Validation Report

Compound: Trichlorfon

Reference: Kampo, M.A., Andrashko, V.V., Levaniuk, V.F., Gryzhak, I.P., The Effect of chlorophos on the energy metabolism in the placenta and organs of the intrauterine fetus. Pharmakol. Toksikol 2,208-210, 1975.

Area of Concern: Reproduction/teratology

Project Manager: George Bagley

Reviewer please respond below

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1. Test Methodology or Protocol ( ) Valid ( ) Not Valid
   Comments:

   The method section was very brief. The information presented was good as far as it went. No metion made of the method used to determine TCF in tissues.

2. Results, conclusions or summary ( ) Support ( ) Do Not Support Results or Conclusions of Paper
   Comments:

   1. Apparently statistical evaluation of the data was done. The decrease in fertility observed at 15 days but not at 29-30 days may be more of a reflection of the variable control values than a compound effect. If the control values really do run around 9.0±0.55, then an effect was achieved. One would have to know the range of values for that strain of rabbit before judgment could be made.

3. Additional Investigative Contacts or Supportive Literature Sources. (List and Summarize. Use Reverse Side or Additional Sheets If Necessary.)

K Diane Courtney
Reviewer's Signature

TEB/HERL
Branch

Oct 26, 1977
Date

2. Results (continued)

2. Of note was the observation that no malformations were produced.

3. The data concerning the day 15 oxygen consumption data are scant.

4. The day 29-30 oxygen ocnsumption data appear good with the exception that the brain did not show a dose dependent reaction. The lower dose produced a greater reduction of oxygen consumption than the higher dose.

5. The conclusion that the placenta was affected first and then the fetus was not supported by the data.

I think a good attempt was made in this paper; however, it lacks details and data.

THE EFFECT OF CHLOROPHOS ON THE ENERGY METABOLISM IN THE PLACENTA AND ORGANS OF THE ITRAUTERINE FETUS

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Most chemical poisons of organochlorine, carbamite and organomercuric nature have an embryotropic effect (T.K. Trifonov, et al, 1969; L.I. Komarova, 1970; L.V. Marston, 1967; I.P. Zhalbe et al; 1968; V.I. Vashakidze, 1966, 1970; A.I. Shteinberg and M.V. Ozhovan, 1971; V.A. Goncharuk, 1968; Mestitsova and Bero, 1966). Organophosphorous derivatieves are not insignicant for pregnant animals and their offspring (V.A. Gofmekler and B.B. Khuriev, 1971; V.A. Gofmekler and S.A. Tabakova, 1970; Horvath, 1966; Stewart and Finch, 1966). A widely used pesticide, chlorophos is one of the compounds whose effect on organism could be considered as a type of effect which is typical for both organophosphorous and organochlorine compounds. The purpose of the paper was to study the effect of different doses of chlorophos on some aspects of the energy metabolism in the placenta and organs of introuterine fetus.

RESEARCH METHODS

About 60 pregnant female-rabbits were used for the experiment. Aqua solution of chlorophos in a dose of 50mg/kg and 75mg/kg was administered into animals perorally through a sound daily starting on the first day of pregnancy. The control animals were fed with 10 ml of distilled water daily. The animals were killed with air embolism on

the fifteenth and sixtenth day and on the twenty-ninth and thirtieth day of pregnancy; the intensity of tissure breathing and chlorophos content were established in the placenta and in the organs of introuterine fetuses: liver, brain ,29-th day of pregnancy, or in granulated fetuses, 15-th day of pregnancy, using the direct manometer Varburg method. (A.A. Pokrovski and L.G. Ponomareva, 1965). General state of pregnant female-rabbits, the pregnancy course, number, weight and the state of introuterine fetuses were evaluated also.

RESULTS AND DISCUSSIONS

Chlorophos did not cause anomalies in the course of pregnancy (bleeding, miscarriages) or visible anomalies in development for 29-30 day old fetuses. Fertility decrease was observed on the fifteenth to the sixteenth day of pregnancy; 7.4 ± 0.43 , with a dose of 50mg/kg, and 7.0 ± 0.28, with a dose of 75mg/kg, fetuses against 9.0 0.55 for the control ($P > 0.05$ and > 0.01). These distinctions did not exist for the female-rabbits on the twenty-nineth or thirtieth day of pregnancy: 7.6 ± 0.63 and 7.5 ± 0.44 for the fetus against 8.3 ± 0.55 for the control ($P > 0.05$ and $P > 0.05$).

Poison was not detected in the placenta and in the fetus tissure. This apparently could be explained by either specific properties of the tissure under observation (especially placenta) causing fast decomposition of chemical poison to metabolites (undetected by this method) or this could be explained by insufficient sensitivty of the method.

Breathing of placenta tissures and fetus organs decreased when

affected by chlorophos. Maximum effect in the placenta (64%) was observed on the fifteenth or sixteenth day of pregnancy and it was caused by administration of chlorophos in a dose of 75 mg/kg. Maximum drop of oxygen absorption intensity was observed in the fetus liver on the twenty-nineth or thirtieth day of pregnancy. (See Table). This is understandable if one considers some hepatitis of chlorophos which can not only disrupt chemical processes governed by liver but they can also directly affect the functional state of the organ itself. (V.G. Tsapko, 1966).

The drop of tissure breathing intensity becomes more significant with the preparation dose increase or with prolongation of time of its effect on a pregnant female-rabbit. In this case, it is the placenta that is affected in the first place, at least at the early stage of pregnancy, and then introuterine fetus becomes affected also. All this can be explained by a barrier and trophyc function of the placenta. Disruption of oxidizing process observed in the placenta can prevent normal supply of oxygen and other alimentation to the fetus.

CONCLUSIONS

Thus, the intensity of tissure breathing in the placenta is disrupted as a result of chlorophos effect and organism on a pregnant female-rabbit; this leads to disruption of oxidizing processes for vitality important organs of fetus.

It is important to consider a possible embryotropic effect of chlorophos when it is used regularly and extensively for medical and agricultural disinfection.

TABLE 1

Intensity of tissure breathing of the placenta and intrauterine organs of fetuses observed on the twenty-ninth or thirtieth day of pregnancy for pregnant female-rabbits recieving chlorophos and for the control (in mkl of O_2 per 100 mg of weight tissure weight).

statistical index	control			chlorophos 50 mg/kg
	placenta	liver	brain	placenta
$\frac{n}{M \pm m}$ / P	10 35,82±1,49 —	10 49,62±4,72 —	10 48,13±2,74 —	10 24,24±2,12 <0,001

statistic. index	chlorophos				
	50 mg/kg		25 mg/kg		
	liver	brain	placenta	liv.	brain
$\frac{n}{M \pm m}$ / P	10 26,35±2,24 <0,001	10 41,01±1,19 <0,001	9 24,03±1,66 <0,001	9 30,97±3,52 <0,01	9 32,6±2,15 <0,001

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