Agent Orange health related outcomes of population living in herbicides sprayed area of Quang Tri Viet Nam by Epidemiological cohort study

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Abstract

Well designed retrospective cohort study was carried out in the South herbicides sprayed Cam Chinh commune, Cam Lo district, Quang Tri province, and in the North unsprayed Cam Phuc commune, Cam Xuyen district, Ha Tinh province with samples size of 4087 and 3832persons. Combining to epidemiological survey, the environment assessment was taken, soil samples, bio- and human samples were collected for 2,3,7,8-TCDD residuals analyzing.

The results of the study suggest that in present time, AO/Dioxin is resided at high concentration in the samples taken of former installation location, in level of 14, 18 pg/g. Statistically analytical result of disease model shown that area applied herbicide have high risk of disease belong to bone connective system, genitourinary, blood endocrine, skin and increases risk of infectious disease. That corresponds to estimations from previuos research. *The pathologies with sufficient evidence* to be considered of Agent Orange/Dioxin exposure related are: Sciatica, Chronic sinusitis, Angina pectoris, Low back pathology, Dermatosis palpulosa nigra.

Introduction

During the chemical war from 1962 to 1971, the US military sprayed more than 19 million gallons of herbicides over the land of South Viet Nam, among them there was 11 million gallons Agent Orange (AO), that contaminated unwanted highly toxic compound, 2,3,7,8-TCDD, dioxin².

Dioxin may cause harmful effects on the whole body, and can affect separately the functioning of systems, such as nervous system, immune responses, carcinogenicity, hepatotoxicity, metabolic toxicity, enzyme toxicity^{1,5,6}

The studies on the effects of Agent Orange have shown an association between exposure to herbicides and longlasting effects on human health ^{3,4} But these studies had some limitations; like the exposure assessment was mainly historical of spraying archivement and interviewing but not analytical; the study errors like chance, bias, and confounding poorly ruled out with reasonable confidence.

In order to provide a deep insight into the relation between exposure to AO/Dioxin health outcomes, surmount the mentioned limitations, these conducted study based on strictly epidemiological disciplines for the assessment of exposure and health related outcomes.

Materials and Methods

Subjects:

Cases are the people, living in sprayed Cam Chinh commune of Quang Tri province, in sample size of 4087 Controls are the people living in unsprayed Cam Phuc commune, Ha Tinh province, in sample size of 3832 Both are located in the central of Viet Nam, with the relatively similar socio-economic circumstances.

Methods:

An Environmental Exposure Assessment had been taken, soils, sediments, and animal tissue samples, based on the digitalized map of herbicides spraying. All of these samples were analyzed for TCDD in Japan

A Cohort Retrospective survey, based on epidemiological interviewing was implemented by highly trained nurse-interviewers. Information collected included personal habits comprising smoking, alcohol drinking, contraceptive drug use, history of pesticide contacting, status of health, reproductive health. The children under 16 ages and congenital deformities was checked by local pediatricians

The human samples, blood, breast milk, fat tissue were collected for residual TCDD analysis.

Methodology approarch: data were processed and analyzed by EPIINFO 6.04, STATA 7.0 softwares, using stratified analysis, multiple logistic regressions, the results evaluated in correspondence with the epidemiological disciplines, as follow:

- The statistical relation between AO/Dioxin Exposure and the Health Outcomes: RR/OR; CI; p value.
- Errors removing/or restricting (chance, bias, and confounding)
- Cause-effect relationship verifying, giving the overtop for Strength of Association, Consistency of Association, Biologic Plausibility,

Study limitations:

The research is still limited in proceeding of implementing, because the individual health information collecting is not perfect enough due to the health record management and archive was not well done. And the interviewing has some difficulties since the knowledge of residences is still restricted.

Results and Discussion

Environmental Assessment

Although chemical war has stopped for over 30 years, dioxin still in residuals in some soil samples from former military installation of sprayed Cam Chinh, in low concentration level, that satisfy guidelines for agriculture usage as planting, livestock breeding, aquatic cultivating, excluding soil sample of former instalation Khe Ram. Analytical results of biosamples produced in study area shown that it was not identified existence of 2,3,7,8-TCDD in that excluding several congeners with micro toxic level and low concentration. Thus all analyzed samples are not contaminated by Dioxin and obtain safety standard for human food.

Epidemiological results

Structure of Illness:

The results of the study show the statistically significant differences of disease incidences between exposed Cam Chinh and unexposed Cam Phuc populations (48.6% versus 42.2), RR=1.15; CI. 1.11-1.21; p<0.001. *Table 1:* Disease incidences of investigated peoples

Diseases of	Exposed $(n = 4087)$		UnExposed ($n = 3832$)		$\mathbf{DD}(\mathbf{CL})$	
	Frequency	Incidence (%)	Frequency	Incidence (%)	RR (<i>CI</i> .)	р
Nervous system	366	8.9	323	8.4	1.1 (0.92-1.23)	<0.5
Circulatory system	125	3	95	2.5	1.23 (0.95-1.61)	>0.5
Digestive system	187	4.6	159	9.8	1.1(0.9-1.36)	>0.5
Respiratory system	202	4.9	346	9	0.55(0.46-0.65)	< 0.001
Connective tissue	406	9.9	265	6.9	1.44 (1.24-1.67)	<0.01
Genitourinary system	95	2.3	63	1.6	1.41(1.03-1.9)	< 0.05
Skin & subcut. tissue	143	7.4	101	2.6	1.33 (1.03-1.71)	< 0.05
Blood & Endocrine	84	2.1	29	0.6	2.7(1.75-4.1)	< 0.001
Teeth, mounth, eyes	130	3.2	89	2.3	1.37(1.1-1.79)	<0.01
Infectious	117	2.9	63	1.6	1.74 (1.29-2.36)	< 0.001
Unmalignant tumour	37	0.9	31	0.8	1.12 (0.7-1.8)	>0.05
Cancer	29	0.7	16	0.4	1.7(0.9-3.12)	>0.05
Incidence /person	1.5		1.2		$X^2 = 0.64$	< 0.05

Detailed diseases by systems

Nervous system:

Neurasthenia takes a highest proportion.

