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Effects of TCDD [2,3,7,8-Tetrachlorodibenzo-P-Dioxin (TCDD)] on the Early Stage of Pancreatic Carcinogenesis Induced by Azaserine in the Rat Pancreas

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Abstract: TCDD (2,3,7,8-tetrachlorodibenzo -p-dioxin), an addictive substance in cigarettes, has been implicated in the pathogenesis of pancreatic carcinoma. This compound has not been tested previously for carcinogenicity towards the pancreas, although TCDD is a known liver carcinogen. The present study was designed to ascertain whether TCDD may have a promoting effect on the development of precursor pancreatic lesions on the rat exocrine pancreas. For this purpose, 30 out of a total of 60 male Leeds rats aged two weeks received a single weekly i.p. injection of azaserine (30 mg/kg body weight) for 5 weeks. The rest of rats (n=30) were used as control groups during the injection period. At 6 weeks of age, azaserine-initiated (n=30) and untreated control (n=30) rats were divided into 4 groups separately each, as follows; Group: 1, UnCt (Untreated control rats) (n=15); Group 2, AzCt (Azaserine-initiated control rats) (n=15); Group 3, TCDD (untreated normal rats fed TCDD, 0.038 µg/kg diet TCDD) (n=15); Group 4, AzTCDD (Azaserine- initiated rats fed TCDD, 0.038 µg/kg diet TCDD) (n=15) for 6 months. Rats were killed and pancreata weighed and prepared for quantitative histologic analysis of atypical acinar cell foci (AACFs), which are putative preneoplastic lesions. Both the number and size of AACFs were analysed. In rats fed TCDD, the ACFF burden was higher than in control rats ($P<0.05$). TCDD feeding to rats injected with azaserine led to a significant increase in AACF burden over control values. The increased size and number of acidophilic AACF of rats fed TCDD (Group 3) and the pancreata of AzTCDD treated rats fed TCDD (Group 4) may indicate an enhancing effect of TCDD. This limited experiment suggests promoting effects of 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD), but further studies of longer term and with large doses of TCDD are needed to allow the assessment of whether TCDD affects growth of azaserine induced preneoplastic pancreatic lesions.

Key Words: TCDD, azaserine, pancreas

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