Original Article

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Evaluation of Teratogenic Potential of Ondansetron on Developing Chick Embryo

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Abstract

Objective: To determine the teratogenic potential on developing chick embryo after injection of ondansetronto the fertilised egg and comparing it withembryos of controls. *Methodology*: The present study was conducted inthe Department of Anatomy in our Institute.Fertilised chicken eggs were exposed toondansetron by injecting the drug through air sac on 3rd Embryonic Day (ED). The control group and the experimental group were examined intermittently by candling method to check death of embryos. Survived Chicken eggs were dissected out on day 19th of incubation and were carefully observed for any major congenital abnormalities. The embryos thus dissected out were subjected to estimation of crown-rump length (CRL), changes in weight of egg (before and after incubation), volume of embryos. *Results*:The mortality in experimental group was significantly higher as compare to control ones. All the other parameters studied in this study are non-significant statistically. *Conclusion*: The outcome of study is suggestive of no significant effect on various parameters used to evaluate teratogenicity but significant mortality is sign of concern.

Keywords: Chick Embryo; Ondansetron; Teratogen; Mortality.

Introduction

Ondansetron is a serotonin 5-HT_3 receptor antagonist used mainly as an antiemetic to treat nausea and vomiting, commonly following chemotherapy. It is also used off-label to treat hyperemesis gravidarum in women, but there is no conclusive data available on its safety in pregnancy, especially during initial months of pregnancy.

Chick embryo is a popular experimental model for developmental studies. It has certain practicaladvantages like easy experimental manipulation, richhistory in developmental biology and the shortincubation time, which emphasize the importance of thechick embryo, as a model animal forsuch developmental studies [1].

Early development of the embryo takes place in the blastoderm. The albumen surrounds the yolk and protects the potential life of developing embryo. It is an elastic, shock-absorbing semi-solid with high water content. The yolk and albumen are prepared simultaneouslyto sustain life - the life of a growing embryo- for twenty one days, in the case of the chicken. This entire mass is surrounded by two membranes and an external covering called the shell. The shell provides for an exchange of gases and a mechanical means of conserving the food and water supply within [2].

Early chick mortality may be associated with disease, inadequate brooding temperatures, heat stress and poor management in hot climates [3].

Aim

To determine the teratogenic effect of ondansetron on developing chick embryos after injecting the drug on 3rd day of incubation. Study also aims in comparing the mortality among two groups by noting the number of dead embryos.

Material and Methods

An incubator (Yorko make) with capabilities for

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maintaining and monitoring temperature and humidity and turning the eggs periodically, was used forincubating the eggs. The temperature in the incubator was maintained at 102°F and the relative humidity was kept between 70-80% [2].

Total of hundred developing chick embryos were utilized for this study with due permission from Institutional Ethics committee. Out of which first fifty were kept in control group and other half in experimental group. The eggs of experimental group were injected with 1.0 mg (this dosage was calculated as non-lethal from our previous experiments) of ondansetron dose [4]. The developing eggs were allowed to develop and were check intermittently for their survival with candling method. Weight of egg before putting them in incubator and weight of egg after 19th day(gm) were noted using digital weighing balance. The volume of embryos were estimated using fluid displacement principle. Crown Rump(CR) Length in cm for all the groups was also measuredfor each survived embryo by passing a thread from root of beak along the back to the tip of coccyx and then measuring length of thread.

The embryos were also grossly observed for

1) Abnormalities of head and neck.
2) Deformities of limb.
3) Abnormalities of beak.
4) Deficient abdominal wall.

Data collected was fed in the computer and statistical software (Epi info) was used. The variable fed into the data analysis software was termed as 'survivability' where a value of '1' denoted alive embryo and a value of '2'denoted dead embryo.

Results

The embryos were carefully examined for any gross malformations. None of the embryo treated with ondansetron showed any deviation from normal anatomical structure. The table shows the mortality of embryos in both groups. The number of embryos survived in control groups were 44 and number of survived eggs in experimental group were 41. The mortality in experimental group was bit higher and statistically significant when compared with the controls. The comparative account of mortality is shown in Figure 1.

The initial weight of eggs that was just taken prior to keeping them in incubator and final weight was the weight taken just prior to opening of egg. The difference of final and initial weights were treated as decrease in weight. The decrease in weight were statistically non-significant (Figure 2).

