

STUDIES ON THE TERATOGENIC EFFECTS OF CLINDAMYCIN HYDROCHLORIDE ON THE CHICK EMBRYO

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SUMMARY

Two doses 7.5 and 15 mg/50g of Clindamycin Hydrochloride were injected into the egg yolk of embryonated eggs of hens on the 5th day of incubation. Consistent effects of Clindamycin were embryo lethality (100%), retardation of growth (10.3 to 10.7%), ectopic viscera (34.5 to 42%) and a low incidence of anomalies like thin debilitated toes and feet (7 to 10.7%) and alopecia respectively (24.1 to 35.7%) etc. Results suggest that exposure to Clindamycin would cause serious reproductive problems in avian species.

INTRODUCTION

The discoveries of Antibiotics have been among the great achievements of our time with therapeutic applications on both human and veterinary medicine. Subtherapeutic applications are widely used for disease prevention, growth promotion and feed efficiency in livestock and poultry production. Such a large use of antimicrobial agents are expected to have a great impact on human and animal health, agriculture, ecology and public health. Clindamycin hydrochloride (Dalacin C) is a semi-synthetic product by a 7 (S) chlorosubstitution of the 7 (R)- hydroxyl group of the parent compound Lincomycin. It is active against gram-positive aerobes and highly active against both gram-positive and gram-negative aerobic pathogens (Bonder et al., 1972) and easily absorbed from the intestinal tract (Lewis 1967 and Upjohn, 1987).

Experimental study showed that syrian hamsters are exquisitely sensitive to Clindamycin, as little as 1 gm./kg of Clindamycin given systemically

causes a fatal colitis. Also the application of Clindamycin topically daily to the shaved backs of syrian hamster in a hydroalcoholic vehicle (0.1 gm.) was lethal to more than half the hamster and 1 gm. to all the animals (Feingold et al., 1979). Rats administered Clindamycin in dose of 600 gm./kg/day for six months, had soft fecal pellets and high mortality rates while dogs orally dosed at 600 gm./kg/day for 2-6 weeks had vomiting and lost weight (Weber et al., 1978). Clindamycin readily crosses the placental barrier, besides, foetal liver can concentrate the drug (Philipson et al., 1973, 1976). Safety for use in pregnancy has not been established (Upjohn, 1987). Therefore this work is planned with the aim of establishing the effect of Clindamycin on the development of embryonating chicken eggs.

MATERIAL AND METHODS

Clindamycin hydrochloride (Dalacin c), 150 mg capsules Provided by Upjohn, Belgium, was reconstituted with sterile distilled water. The freshly Prepared solution was used all over the experi-

ment. Fertile eggs (approximately 50 g. weight) were obtained from the Faculty of Agriculture, Cairo University. The eggs were incubated, during this period they were kept under optimum conditions of temperature, humidity, air ventilation and turning of eggs. A total of 85 fertile Fayoumi eggs with 5 day old alive embryos were taken and divided into 3 groups of 28, 28 and 29 eggs respectively. The 1st group (control) eggs were injected 0.1 ml of sterile water in the yolk sac, the 2nd. and 3rd groups received 7.5 and 15.0 mg clindamycin/egg (1/20 and 1/10 therapeutic dose according to Upjohn (1987). The eggs were candled on alternate days post injection up to the 20th day of injection. At the end of incubation period embryos were inspected for deformities. Skeletal examination was carried out, using Alizarin red (s) according to Romeis (1948).

RESULTS AND DISCUSSION

The effect of Clindamycin on the development of

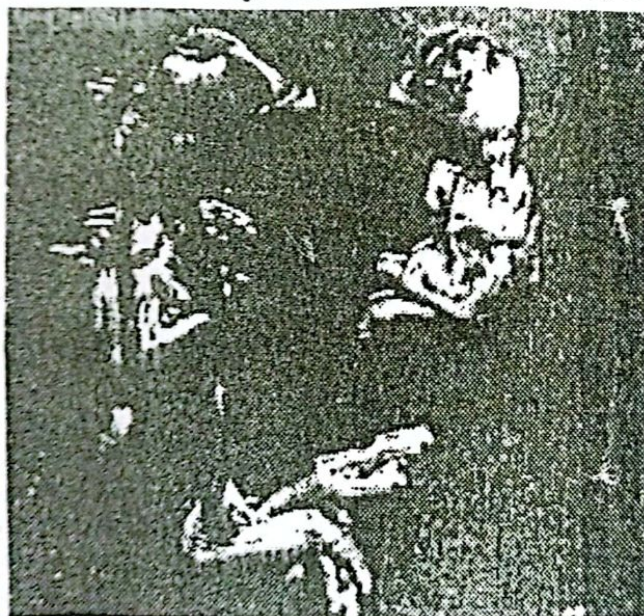


Fig.(1): Chick embryo showed dwarfed growth, thin debilitated toes and feet and alopecia (right) in comparison to control (left), both same age, 20 days.

