maturity period like: spasm, epilepsy, Huntington which are totally suggested as the “cerebellar cognitive affective” sandrom. Such a sandrom is accompanied with the visual and oral Insufficiency (Signals) signs (14,15).

Studies have shown that 23-85 percent of pragnent mothers who received this drug, occurrence of malformation has been observed in their fetus. Yet, there is not enough information on the trathological effect of this drug on the different structures of the newborn fetus(3). In this study, it has been tried to show the placental blood barrier transfer of this drug, and its known cytotoxicity effect, the probable amount of vincristine damage to the formation of cerebellum in newborn fetus.

Materials and Methodology:

In this study, male and female mice with swiss race, and with the weight of 30±3 were selected. Equal numbers of female mouse were put beside the same numbers of male mouse during the prostrus phase from the strus cycles (uring night). The test of vaginal Smir was done at 8 a.m. so that the first day of pragnency was determined by the observation of spreme in esmir and by the formation of vagenal plaks. As such, a total number of 20 mouse were pragnent. then the pragnent mice were assigned in two groups of control (n=10) and treatment (n=10) randomly. with respect to the frequency of tratological occurance, following the usage of drug during the period of organogens (13,5), and the beginning of initial growth of cerebellum in that period, 3 mg/kg of Vincristine was injected to the treatment group on the 10th and 11th days of pragnency (9,11). Also, the control group were injected by the normal salin during the same days. After the pragnency days, out of total newborn fetus, 48 ones from control and treatment groups, were selected for the present study randomly. After performing histotechnic and coloring phases, in order to investigate the changes occurred in the cerebellar structure observations were made under the light microscope using hemotoxiline-ozoine method. Also, in order to investigate the parameters of the obtained data, mean±SEM was selected between the control and treatmen groups. For statistical analyses t-test and SPSS software were performed.

Results

External morphological observations from the newborn fetus of treatmen group showed meaningful decrease (p<0.001) in weight and size of the skull,
and the growth of the new born fetus compared with those of the control group (Table 1).

Table 1. Shows the average parameters of external morphological observations after the injection of 2 dose vincristine on the 10th and 15th days of pregnancy, each parameter is presented as mean±SEM (n=20).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Group</th>
<th>Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight of fetus/Geran</td>
<td>04.0 ± 63/1</td>
<td>04.0 ± 97/0</td>
</tr>
<tr>
<td>Length of tallness/mm</td>
<td>51/0± 76/24</td>
<td>65/0 ± 97/19</td>
</tr>
<tr>
<td>Width of skull/mm</td>
<td>13/0 ± 77/7</td>
<td>11/0 ± 79/2</td>
</tr>
<tr>
<td>Length of skull/mm</td>
<td>26± 56/10</td>
<td>8/0± 13/9</td>
</tr>
</tbody>
</table>

*Shows the meaningful difference from control group (p<0.001).

On the basis of microscopic observations from the initial growth of cerebellum in the newborn infants of control group, three-layer cells of cerebellar cortex were visible and distinguishable from each other. cerebullem was in foliated shape initially, and the development of pia matter around the cerebellum was observable.

In treatment group, the layers of molecular cells, purkenz and oranulex, compared with those of control group had irregular tissues and seemed distorted so that the cerebullem had no foliated shape, with no initial chins, and it was observable with a completely initial shape (images 1 and 2).

Image 1: shows the microscopic view from the tissue of the cerebellum with three layers (black flash), Meningeal membranes (white Flash), Control group (magnified as 10*H&E).

Image 2: Shows the microscopic view from the tissue of cerebellum, Meningeal membranes (white Flash), the interstitial space of white material of cerebellum (*), experimental group (magnified as 10*H&E).

By observing the white material of cerebellum in treatment group compared with the normal condition of white material in control group showed a deficiency in tropil tissue that accompanied with the decrease of color-receiving and increase of interstitial space, and decrease of density in neurogilian cells. Also, in experimental group dismyelinateion of nervous cords in white material of cerebellum was observed (images 3,4).

The presence of purkenz cells in experimental groups’ cerebellar cortex was rare compared with the density of purkenz cells in control group (images 3,4).
Regarding the Meningeal membranes around the cerebellum, the treatment group had a soft tissue pleotosis and edematosis compared with the normal condition of the control group's Meningeal membranes (images 3, 4).

