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EFFECT OF ASPIRIN ON LUNGS OF DEVELOPING MICE

Anatomy

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ABSTRACT

Aims and Objective: Aspirin a non-steroidal anti-inflammatory drug having antipyretic,analgesic and anti-inflammatory actions.It is also used in prevention of myocardial infarction.However its effect on the lungs of developing embryo has not been explored yet.

Material and methods: Aspirin was given to pregnant mice in the dose of 100mg/kg body weight and the lungs of 19th day fetus was studied for any microscopic changes.

Results: Aspirin induced rupture of alveolar lining to produce large haemorrhagic lacunar spaces. Aggregation of lymphocytes can be seen interspersed between the pneumocytes as well as in the interalveolar connective tissue space. Necrosis of cells has lead to clumping of cells.

Conclusion: Aspirin has toxic effects on lungs of developing embryo so should be used with caution in pregnancy.

KEYWORDS

ASPIRIN, PLATELETS, HAEMORRHAGE, TERATOGENESIS

INTRODUCTION

Aspirin is one of the Non-steroidal anti-inflamatory drugs.It has antipyretic, analgesic and anti-inflammatory actions.

Several previous studies showed that NSAIDs use on late pregnancy can be associated with severe adverse neonatal outcomes including increased risks of persistent fetal pulmonary hypertension, increased risk of congenital heart defects, intracranial hemorrhages, renal toxicity in fetus, and orofacial clefts.

Despite more than 100 years of use, acetyl salicylic acid (aspirin) has only been recognized for the prevention of myocardial infarction (MI) and ischemic stroke for the past 25 years. Over this period, based antithrombotic effectiveness of aspirin is related to its inhibition of the cyclooxygenase (COX) enzyme that metabolizes arachidonic acid to a variety of prostanoids, including thromboxane A2 (J. R. Vane et al, 1971). Platelet-derived cyclooxygenase-1 (COX-1) generates thromboxane A2, a potent vasoconstrictor and platelet agonist.With the inhibition of platelet COX-1 activity, there is a decrease in platelet aggregation, leading to a reduced thromboembolic potential and prolonged bleeding time. Thus, it is not surprising that the major risks associated with aspirin relate to bleeding complications.

Looking at very few and inconclusive reports about the teratogenicity of aspirin and histopathological changes induced by it on the lungs of the developing fetus, the present study has been undertaken. In the present study, the drug has been experimented upon the swiss albino mice to elucidate its effects on the offspring.

MATERIAL AND METHODS

Adult female swiss albino mice weighing 20- 25 gm (average age of 80-100 days) were used after approval of institution The female mice in their pre-oestrous phase were transferred in the evening to the cages having a male mice in the ratio of 2:1. The presence of vaginal plug on the following morning indicated pregnancy and was designated as day zero(0) of gestation. The pregnant mice were divided into following groups

Group 1 : Control (given equivalent amount of tap water)
Group 2 : Treated with Aspirin 100mg/kg of body weight from day 3 to day 5 of gestation.

The mouse of each group was sacrificed on day 19th of gestation by deep ether anaesthesia and fetuses were collected after uterotomy . After gross examination and photography the fetuses were preserved in 10% neutral formalin solution for seven days. After fixation the lungs of the embryos were dissected out . For histological study the lungs were processed, sections were cut and stained with hematoxylin and eosin.

OBSERVATION AND RESULTS

Although Aspirin has been proven to be beneficial in resolution of various acute lung injuries, in high doses it can damage the normal cytoarchitecture.

On histological observation the treated lungs shows many pathological changes. The slide shows rupture of alveolar lining at various places. Due to the rupture adjacent alveoli have fused together to produce large empty lacunar spaces. Haemorrhage is clearly evident in the alveolar spaces. Aggregation of lymphocytes can be seen interspersed between the pneumocytes as well as in the interalveolar connective tissue space. Necrosis of cells has lead to clumping of cells. On highpower pyknotic changes can be seen in the pneumocyte nuclei

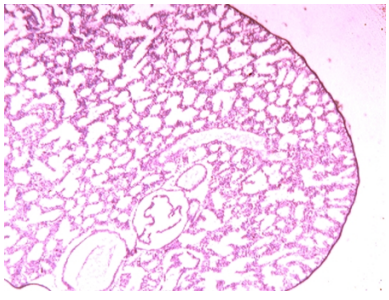

Figure 1 : Photomicrograph showing control lungs (H & E, 100 X).

