Effects Of Retinoic Acid On Survival Percent And Growth Of Swiss Albino Mice

Dr Rashmi Sharma And Ashok Gupta

Department Of Zoology, SPC GCA Ajmer, Rajasthan, India

Abstract: The development of an organism is a complex process of embryogenesis involved cell proliferation, differentiation, migration and organogenesis. Teratology is the branch of biology that deals with abnormal development. Many agents interfering the development process can cause malformations in the embryo. The study of these congenital abnormalities is called teratology and agents which are responsible for causing these malformations are called teratogens. Susceptibility to teratogens depends on the genotype of the organism, including species as well as strain differences. Etienne Geoffrey Saint Hilaire and his son in 1820 started experiments on chick embryo by disturbing its environment in different ways at different embryonic stages. They found some anomalies like Trioncephally, atrophy of eyes and spina bifida in his experiments (Tuli, 1968). In 1877 Dareste reported some anomalies like Trioncephally, atrophy of eyes and spina bifida in his Experiments (Tuli, 1968). Retinoids are essential for spermatogenesis, placental development, foetal morphogenesis and growth. The role of vitamin A in vision is well known. Active derivative of vitamin A (Retinoids) play an important and multiple role in Mammalian development and homeostasis (Sapin, et.al. 1997, Dup et al 1997). These essential dietary compounds are needed in very small quantities, they are not synthesized by the animals and are obtained from external sources in the form of β carotene (C40H56). In cells of intestine β carotene is converted into vitamin A alcohol and is transported by blood to liver where it is esterified and stored as vitamin A palmitate. RA is not stored in liver but is derived from retinal and it is biologically the most potent form of vitamin A. Vitamins are organic compounds which are divided into 2 categories i Fat soluble (A,D,E,K) And ii water soluble (B and C). Vitamin A belongs to fat soluble category of vitamins. A fat soluble substance essential for life was first discovered in egg yolk in 1909 by Stepp (Pawson, 1981; Robert and Sporn, 1984). It was confirmed by McCollum Devis in 1913 when he found a compound with similar biological activity in butter fats, egg yolk and cod liver oil and was named fat soluble vitamin A. In the present study effects of different doses on survival rate on different development stages of Swiss albino mice are studied.

Key words: Retinoids, Teratological, Swiss albino mice, Survival percentage.

I. Introduction

Teratology is a branch of Embryology that deals with abnormal development. The development of an organism is a complex process of embryogenesis involved cell proliferation, differentiation, migration and organogenesis. Many agents interfering the development process can cause malformations in the embryo. The study of these congenital abnormalities is called teratology and agents which are responsible for causing these malformations are called teratogens. Susceptibility to teratogens depends on the genotype of the organism, including species as well as strain differences. Teratological experiments was started from 1820s with the studies of Etienne Geoffrey Saint Hilaire and his son on chick embryo by disturbing its environment in different ways at different embryonic stages. They found some anomalies like Trioncephally, atrophy of eyes and spina bifida in his Experiments (Tuli, 1968). In 1877 Dareste reported some congenital malformation in the chick embryo by environmental disturbance. Retinoids are essential for spermatogenesis, placental development, foetal morphogenesis and growth. The role of vitamin A in vision is well known. Active derivative of vitamin A (Retinoids) play an important and multiple role in Mammalian development and homeostasis (Sapin, et.al. 1997, Dup et al 1997). These essential dietary compounds are needed in very small quantities, they are not synthesized by the animals and are obtained from external sources in the form of β carotene (C40H56). In cells of intestine β carotene is converted into vitamin A alcohol and is transported by blood to liver where it is esterified and stored as vitamin A palmitate. RA is not stored in liver but is derived from retinal and it is biologically the most potent form of vitamin A. Vitamins are organic compounds which are divided into 2 categories i Fat soluble
Vitamin A belongs to fat soluble category of vitamins. A fat soluble substance essential for life was first discovered in egg yolk in 1909 by Stepp (Pawson, 1981; Robert and Sporn, 1984). It was confirmed by McCollum Devis in 1913 when he found a compound with similar biological activity in butter fats, egg yolk and cod liver oil and was named fat soluble vitamin A. The name of vitamin was given by Dummond in 1920. The natural and synthetically obtained vitamin A is found in several forms of Alcohol (Retinol), aldehyde (Retinol palmitate), acetate and retinoic acid. They were collectively known as retinoids. Retinol or alcoholic form of vitamin A is an unstable organic compound. They are easily oxidized specially in the presence of heat. The ester form of vitamin A are fairly stable. When vitamin A is taken in the form of esters (Palmitate/acetate), its converted into Alcoholic form (Retinol) in the intestinal cells to be carried to liver, where it is converted to palmitate form for storage. Retinoic acid is not stored in the liver but it is derived from retinol and it is biologically most potent form. In the present study effects of different doses on Survival rate on different development stages of swiss albino mice are studied.

II. Materials And Methods

The mice were obtained from mice breeding center, Department of Zoology M.D.S.U. Ajmer. Animals were fed synthetic diet mice feed pallets (Brook Bond Lipton India Ltd.) Supplemented with germinated grains, seasonal green vegetables, multivitamin drops and water ad libitum. Tetracycline mixed in water in water was regularly given. There are four virgin female mice 25+1gm were caged with fertile healthy male in the evening and these were examined for presence of vaginal plug, the next morning. The day appearance of vaginal plug was considered as day 0 of pregnancy.

