THE EFFECTS OF DIOXIN EXPOSURE ON THE OCCURRENCE OF BIRTH DEFECTS: A CASE CONTROL STUDY AT TUDU HOSPITAL

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Introduction:

Dioxin (TCDD or 2, 3, 7, 8-tetrachlorodibenzo-para-dioxin) is a toxic contaminant from the herbicides, used widely by U.S Army in South Vietnam from1962-1971. During the Vietnam War, the U.S military sprayed a very large amount of herbicides on about 1.7 million hectares, 61 % of which was Agent Orange.[1,2,3] In Vietnam, Tudu Obstetrical and Gynecology Hospital has been doing 7 case-control studies to examine the relation between dioxin and birth defects, still births, miscarriage, male infertility, choriocarcinomas, hydatidiform mole, and ovarian tumors. We report here the first stage of our research on birth defects.

Methods:

This was a matched case control study. 372 cases were women who gave birth to children with birth defects at Tudu hospital. 730 controls were women who had healthy babies at Tudu hospital. Dioxin exposure was the exposure factor. We used Agent Orange spraying maps of the U.S. military during the Vietnamese War to define the exposed areas.[2,3] Based on subjects' domociles and time lived in the areas, we divided subjects into 5 of exposure levels:

-Level I*:* Subjects were exposed directly* and they lived in the exposed areas before 1975 with more than 15 years
-Level II*:* Subjects were exposed directly, and they lived in the exposed areas before 1975 with up to 15 years
-Level III*:* Subjects were exposed indirectly**, and they lived in the exposed areas before 1975 with more than 15 years.
-Level IV*:* Subjects were exposed indirectly, and they lived in the exposed areas from 1980 (or level III but less than 15 yrs)
-Level V*:* Subjects weren't exposed and didn't live in the exposed areas.

* Physically present in the areas during the time of being sprayed and had direct skin contact with exposure.
** Physically present in the exposed areas but not during the time of being sprayed and haven't had direct skin contact with exposure.

Data was collected in Tudu hospital. We conducted in-depth qualitative interviews with subjects during their early post partum period.

Result:

From May to December 2001, 372 cases were recruited from over 22,791 births. 1.63% was the birth defect rate for Tudu hospital. We found the category of face or head defects was highest among the birth defects (38.4%). Next were the birth defects relating to the alimentary (22.5%) system. The other birth defects were 39.1% as shown on table 1.

Table 1: Birth defects at Tudu Hospital 2001.

Birth defects	Number of cases =372	Percentage of total birth defects
1. Face, head	142	38.4%
2. Spinal	12	3.1%
3. Limb	19	5.2%
4. Down syndrome	20	5.5%
5. Alimentary system	84	22.5%
6. Respiratory system	10	2.8%
7. Urogenital system	29	8.3%
8. Other birth defects	72	19.4%

Table 2: Characteristics of the current pregnancies:

Characteristics	Cases (n=372)	Controls (n=730)
Internal diseases before pregnancy	8 (2.1%)	34 (4.6%)
Internal diseases during pregnancy	28 (7.6%)	56 (7.5%)
Syphilis positive test	1 (0.3%)	0 (0%)
Hepatitis B positive test	6 (1.7%)	21 (2.9)
HIV testing positive	3 (0.7%)	0 (0%)
Mean gestational age	28.5±7.5wks	39.2±1.6wks
Delivery methods*:*		
C-section	57 (15.3)	45 (6.1%)
Extraction delivery	5 (1.4%)	61 (8.3%)
Spontaneous	310 (83.65%)	624 (85.6%)
	17 (4.5%)	10 (1.5%)
Multiple pregnancy		
Mean birth weight	1576 ± 1053g	3165 ± 381g
Gender:		
Male	185 (49.8%)	364 (49.8%)
Female	165 (44.3%)	366 (50.2%)
Unclear	22 (5.9%)	0 (0%)
	89 (24%)	730 (100%)

After delivery, the survivor rate beyond one day in the control group was 100% while the survivor rate in the case group was 24%. We should consider the surival rate of the cases because, within 7 months, the 89 abnormal babies were entered into society from Tudu hospital (Table 2). They will be a burden for not only their families but also for society.

Table 3: Past history of risk factors relates to pregnancy

	Cases (n=372)	Controls (n=730)
Drinking	9 (2.4%)	4 (0.5%)
Smoking	3 (0.7%)	1 (0.2%)
Chemical contacting	19 (5.2%)	5 (0.7%)
Using medicine for chronic diseases	20 (5.5%)	20 (2.7%)

The rate of alcohol drinkers in the cases group was not high, but it was higher than those of drinkers in the control group (2.4% vs. 0.7%). The difference was obvious when looking at the subjects' past history of harmful chemical contact (5.2% versus 0.7%). The same was found when we investigated the subjects' past history of using medicine for their chronic diseases such as goiter, sedatives, epilepsy, and anti-coagulation medicines. 5.5% of cases were users, but only 2.7% of controls were user of these medicines (Table3)

Table4: The relation between the exposure levels and birth defects:

Exposure levels	**Cases**	**Controls**	**OR**	**P value**
Level I&II	19	3	15.18 (4.2-65.21)	0.001
Level IV	61	96	1.52 (1.04-2.22)	0.02
Level IV	98	166	1.42 (1.04-1.93)	0.02
Level V (Ref)	194	465	1	*

Because group I and group II (Level I & II) both had small numbers, we combined them in a group called "Group I&II" in Table 4.