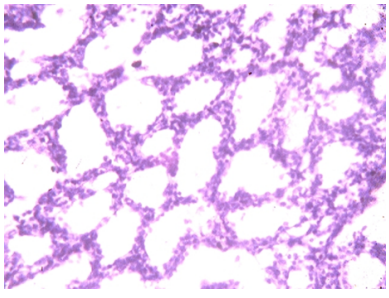

Figure 2 : Photomicrograph showing control lungs (H & E, 400 X).

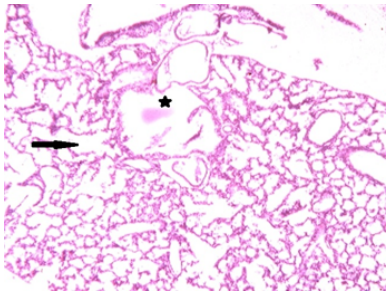

Figure 3 : Photomicrograph showing treated lungs (H & E, 100 X). empty lacunar spaces (→), haemorrhagic area (★).

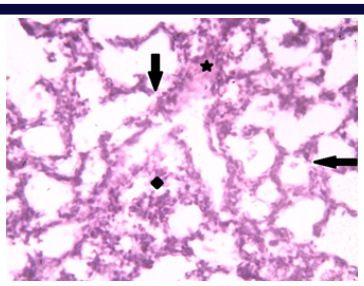

Figure 4 : Photomicrograph showing treated lungs (H & E, 400 X). Showing breakage of alveolar lining (→), hyalinization (★) and cellular aggregation (♦).

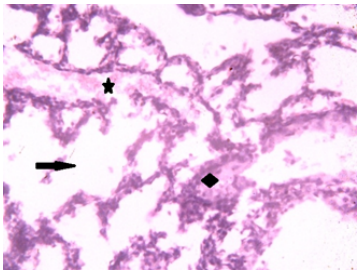

Figure 5 : Photomicrograph showing treated lungs (H & E, 400 X). Showing empty lacunar spaces (→), haemorrhage (★) and hyalinization and aggregation of cells (♦).

DISCUSSION

Aspirin has been utilized for many years as a therapeutic agent because of its well known analgesic, antipyretic and anti-inflammatory activity. In the recent years, many unwanted side effects have been observed both on animal studies and clinical trials .

Abraham M (1981) observed that instillation of Aspirin (50 to 90 mg/kg fetal body weight) in to the rumina of fetal lambs resulted in significant increase of pulmonary arterial pressure, which was directly related to constriction of the ductus arteriosus. Such pressure elevation may act as a trigger to increase muscular development in the small vessels of the lung, which interferes with the rapid reduction in pulmonary vascular resistance normally occurring after birth.

Alex Schoenfeld et.al. (1992) reported constrictive effect of Aspirin on fetal ductus arteriosus.They stated that Aspirin use during pregnancy is related to teratogenesis, maternal bleeding, fetal and neonatal bleeding, effects on the pulmonary circulation.

Namieta M. et al. (2000) performed a study on effects of NSAIDs on fertility, pregnancy and lactation. They found that Aspirin can cross the placenta and cause congenital anomalies in animals. Chronic or intermittent use of high dose of Aspirin leads to premature closure of ductus arteriosus in the fetus.

Although Aspirin has been proven to be beneficial in resolution of various acute lung injuries, in high doses it can damage the normal cyto-architecture. Leslie. J crofford (2001) studied the use of analgesic, anti-inflammatory agents in asthma and prevelance of aspirin hypersensitivity. They observed that Aspirin exacerbated respiratory disease (AERD), or aspirin induced asthma is characterized by asthma and rhinitis triggered by the ingestion of aspirin and NSAIDs. They proposed that the mechanism underlying is the inhibition of synthesis of protective prostaglandins resulting in an increase in the synthesis of cysteinyl leukotrienes by eosinophils and mast cells. The microscopic observation in the present study revealed rupture of alveolar lining, massive haemorrhages, necrosis of cells and aggregation of lymphocytes interspersed between the pneumocytes as well as in inter alveolar connective tissue space.

Antonucci et al. (2012) observed that Aspirin given to pregnant women crosses the placenta and causes embryo-fetal and neonatal adverse effects. It affects the brain, kidney, lung, skeleton, gastrointestinal tract and cardiovascular systems of the developing fetus.

Thus it can be hypothecated that Aspirin, due to its toxic effects on various organs in the developing fetus can affect the normal developing pathways in high doses.So this drug should be used with caution in pregnancy.

CONCLUSION

Thus as concluded from these studies, it is suggested that Aspirin although widely used may cause toxicity and teratogenicity. Clinicians, therefore, should carefully justify the aspirin therapy to pregnant mothers at the early stages.

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