AN EVALUATION OF CARDIOVASCULAR OUTCOMES AMONG U.S. WORKERS EXPOSED TO 2,3,7,8-TCDD-CONTAMINATED SUBSTANCES

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1. Introduction

The evidence for an association between 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure and adverse effects on the cardiovascular system is conflicting. Data from three mortality studies suggest that TCDD exposure may be associated with an increased risk for cardiovascular disease mortality [1)2)3)]. Several other mortality studies of TCDD-exposed occupational cohorts did not find a significantly elevated risk for cardiovascular disease [4)5)6)7)8)]. Although several cross-sectional medical studies have also examined the association between TCDD exposure and effects on the cardiovascular system [9)10)11)12)13)], statistically significant associations were found only in the study of U.S. Air Force Ranch Hand personnel responsible for spraying TCDD-contaminated Agent Orange in Vietnam [9)]. Although the overall conclusion from the Ranch Hand study was that there was no apparent association between cardiovascular disease and TCDD exposure, an elevated risk was observed for peripheral pulse abnormalities in four vessels, medical record-verified hypertension, and non-specific ST- and T-wave changes on ECG. In addition, findings from cross-sectional medical studies suggest that TCDD exposure may be associated with several risk factors for cardiovascular disease, including disorders of lipid metabolism [9)10)14)], and glucose intolerance [9)15)]. This paper provides a brief report of the cardiovascular findings from a large cross-sectional morbidity study of TCDD-exposed workers formerly involved in production of 2,4,5-trichlorophenol (2,4,5-TCP) or one of its derivatives

2. Methods

As part of a cross-sectional medical study of workers employed at least 15 years earlier in the manufacture of 2,4,5-TCP or one of its derivatives at two U.S. chemical plants, we examined the association between TCDD exposure and various cardiovascular outcomes. Information on worker and referent health status was collected through a comprehensive set of standardized interviews and medical examinations. The medical examinations included a general physical examination (including blood pressure measurement in each arm while the participant was seated), Doppler examination of the peripheral pulses, chest X-ray, and electrocardiogram (ECG). The

cardiovascular outcomes of *a priori* interest were myocardial infarction, angina, arrhythmia, hypertension, and abnormal peripheral arterial flow. Myocardial infarction and arrhythmia were considered present if the participant reported that a physician had diagnosed this condition, or the participant had ECG evidence for the condition. A participant was defined as having hypertension if the participant had a self-reported history of physician-diagnosed hypertension, or if an elevation was detected in either the systolic (>140 mm/Hg) or diastolic pressure (>90 mm/Hg) on examination. A participant was defined as having APAF if either the resting index, the recovery index one minute post occlusion, or the recovery index two minutes post occlusion was less than 0.97 in either leg [16)17)]. Finally, angina was defined as a self-reported history of physician-diagnosed angina. To evaluate the association between TCDD exposure and each of the cardiovascular outcomes of *a priori* interest, unadjusted odds ratios were calculated and tested for significance using a chi-square test, and adjusted odds ratios were determined using logistic regression analyses.

3. Results

A total of 281 workers and 260 unexposed referents participated. The workers had substantial exposure to TCDD, as evidenced by significantly elevated mean serum TCDD concentration of 220 pg per gram of lipid, compared with 7 pg per gram of lipid among the referents. No association was found between TCDD exposure and any of the cardiovascular outcomes that were investigated, including myocardial infarction, angina, cardiac arrhythmias, hypertension, and abnormal peripheral arterial flow.

4. Discussion and Conclusions

Our data do not support an association between long-term, high-dose TCDD exposure and any of several adverse cardiovascular outcomes. Although our study had sufficient power to detect a 1.5-fold elevation in risk for cardiac arrhythmias, hypertension, and abnormal peripheral arterial flow, our study had low power (approximately 50%) to detect a similar elevation in risk for myocardial infarction and angina.

One explanation that should be considered in interpreting negative results in cross-sectional studies may be the "participation bias" from those affected with severe or fatal cardiovascular disease being incapable of participating [18)]. For this explanation to be true, one would expect to see elevated cardiovascular disease mortality among the cohorts from the two chemical plants studied. Workers from the two plants in our study were included in a large cohort mortality study of U.S. workers involved in the production of TCDD-contaminated substances [4)]. The study by Fingerhut et al. [4)] did not find an elevated risk for either cardiovascular disease mortality or ischemic heart disease mortality in either plant, even among those with the highest durations of exposure (personal communication, 1990). Furthermore, to assess the potential magnitude of participation bias in our study, a phone interview was attempted with all of the workers who refused to be examined, and a sample of referents who did not participate. The proportion of examined and refusant workers who reported a history of myocardial infarction, or angina were not statistically significantly different. Similar results were found for the referents. These results suggest that participation bias is not responsible for our study findings.

In conclusion, our study found that workers with high occupational TCDD exposure at least 15 years earlier, many of whom continued to have persistently elevated TCDD body burdens, had no increased risk for any of the cardiovascular outcomes that we investigated. Our findings are consistent with other cross-sectional medical studies of TCDD-exposed individuals. Although several mortality studies of TCDD-exposed cohorts found significantly increased risks for cardiovascular disease mortality, similar increased risks were not observed in other mortality studies. The data available do not provide definitive conclusions but indicate that further examination of the association between TCDD exposure and cardiovascular disease should be pursued.

5. References

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