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PRENATAL EPINEPHRINE INDUCED TOXIC CHANGES

Anatomy

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ABSTRACT

Epinephrine or adrenaline is a naturally occurring catecholamine. It is a hormone, neurotransmitter and medication. It is normally produced by both the adrenal glands and certain neurons. It plays an important role in the fight or flight response by increasing blood flow to muscles, output of heart, pupil dilatation and blood sugar. It acts by binding to alpha and beta receptors.

As a medication it is used to treat a number of conditions including anaphylaxis, cardiac arrest and superficial bleeding. It may also be used for asthma when other treatments are not effective and this is one of the life saving drugs. There might be emergent occasions where doctors have to administer it to pregnant women. Safety of its use in pregnancy is unclear. So in present study attempts have been made to explore its prenatal effects by reviewing previous studies performed on the topic.

KEYWORDS

Cardio-vascular malformations, Teratogenesis.

INTRODUCTION

Epinephrine was first isolated by Napoleon Cybulski in 1895.[1]. It is a hormone, neurotransmitter and medication. It is normally produced by both the adrenal glands and certain neurons. It plays an important role in the fight or flight response by increasing blood flow to muscles, output of heart, pupil dilatation and blood sugar. It acts by binding to alpha and beta receptors. As a hormone , epinephrine acts on nearly all body tissues. Its actions vary by tissue type and tissue expression of adrenergic receptors. For example , high levels of epinephrine causes smooth muscle relaxation in the airways but causes contraction of the smooth muscle that lines most arterioles.

Epinephrine acts by binding to a variety of adrenergic receptors. It is a nonselective agonist of all adrenergic receptors.[2] Epinephrine's binding to these receptors triggers a number of metabolic changes. Binding to alpha-adrenergic receptors inhibits insulin secretion by the pancreas, stimulates glycogenolysis in the liver and muscle,[3] and stimulates glycolysis and inhibits insulin mediated glycogenesis in muscle.[4] Beta adrenergic receptor binding triggers glucagon secretion in the pancreas, increased ACTH secretion by the pituitary gland and increased lipolysis by adipose tissue. Together these effects lead to increased blood glucose and fatty acids, providing substrates for energy production within cells.

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It has been seen that the teratogenic effect of different drugs differ in different species and even in different strains of the same species and also in different tissues of an animal. Therefore, such testings in different species and strains of the experimental animal becomes essential to have a reliable clue of the suspected teratogens. If thalidomide had also been tested on animals for its teratogenecity prior to its clinical use probably birth of thousands of malformed babies in 1961 tragedy, could have been prevented.[5]

REVIEW LITERATURE

Hodach et al.(1975) in their work on chick embryos in ovo administered a single dose of Epinephrine at concentration ranging from 0.4 x 10^{-9} to 20 x 10^{-9} mol/5ul saline during stages 20-27 Hamberger and Hamilton.[6] Cardiovascular anomalies were produced in 743 cases. They obtained absence of right third, left third, right fourth aortic arches. They found absence of right and left ductus arteriosus, hypoplasia of right fourth arch, anterior displacement of base of aorta as a third, fourth and sixth arch anomalies. The frequency of anomalies was significantly reduced by pretreatment with propranolol.

Gilbert et al.(1976) in their study showed that cocaine potentiated the effects of epinephrine in terms of aortic arch malformations in embryonic chicks. Cocaine itself produced aortic arch malformations when administered in large doses. In 1977 they further used in their work theophylline and caffeine which do not produce but potentiated aortic arch malformations induced by Epinephrine in experimental animals.[7]

Gregory M. Rajala et al.(1984) in their study on chick embryos showed that the mean heart rate values for Epinephrine treated embryos were significantly less than values obtained for untreated and saline treated control embryos. Dysrhthmias were characterized by periods of bradycardia alternating with periods of asystole and were confirmed by ECG. It suggests that Epinephrine induces cardiac conduction disturbances.[8] Gregory M. Rajala et al. (1988) showed that absence of one or more aortic arches occurred more frequently in embryos treated with Epinephrine.[9]

Matthias O.Cheung et al. (1977) performed a study on 5 days old chick embryos and found that Ephinephrine produced aortic arch anomalies and related to the induction of hypoplastic right pulmonary artery with absent or hypoplastic right ductus arteriosus.[10]

Kroese J.M et al. (2004) in a study on chick embryos observed that Epinephrine administration caused a significant increase in heart rate, peak and mean velocities, peak acceleration, peak and mean blood flows, stroke volume.[11]

DR Lenselink, RS Kuhlmann et al. (1994) in their study on chick embryos found that Epinephrine was significantly involved in adrenergic cardio-vascular teratogenesis.[12]

CONCLUSION

From the present study on prenatal effects of Epinephrine administration following conclusions can be withdrawn. When treated chick embryos were examined for malformations of viscera of gastrointestinal and urinary tracts and anomalies of brain, they did not show any adverse effects. This indicates the selective action of epinephrine at the level of beta receptors of developing heart. Mainly the third, fourth and sixth arches are involved after the administration of epinephrine. However, all the internal anomalies observed in these experiments were associated with malformations of fourth arch only.

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