Subjects who were in the exposed level I & II are 15 times more likely to have babies with defects than subjects who weren't presumed to have any exposure. On the other hand, women who had ever potential direct contact with dioxin during the war in South Vietnam are 14 times more likely to have babies with birth defects than women who had never been exposed.

Subjects who were in the exposure level III are 1.52 times more likely to have babies with defects than subjects who weren't potentially exposed at all. On the other hand, women, who didn't have direct contact with dioxin during the war but lived in exposed areas more than 15 years and before 1975, are 1.52 times more likely to have babies with defects than women who had never been exposed.

Subjects who were in the exposure level IV are 1.42 times more likely to have babies with defects than subjects who weren't exposed at all. On the other hand, women, who didn't have direct contact with dioxin during the war but lived in potentially exposed areas after 1980, are 1.42 times more likely to have babies with defects than women who had never been exposed.

Discussion:

This report is a part of our research that was planned to be completed on December 2002. Data were collected and analyzed within 7 months from May 2001 to December 31 including 372 cases and 730 controls. The study is intended to provide information regarding possible dioxin risk factors for birth defects so that this information may be used in future studies and interventions. This study suggests an association between dioxin exposure and birth defects. We will apply the results found in caring for all pregnant women in our Primary Health Care. We will document for all Health Units different average dioxin levels where the exposed pregnant women should be provided with more health monitoring and care. This long–term monitoring will limit the pregnancies with malformations. Diagnosis will be made sooner of pregnancies with fetal defects, so health providers can intervene in a timely and suitable manner .[4,5]

This is ongoing research. More data need to be collected for examining relation between the exposure and each specific kind of birth defects. More samples are expected which will enhance the study power. Then we will use logistic and multilevel regression to assess causal relation separately by dioxin and each category of birth defect. This analysis model will be used for controlling confounder factors and for measuring the effect modification.

Past exposure variables may be subject to recall bias, but attempts have been made to make questions easier to answer and a pilot study was conducted to determine the feasibility of the birth defect questions. However, this issue still remains in our research. Due to lack of funding and other considerations, dioxin blood analyses was not using for estimating exposure level. We hope this biological and evidences will better estimate of dioxin and validate our surrogate of exposure, fixed wing aircraft spraying records, in the next stage of our study.

Reference:

1. 10-80 Committee, Vietnam. 1980's. Basis investigation on the exposed areas.
2. Clark Smith, Don Watkins. 1993. Vietnam Map Book
3. US Army. "Joint Services Environmental Support Group" Services Herbs tape 12 September 1985.
4. L.C.Dai, L.B.Thuy, H.K.Chi, N.T.B.Tuyet, N.T.Hue, N.T.Ly, T.V.Hien, V.T.T. Nhu, N.L.Cung N.T.Lan. 1995. Statistical data of Birth defects at Bien Hoa–Thu Dau Mot-Vung Tau City. 10- 80 Committee document.
5. N.T. N. Phuong, L.T.D.Huong. 1983.The effects of Chemical Agent on pregnancies, basic epidemiology investigation on the South Vietnam's provinces. Long term effect of chemical war on South Vietnam. 10-80 committee, chapter III, p63-68.
6. Schecter A.J., Dai L.C., Bao T.V., Päpke O. Semen and blood dioxin and dibenzofuran levels in Vietnamese and Americans. 1981. Organohalogen compounds.Vol.38.1981.171– 174.
7. Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides. Veterans and Agent Orange, update 1996. National Academy Press. 1997, p1-14, p15-36.
8. Devito M.J., Birnbaun L.S. 1994. Toxicology of Dioxins and Related Chemicals. Dioxin and Health. Schecter A..Plenum Press, New York. 139 – 155
9. Erickson J.D., Mulinare J., Mc Clain P.W., et al. 1984. Vietnam veterans' risks for fathering babies with birth defects. JAMA. 1984, 252, 903 – 912
10. Mastroiacovo P., Spagnolo A., Marni E., Meazza L., Bertollini R.,1988. Segni G. Birth defects in the seveso area after TCDD contamination. JAMA. 1988, 259, 1668 – 1672.
11. Oklahoma Agent Orange Foundation. Vietnam map book – a self help guide to herbicide exposure. 1981.
12. Schecter, A., O. Papke, M. Ball, Hoang Dinh Cau, Le Cao Dai, Nguyen Quang Ming, Hoang Trong Quynh, Nguyen Ngoc Thi Phuong, Pham Hoang Phiet, Huynh Kim Chi, Dieu Thieu Vo, J.D. Constable and J. Spencer 1992. "Dioxin and dibenzofuran levels in blood and adipose tissue of Vietnamese from various locations in Vietnam in proximity to Agent Orange spraying," Chemosphere, 25(7-10):1123-1128.
13. Schecter, A., Le Cao Dai, Le Thi Bich Thuy, Hoang Tri Quynh Minh, Hoang Dinh Cau,Pham Hoang Phiet, Nguyen Thi Ngoc Phuong, J.D. Constable, R. Baughman, O. Papke, J.J. Ryan, P. Fürst and S. Raisanen. 1995. "Agent Orange and the Vietnamese: the persistence of elevated dioxin levels in human tissues," American Journal of Public Health, 85(4): 516-522.
14. Schecter A, Dai L. C., Papke 0, Prange J, Constable J. D., Matsuda M., Thao V. D., Piskac A. L. 2001. Recent dioxin contamination from Agent Orange in residents of a southern Vietnam city. Journal of Occupational and Environmental Medicine, May 43(5): 435-443.