In the observations made from the structure of the fourth ventricle around the cerebellum in the control group, the coroidial tissue was developed completely, and the cover coroidal cells had a normal condition. In the experimental group, the structure of the fourth ventricle was pleotosis and the cover coroidal cells, due to the necrotic appearance, had lost their uniformity and coroidal tissue was distorted.

Necrotic casts accompanied with fibrin leakage, following the damage to coroidal capillaries of the fourth ventricle space, was clearly observable (5, 6).

- Image 3: Shows microscopic view of cerebellar tissue, purkenz cell (black flash) Meningeal membranes, interstitial space of white material (*), experimental group (magnified as 40x H&E).

- Image 4: Shows microscopic view of cerebellar tissue, purkenz cell (black flash) Meningeal membranes, interstitial space of white material (*), experimental group (magnified as 40x H&E).

- Image 5: Shows a microscopic view of the coroidal girid of the fourth ventricle in the vicinity of cerebellar tissue, control group (magnified as 40x H&E).

- Image 6: Shows a microscopic view of the cerebellar tissue accompanied with the pleotosis and appearance of necrotic casts in the ventricle space (*) and the development of blood veins in cerebellar tissue (black flash), control group (magnified as 40x H&E).
Aputz occurrence in cover cells of coroidal girid was one of the other observations made in experimental group compared with those of the control group. Apupetus, with an increase in cytoplasm atozitophil, condensation, and segmentation of Kromatin nuclear, and at last, formation of apitozi mass was observable (image 7). Apupetuz occurrence was also observable sporadically in the neurogolbyay cells of white material of cerebellum (image 8). In sum, the changes which were indicator of apoituz in neural cells of cerebellar cortex were rarely observable.

Discussion and Conclusion

Damages to cerebellar structure are often investigated in the experimental models of pregnancy period, foetal inflammation, brain schemes, and prebirth studies.

Also, in this study, on the basis of observations made, the descriptions made it obvious that the structure of cerebellar from the organuz period to the end of pregnancy, is pertain to meaningful, irreversible damages (to cerebellum) so that the given damages during the pregnancy period (in human life) or after the birth may affect fetus spiritually or cause problems during the maturity period.

In a study performed by Haton and et al (2007) on the development of cerebellum in sheep fetus, with the interfere of andotoxin indicated the meaningfulness of the damages to the cerebellar structure in the later period of pregnancy.

In a study, Neki and sherini(2002) emphasized the malformation event in the process of development in cerebellar Cortex.

Also, they asserted that the interference of anti-mitotic activity drugs or X ray in newborn mice creates initial damages to the pia matter of Meningeal membranes (10). In addition, in the present study, on the basis of observations made, the damages to newborn fetus of experimental group, due to vincristine, pleotosis and edem in pia matter around cerebellum were reported.

Kamper and Yuman (1998) studied in the field of neuroathology. They referred to a higher percentage of damages to puzkenz structure of cerebellum with a decrease in the number and some times in the size of prukenz cells of cerebellum. Also, in the present study, the dense condition of prukenz cells in experiment group was emphasized, which is an evidence for the destructive effect of Vincristin on the mitotic activity of purkenz,prakash and et al (2007) in a study on mice which was done from the 10th and 12th days of pregnancy (organoz period) showed that cytonoxic cyclo cephamid had no significant halting effect on the cover cells of croidi girid and also it caused apupetu, infusion in the mice brain cells (13). In this study, also, it has been showed that Vincristine had effects on the cover cells of Kroidi tissue in experimental group with the segmentation of Kromation nuclear apupetuz and its effect on the cells of white material of cerebellum with the occurrence of apupetuz was reported.

Conclusion

On the basis of results obtained from this study and findings of the previous studies, it can be concluded that the effects of drugs with anti-miotic activity (Cytotoxic) includes:
• Haltering the segregation/proliferation of cells in the cerebellar cortex.
• Improving infusion of apupetuz in the coroidi cell girid and the tissue of the cerebellumitsel.

In sum, the present study indicated some new events, in line with the proof of infusion mechanism, retardation in the formation of cerebellum in mice fetus, by one of the chemotherapy drugs namely, vincrisistine, during the intr-urine lives, also, the infusion of apupetuz and the distortion of cell structure were presented.

Reference

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