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Research Article

Teratogenic effect of maternal oral ingestion of aspirin on neural tube development of foetal wistar rats

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ABSTRACT

This is an experimental study to investigate the influence of maternal oral ingestion of aspirin on the neural tube development of wistar rat foetus. Ten albino rats consisting of 8 females and 2 males (weight range 200g-250g) were collected and used for the experiment. The 2 males were separated from the 8females which were then divided into 2 groups A and B. Three female wistar rats were then taken from each group to form classes A and B, while the remaining 2 females formed the control class C. They were then placed in an enclosure for 2 days with the males after which they were examined for signs of copulation. Water containing aspirin in varying doses was then administered to the rats in classes A and B on the various gestational days. The female wistar rats were sacrificed on Gestation Day 18 and the neural tubes of the developing foetuses were examined for any anomalies. Foetuses from classes A and B both showed decrease in the average head length with slight decrease observed in class A and significant difference (P<0.05) in Class B when compared to the control C. Slight decrease in the mean body length was observed in both classes without any significant difference in reference to the control class (class C).

Keywords: Aspirin, neural tube, wistar rats and foetuses

INTRODUCTION

Teratology is the study of abnormalities of physiological development. It is often thought of as the study of human birth defects, but it is much broader than that, as it incorporates other non-birth developmental stages such as puberty and other non-human life forms as in plants. Other forms of developmental toxicity include all manifestations of abnormal development such as growth retardation or delayed mental development without any structural malformations (Rogers, 1996).

The unborn baby though appears to live in a protected and comfortable environment is not entirely immune to the larger world surrounding the mother. Teratogenic agents affect genes and protein production in several ways. They may damage genes and make them incapable to operate by substituting themselves in the genetic code. It has been observed that thousands of babies that are born deformed or mentally retarded every year are the results of events that occur in the mother's life, and such events are classified as teratogens. Sneader (2000) observed that teratogens are any agents that can cause abnormalities of foetuses and such agents include: drugs, chemicals, infections, maternal

health state, alcohol, smoking and pollutants. Prenatal period is a very sensitive period in the life of the human organism, and the danger of structural defects caused by teratogens is greater in the embryonic stage.

Over the years psychologists have devoted keen interests in studying the effects of maternal physical health condition on the unborn baby. Statistics show that the outbreak of rubella in 1964-1965 recorded 30,000 prenatal and neonatal deaths and more than 20,000 infants were born with malformations, including mental retardation, cataracts or blindness, deafness and serious congenital heart disorder and others (Sneader, 2000). Rogers, (1996) observed that the infectious risk is high if the disease appears early in pregnancy as in the third and fourth weeks and the second month of pregnancy, and may result in spontaneous abortion. He further stated that one-third of babies delivered through a birth canal affected by genital herpes die at birth and one fourth of such newborns manifest serious brain damage later in life.

Teratogenic agents can be divided into two categories namely: environmental and genetic, based on their etiology. Each category of agents utilizes different pathological processes that result in embryo pathology. About 20-25% of human malformations observed in the first year of life are caused by genetic agents (Rogers, 1996). Birth defects caused by these teratogenic agents have a range of pathological processes that are determined prior to conception, due to the presence of inherited or newly acquired genetic abnormalities. The causal mechanisms underlying these processes include, but are not limited to gene deficiency, gene abnormality, chromosome rearrangement, chromosome deletion and chromosome excess. Although environmental factors may modify the development of the genetically abnormal embryo, the genetic abnormality is the major contributor to the pathologic process (Brent and Beckman, 1990).

Approximately 10% of human malformations observed in the first year of life are caused by environmental agents, which have several characteristics in common (Brent and Beckman, 1990 and 1994). They include Nicotine (tobacco), Caffeine, Ethanol (alcohol), Isotretinoin (13-cis-retinoic acid), Aminopterin, Methotrexate, Androgenic hormones, Enalapril, Coumarin (including Warfarin) and Aspirin, also known as acetylsalicylic acid. It is a drug which is often used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti-inflammatory (Sneader, 2000).

Studies of effects of teratogenic agents on the unborn baby during the prenatal period are many and diverse. These effects can be very disastrous to the developing human being as the risk incorporates a continuum of biological and environmental conditions, ranging from mild oxygen deprivation at birth to very serious genetic defects. Hence the use of wistar rats as opposed to the use of human foetuses.

The easy accessibility of aspirin to the general public due to its cheapness and popularity makes it potentially dangerous as a teratogen if administered to the gestating mothers, posing a potential risk to the developing foetus. Generally, most pregnant women especially in rural areas take medicines including aspirin, based on their basic knowledge picked up from different places or being treated by quack doctors. Aspirin is usually given as a pain-killer even during pregnancy and this may result in various birth defects depending on the doses given and the period of pregnancy in which it was administered. Chronic high dosage exposure of pregnant women to aspirin has been associated with low birth weight and a variety of maternal and placental complications (Brent and Becham, 1990).

This study was carried out in Bowen University Iwo, Nigeria, to examine the teratogenic effect of aspirin on the development of the embryonic neural tube in relation to the closure of spinal canal. The objective is to seek or observe anomalies in the development of the foetal spinal cord as a result of maternal ingestion of aspirin.