The mean values for volumes of embryos are also depicted in table 1 and Figure 3. These values for experimental group when compared statistically with their control counterparts also showed non-significant deviation. The mean values for CR length were also non-significant in two groups. Graphical representation of all is shown in Figure 4.

Table 1: An evaluation of teratogenic potential of ondansetron on developing chick embryo

S. No	Parameter	Control	Experimental	P value
1	Mortality	12%	18%	Significant
2	Decrease in Weight	3.99 ±0.92	3.81±1.12	0.212 (p>0.05), NS
3	CR Length in cm	5.93 ± 0.36	5.87 ± 0.44	0.225 (p>0.05),NS
4	Volume of Embryo	5.67±0.62	5.66±0.61	0.47 (p>0.05), NS

Fig. 1:

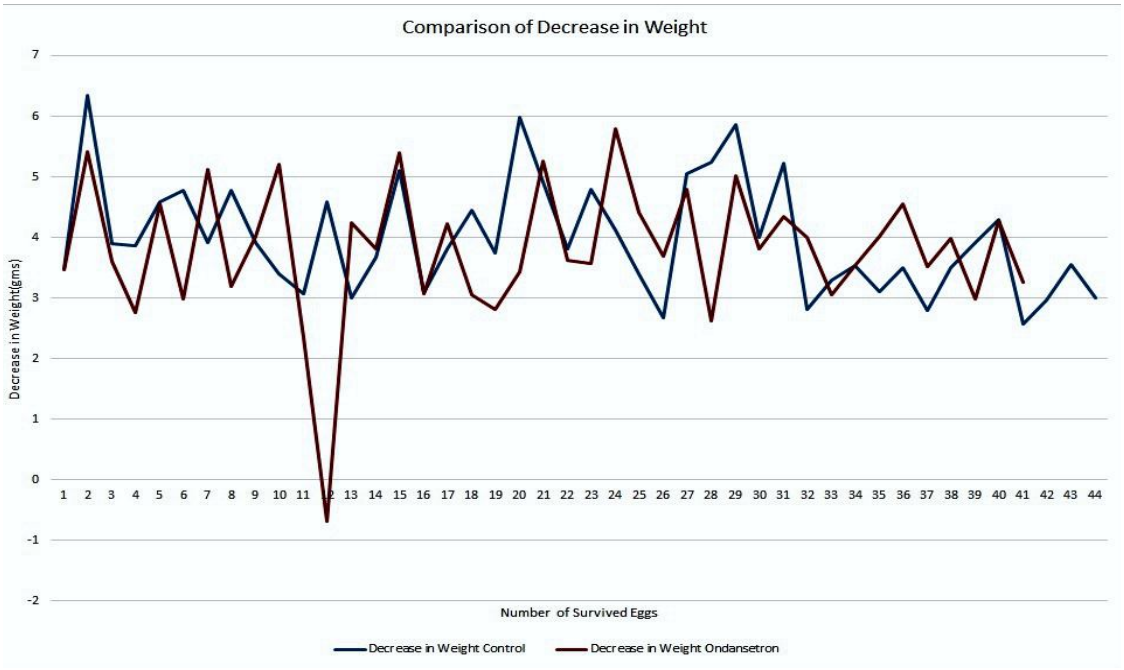

Fig. 2:

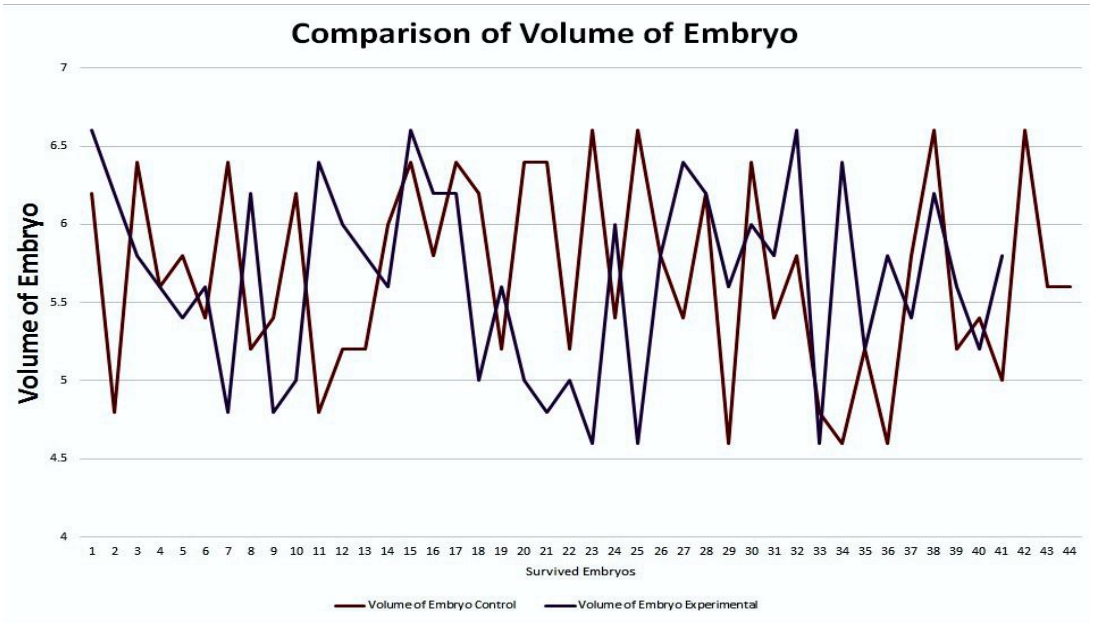

Fig. 3:

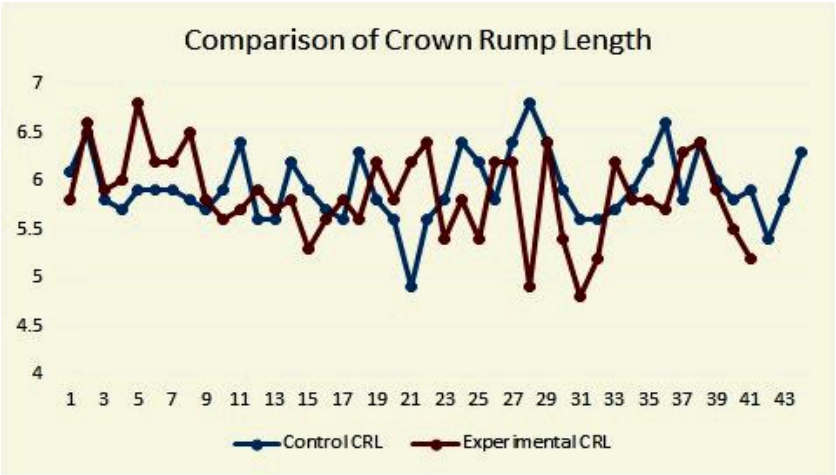

Fig. 4:

Discussion

The present study is an attempt to evaluate the embryotoxic effects of the Ondansetron. This is first detailed analysis of ondansetron toxicity in the chick embryo for which there are no detailed data available in literature to the best of our knowledge. We were not able to find single study which has employed ondansetron as target drug for developing chick embryo. We selected the ondansetron because of its widely usage during emesis. Moreover self-medication amongst people of this subcontinent is not so uncommon. The selection of drug dosage in this study was based on our own previous study.

Good hatchability depends on meeting all crucial incubation parameters and conditions. One of these important parameter is weight loss. In general, eggs should lose 11-13% of initial weight during the first 18 days of incubation. Weight loss in hatching eggs is caused by the regular evaporation of water from the eggs and inseparably linked to achieving optimum embryonic development during incubation.

This weight loss from the egg is essential for the formation of the air cell and at the same time, the evaporation of water from the egg facilitates optimized water, mineral balances in the different embryonic compartmentsformed during the embryonic development.

As soon internal egg temperature rises, evaporation through the shell and the transport of water from the albumen to sub-embryonic cavity increase. The reasons of weight gain in one case is beyond our knowledge and an extensive literature search for this observation did not yield any explanation.

We were not able to find any gross malformations in any chick and major reason behind it can be that chicks were allowed to hatch full term. Had there been any malformation the chick would have not survived. Many different researchers have reported malformations in development of organs or body with the use of chemicals specially insectisides [5].

Conclusion

The mortality of chicks in experimental group is very significant observation. The remaining parameters observed in experimental group showed non-significant deviation from control groups.This warrants further advance studies with larger sample size.

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