chick embryo, injected in the yolk sac in dose of 15.0 mg and 7.5 mg/egg, in Fertile Fayoumi eggs was determined (Table 1). Both the doses caused death of all the experimental embryos. At 15 mg/egg dose level more embryos (26.67%) died by 8-12 day than those (16.67%) given 7.5 mg Clindamycin per egg. Between 13 to 20 days more than 50% embryos in both the groups died. Remaining eggs having died by full term of incubation.

Among abnormalities, ectopic Viscera was the most common, ranging from 34.5 to 42.9 percent at 7.5 and 15.0 mg/egg dose level. Retardation of growth and abnormally thin and debilitated toes and feet each accounted for 7 to 11 percent abnormalities. Miscellaneous deformities (general congestion of the Viscera, haemorrhagic patches of the lungs) were recorded. No skeletal abnormalities were detected.

Search of the available literature revealed no investigations concerning the teratogenic effect of Clindamycin in pregnant female. Kosa et al. (1985) mentioned that safety in gestating bitch has not been established also safety for use in pregnancy has not been established (Upjohn 1987). The concentration of the drug or its bioactive metabolites (N-demethyl Clindamycin and Sulphoxide) in foetal blood and tissue after the mother had received multiple doses were high than the mother when received a single dose. Philipson et al. (1973 and 1976) mentioned that Clindamycin is

highly bound to plasma protein (about 90%) in human. Moreover, Clindamycin crosses the placental barrier and foetal liver can concentrate the drug. Silverman et al. (1956) mentioned that highly bound drugs in the mother might play some role in the production of defects and in relatively high mortality rate.

Therefore, it is inferred that, the highly bound

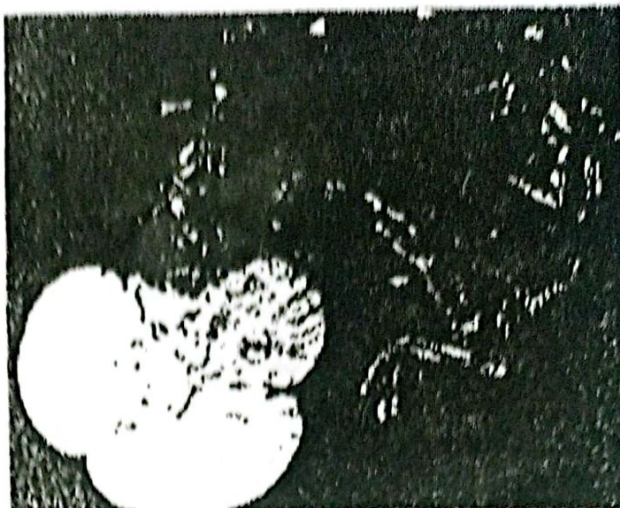


Fig.(2): Chick embryo showed Gastrochisis or defect of abdominal wall accompanied by protrusion of gizzard, intestine and liver (right) in comparison to control(left), both same age,20 days.

Fig.(3): Chick embryo showed delayed indrawing of yolk and retardation of growth (right) in comparison to control(left), both same age,20 days.

Table (1) : Showing Comparison between Clindamycin hydrochloride injected in a dose of 15 and 7.5 mg / egg and control group.

| Teratogenic effects | Control group | Clindamycin | |
|--------------------------------|---------------|-------------|------------|
| | | 15 mg/egg | 7.5 mg/egg |
| Total No . of eggs : | 28 | 28 | 29 |
| Death in shell full term | 2 | 5 | 8 |
| Death in shell 13 to 20 days | 1 | 15 | 16 |
| Death in shell 8 to12 days | None | 8 | 5 |
| Thin debilitated toes and feet | None | 3 | 2 |
| Retardation of growth | None | 3 | 3 |
| Ectopic viscera | None | 12 | 10 |
| Miscellaneous deformities | None | 10 | 7 |

Clindamycin to the plasma protein, its ability to cross the placental barrier and the high concentration of it in the foetal blood and tissue may affect the foetus and lead to fetal death together with malformations.

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