The second are the disorders of peripheral nerves system, there is an unclear increasing in Cam Chinh. Following are diseases such as inflammation of peripheral nerves, schizophrenia, transient cerebral ischaemic attacks & related syndromes.

Circulatory system:

The most occuring is angine pectoris in elevated rate of angine pectoris in Cam Chinh Following are hypotension, hypertension, myocardial inaction, heart arrhythmia.

Digestive system:

The diseases with high frequency are gastritis & duodenitis, ulcerative colitis, intestinal malabsorption. chronic viral hepatitis that can lead to hepatic sclerosis, liver cancer disease increases in Cam Chinh.

Respiratory system:

The high rate belongs to diseases of chronic sinusitis, chronic bronchitis, pneumonia.

Musculoskeletal-connective tissue system:

There are significantly increasing rates of dorsalgia, sciatica, low back pain, arthrosis, ankylosing spondylosis.

Genitourinary system:

Data of the research indicates that diseases of highest rate are calculus of kidney & ureter, urinary tract infection, inflammation of female genital tract, however the difference is not statistically enough.

Primary infertility has occured in Cam Chinh.

Skin diseases:

Dermatosis palpulosa nigra that is detective disease of exposed dioxin increases in Cam Chinh Following are urticaria, prurigo, atopic dermatitis...

Endocrine diseases:

It is observed that goiter disease counts for highest incidence, an exceeding of goiter happened statistically in Cam Chinh in comparing to Cam Phuc.

Diseases of teeth, mouth, eyes:

Generally, disease of these organs as subjective visual disrurbances, diseases of pulp and periapical tissues, conjunctivitis, hearing loss occured undifferently.

Infectious diseases:

Malaria disease is defined with exceeding rate in Cam Chinh compared to Cam Phuc, infected worm, tuberculosis, bacterial menningetis, typhoid & paratyphoid fevers is equal in 2 communes. *Benign noeplasms:*

Benign neoplasms of skin takes a highest rate, following by haemangiomas & lymphangioma, benign noeplasms of breast... without of difference in 2 communes.

Malignant neoplasms:

The high rates are liver cancer, the cancer of stomach, uterus, ovavy in exposed Cam Chinh

Disease's incidence by period of time

In unsprayed commune Cam Phuc, there almost is not change in disease incidence during 40 years, from 1960, before chemical war to study time. While in sprayed Cam Chinh, there is considerable change of incidence, that raised since 1961, reached maximum at years of 81-90, and then come down to the level as before the war.

In Cam Phuc disease's distribution by time duration of 10 years is not distinct. In contrary, in Cam Chinh the incidence of disease is distinct from time duration after chemical war. Disease increased sharply in period of 71-80, 81-90 and go down to ordinary level as period before the war.



Figure 3: Disease's incidence by period of time

Diseases	Exposed	Unexposed	RR	CI. 95%	Р	AFe
Angine pectoris	1.27	0.63	2.03	1.25-3.29	< 0.01	50.8
Chronic sinusitis	1.84	0.73	2.51	1.63-3.88	< 0.001	60.2
Dorsalgia	3.57	1.88	1.9	1.44-2.51	< 0.01	47.4
Sciatica	2.30	1.20	1.92	1.35-2.72	< 0.01	47.8
Low back pain	1.22	0.39	3.13	1.76-5.56	< 0.01	68
Dermatosis palpulosa nigra	0.51	0.21	2.46	1.1-5.6	< 0.05	59.4
Liver cancer	0.20	0.03	7.5	0.9-3.52	< 0.05	

Table 12: Pathologies with sufficient evidence to be considered of Agent Orange/Dioxin exposure

Conclusion

War Agent Orange/Dioxin pollution till to now become the potential risk on human health, that have made the significant differences of diseases structure between the exposed and unexposed populations. The results of research indicated that there is clear connection between AO/Dioxin exposure with elevated rate of some kind of health pathology, such as diseases of bone connective, RR=1.44, CI.1.24-1.67, p<0.001; genitourinary, RR=1.41, CI. 1.03-1.71, p<0.05; blood endocrine, RR=1.74, CI. 1.29-2.36, p<0.001; and skin diseases, RR=1.33, CI. 1.03-1.71, p<0.05.

The pathologies with sufficient evidence to be considered of Agent Orange/Dioxin exposure related are:

Sciatica: RR = 1.92 (1.35-2.72); AFe = 47.8 %

Chronic sinusitis: RR = 2.51 (1.63-3.88); AFe = 60.2 %

- Angina pectoris: RR=2.03 (1.25-3.29); AFe=65%
- Low back pathology: RR = 3.13 (1.76-5.56); AFe = 68 %
- Dermatosis palpulosa nigra: RR = 2.46 (1.1-5.6); AFe = 68 %
- *The factors, as:* age, sex, family economy, wine drinking, smoking, pesticides using have contributed to raise the incidence of diseases, but they are not the confounding factors in this study by stratified and logistic regression analysis
- In generally, the females have higher rate of diseases than males, especially exposed females with significant rates, compared to unexposed woman.
- *Compared to veteran* population of heavy exposure, the strength of differences of nervous and skin outcomes has decreased, and the incidence of cancers is not significant enough.

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