The vaginal plug

After copulation a secretion of seminal vesicles in the ejaculate of the male coagulate to form a plug in the vagina extending from the cervix to the valve, where it is ordinarily Visible and is a convenient external sign that mating has occurred (Green, 1996).

Duration of pregnancy

The gestation period in this species is 19 days and occasionally 20 days. The youngs are most frequently born in the early hours of the morning between midnight and 4 AM.

Objectives

Investigation of the effects of retinoic acid on different developmental stages (5th, 8th, 11th, and 14th) of mouse embryo.
To study effects of RA on organogenesis of skin, liver, heart.
Effect of RA on skeletal elements.

Experimental design

The pregnant females were devided into following groups:
(6 animals per group)
Group A : untreated
Group B : Treated

Doses

Suitable (non lethal or sublethal) doses of RA were screened on mice embryos on different stages of developments. The following doses were found to produce various teratological defects on developing mice embryos
1. 2mg RA /pregnant female.
2. 4mg RA /pregnant female.
III. Results And Discussion

Teratological effects of RA on different development stages of mice embryo:

Survival percent (Sp) and growth retardation (Weight and length). Survival percentage Studies on the effect of RA on percent survival of mice embryos were carried out by Treating the pregnant female at 5th, 8th, 11th, and 14th day gestation with different doses of RA. For each dose of RA (2mg and 4 mg) 3 pregnant female were selected and normal litter of per female was 8-10 embryos. Therefore percent survival was based on 24 to 26 embryos per dose of RA. Untreated The survival percentage (mean) was observed to be 90% in the embryos of untreated Pregnant females.

Dose 2 mg RA
When 2mg RA was administered on 5th, 8th, 11th, and 14th day gestation the survival % was 85%, 59.2%, 69.4% and 79% respectively. (Table 1)

Dose 4 mg RA
When pregnant female of day 5th, 8th, 11th and 14th day gestation were treated with 4mg dose of RA the percent survival was 75%, 50%, 55% and 70% respectively. (Table 2).

Growth Retardation
The growth retardation effects of RA on mouse embryos was calculated in terms of weight and length (snout to base of tail) of the embryos.

Control (Untreated)
The average weight of control embryos was observed to be 2.5 gm and average length was found to be 30mm.

Dose 2mg RA
The weight of embryos of females treated with 2mg conc. of RA was found to be 2.3gm, 1.3gm, 1.52gm and 1.7 gm respectively on the 5th, 8th, 11th, and 14th day gestation period (Table 3).
The average length of 2mg RA treated embryos of pregnant females was 27mm, 22mm, 23mm, and 24mm respectively (Table 3 fig 1).

Dose 4 mg RA
The next higher dose of RA has found to retarded growth of embryos severly. Pregnant female treated on 5th, 8th, 11th, and 14th day gestation showed 2.0 gm, 1.05 gm, 1.32gm, and 1.4gm weight embryos and length of 25mm, 22mm, 23mm and 24mm of the embryos of treated female (Table 4 fig 2).

![Table 1](image)

<table>
<thead>
<tr>
<th>Per female dose of RA</th>
<th>Gestation period</th>
<th>Survival percent (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTROL</td>
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<td></td>
</tr>
<tr>
<td>2mg RA/pregnant female</td>
<td>5th</td>
<td>90%</td>
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<tr>
<td>2mg RA/pregnant female</td>
<td>8th</td>
<td>85.0%</td>
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<tr>
<td>2mg RA/pregnant female</td>
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<td>14th</td>
<td>94.4%</td>
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Table 2

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<td>90%</td>
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<td>4mg RA/pregnant female</td>
<td>5th</td>
<td>70%</td>
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<td>4mg RA/pregnant female</td>
<td>8th</td>
<td>50%</td>
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<tr>
<td>4mg RA/pregnant female</td>
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Table 3

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<tr>
<th>Treatment dose of RA</th>
<th>Gestation age of mice embryos</th>
<th>Average Weight (in gm)</th>
<th>Average Length (in mm)</th>
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<tr>
<td>CONTROL</td>
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<td>2.5 gm</td>
<td>31mm</td>
</tr>
<tr>
<td>2mg/pregnant female</td>
<td>5th</td>
<td>2.3 gm</td>
<td>27mm</td>
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<tr>
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IV. Conclusion and Summary


2 and 4mg of RA on 5th, 8th, 11th, and 14th day of gestation females was found that survival was higher on at 2mg dose level as compared to 4mg dose. Further stage 8th, and 11th were most crucial development stage when survival percent was very low when compared with 14th day gestation stages. This clearly indicate that the dose dependent effect of RA on mouse embryo. Stage 5th was found to be an exception because % survival was higher at this stage as compared to 8th or 11th day gestation stages. The decrease in percent survival of mouse embryo treated with RA is due to its toxic effects. Hypervitaminosis has been found to be toxic in many other mammalian system. (Lammer, 1985).

References

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