MATERIALS AND METHOD

Materials

Food pellets, Fresh clean water, Containment units each consisting of feeding and water apparatus, Aspirin to be administered, Sensitive weighing scale, Syringes, Cannula, Markers, Veneer calliper, Water bath and Thermometer.

Animals

10 albino rats consisting of 8 females and 2 males (weight range 200g-250g) were kept in cages for two weeks, with opposite sexes in different containment units. The weights were taken to ensure that no rat was outside the weight range of 200g-250g which is ideal for parturition.

Preparation of Aspirin

Aspirin tablets were dissolved in water and then regulated to a suitable temperature (20^{0C}) till the tablets dissolved without any basal residue to ensure easy administration.

Experimental Design

- The 8 female wistar rats were divided into two groups of 4 each namely: group A and group B.
- Group A female wistar rats were placed in a darkened enclosed space with two males for 1 hour having a barrier preventing physical contact among the opposite sexes. This process is known as acclimatization.
- The female wistar rats in group A were then divided into two sets and each set was placed together with one male wistar rat each.
- The sets were placed in an enclosed space for 2 days with the males after which their vaginas were examined using a swab test for signs of copulation and confirmed to have copulated.
- The first day of copulation was termed as gestation day one (GD1) and the following days numbered henceforth.
- The same process was repeated for group B
- 3 female wistar rats were then taken from group A to form class A
- 3 female wistar rats were also taken from group B to form class B
- The remaining 1 rat from each group was taken to form class C or Control
- The classes A and B of wistar rats were then administered various doses of prepared aspirin, infused into the drinking water on various gestation days as shown in Tables 1and 2.
- The drugs were administered after prolonged period of thirst.
- Administration did not begin until gestation day six and terminated on Gestation Day 18.
- The female wistar rats were then sacrificed on Gestation Day 18 and any anomaly in the neural tube of the developing foetuses duly noted
- The foetuses of each group were collected and measured with the values collated in a statistical manner.

Table 1. Administration dosages on various gestational days in class **A**

GESTATIONAL DAYS OF CLASS A	DOSAGE OF ASPIRIN (Mg/Kg
6	50
7	50
8	50
9	250
10	500
11	500
12	50
13	50
14	50
15	50
16	50
17	50
18	50

Table 2. Administration dosages on various gestational days in class B

GESTATIONAL DAYS OF CLASS B	DOSAGE OF ASPIRIN (Mg/Kg
6	250
7	250
8	250
9	625
10	750
11	1000
12	250
13	250
14	250
15	250
16	250
17	250
18	250

Measurement

Concise measurements of the foetuses along the spinal cord and brain were taken and recorded. The measurements included:
Head length (HL): measurement from the nape of the neck to the tip of the head
Body length (BL): measurement from the nape of the neck superiorly to the inferior of the spinal cord at the base tip of the body.
Head width (HW): measurement along the width of the head

RESULTS

A total of thirty seven (37) foetuses were collected from the various groups and measured. The results of the experiment were tabulated as mean± standard deviation.

TABLE3. The effect of different dosages of aspirin on different parameters of the neural tube.

PARAMETERS	CLASS C (CONTROL)	CLASS A (LOW DOSAGE)	CLASS B (HIGH DOSAGE)
HL	1.96±0.055	1.84±0.089	1.44±0.089*
BL	3.6±0.122	3.56±0.114	3.46±0.167
HW	1.62±0.084	1.66±0.182	1.76±0.134

* Significant at P<0.05 in comparison with class C (Control)
KEY: Head length (HL): measurement from the nape of the neck to the tip of the head
Body length (BL): measurement from the nape of the neck superiorly to the inferior of the spinal cord at the base tip of the body.
Head width (HW): measurement along the width of the head.

Effects of aspirin on neural tube development

Foetuses in classes A and B both showed decrease in the average head length with slight decrease observed in class A and significant difference (P<0.05) in Class B when compared to the control C. Slight decrease in the mean body length was observed in both classes without any significant difference in reference to the control class (class C).

DISCUSSION AND CONCLUSION

This study observed a decreasing length in the neural tube (spinal cord) of the examined foetuses after measurement of certain parameters: Head length (HL), Body length (BL), but showing significant difference (P<0.05) with administration of high dosages of aspirin.
Results from this study it have demonstrated that aspirin after maternal ingestion at high dosage portends a risk to the neural tube development of foetuses. This drug should therefore be avoided in pregnancy.

References

Brent R, Beckman D (1990). "Environmental Teratogens". Bulletin of the New York Academy of Medicine 66 (2):123-161.
Brent R, Beckman D (1994). "Mechanisms of Teratogenesis". Annual Review of Pharmacology and Toxicology 24: 483-500.
Rogers JM, Kavlock RJ (1996). Developmental toxicology. In C.D. Klaassen (ed.): Casarett and Doull's Toxicology, 5th ed301-331. McGraw-Hill, New York.
Sneader W (2000). "The discovery of aspirin: A reappraisal". BMJ (Clinical research ed.) 321 (7276):1591–1594.