FAECAL AND PERCUTANEOUS ELIMINATION OF TCDD IN TWO PATIENTS WITH CHLORACNE, AND ENHANCEMENT OF FAECAL EXCRETION WITH OLESTRA, A FAT SUBSTITUTE

Alexandra Geusau[1], Michael Meixner[1], Steffen Sandermann[1], Erwin Tschachler[1], Georg Stingl[1], Eva Valic[2], Christian Wolf[2], Hugo Rüdiger[2], Ronald Webb[3], Olaf Päpke[4] and Michael McLachlan[5]

[1] Department of Dermatology, Division of Immunology, Allergy and Infectious Diseases (DIAID), University of Vienna Medical School, Währinger Gürtel 18-20, 1090 Vienna, Austria.
[2] Department of Internal Medicine IV, Division of Occupational Medicine, University of Vienna, Medical School, Vienna, Austria.
[3] Procter and Gamble Company, Cincinnati, Ohio, USA.
[4] ERGO Forschungsgesellschaft GmbH, D-22305 Hamburg, Germany.
[5] Baltic Sea Research Institute Warnemünde, Rostock, Germany.

Introduction

Chloracne, the most sensitive clinical marker known for a former exposure to polychlorinated compounds in humans, led to the diagnosis of a severe 2,3,7,8-TCDD intoxication in two patients in Vienna in the spring of 1998. The patients had the highest blood levels ever measured in adults (144,000 and 26,000 pg/g blood lipids respectively). There is no established treatment for either chloracne or for detoxification of this highly lipophilic compound, which has an estimated half life of 7 years, accumulates in fat tissue, and is hardly metabolised (*1,2*).

Recent work has shown that excretion of native 2,3,7,8-TCDD via the faeces is a major elimination mechanism for contaminated individuals (*3*). Furthermore, the ingestion of Olestra, a dietary fat substitute, has been found to increase the faecal excretion of this compound (*4*). The aims of the current study were to establish whether the elimination of 2,3,7,8-TCDD can be significantly increased by the ingestion of Olestra, to investigate the role of excretion through the skin as a loss pathway, and to assess the potential to increase this excretion by applying petrolatum to the surface of the skin.

Materials and Methods

During a period of 38 days the patients received potato chips containing Olestra ('PRINGLES fat free', 28 g chips contained 10 g Olestra) provided by the Procter & Gamble Company, in varying dosage and application regimens. On days 4-6 of each 7-day regimen stool was collected, pooled, and analysed for 2,3,7,8-TCDD. As a control, stool was investigated from the Olestra-free periods before and after the trial. In addition, a skin test was carried out. On the back of each patient 12 fields were marked. Petrolatum was applied on every second field, and subsequently the fields were covered with Goretex. On days 1, 4, and 7 two of the fields with and two without petrolatum were uncovered and cleaned. The covering and cleaning materials were retained and analysed for TCDD. In addition, the blood levels of TCDD and the body weight of the patients were monitored over a period of 8 months. All of the analyses were performed by the ERGO Forschungsgesell-schaft using methods that had been internally and externally validated in international interlaboratory comparisons (*5-6*).

Results and Discussion

A pronounced faecal excretion of native TCDD of on average 130 ng/d and 29 ng/d was observed for both patients prior to starting the Olestra experiment. When Olestra was added to the diet, there was a dose dependent linear increase of faecal TCDD excretion in the first patient, whereas in the second a saturation effect beyond a daily Olestra intake of 33 g (90 g Chips) was observed. At the highest Olestra dose the intestinal excretion of TCDD was elevated by a factor of 10 in the first patient and a factor of 8 in the second patient compared to the excretion prior to starting the Olestra experiment. This showed that faecal elimination of TCDD does occur and that this elimination can be markedly increased by ingestion of Olestra. This is in agreement with previous work (*3-4*).

TCDD was clearly detectable in the skin lipid/scales collected in the Goretex covers and cleaning material from the skin experiment. A linear relationship between the length of the sampling period and the amount of TCDD was observed in both patients. The daily elimination rate of TCDD via the skin was estimated by multiplying the average quantity per cm^2 and day measured in skin lipids/scales from the back by the total skin surface area of the patients. The resulting fluxes of 44 ng/d for the first patient and 13 ng/d for the second patient demonstrate that percutaneous excretion is a TCDD elimination mechanism of similar magnitude to faecal excretion. However, a marked enhancement of this excretion pathway was not achieved; the skin that was treated with petrolatum yielded only slightly higher TCDD fluxes than the untreated skin.

The relative contribution of faecal excretion and loss via the skin to the overall elimination of TCDD will be discussed along with the overall effect of the Olestra therapy.

Acknowledgements

We thank the patients for their active participation in the study and Andreas Moser for sharing his experience on the gastrointestinal absorption and elimination of PCDD/Fs in humans.

References

1. Flesch-Janys D., Becher H., Gurn P., Jung D., Konietzko J., Manz A., Päpke O.; *J. Toxicol. Environ. Health* **1996**, 47, 363-378.
2. Michalek J.E., Pirkle J.L., Caudill S.P., Tripathi R.C., Patterson D.G., Needham L.L.; *J. Toxicol. Environ. Health* **1996**, 47, 209-220.
3. Rohde S., Moser A., Päpke O. and McLachlan M.S.; *Chemosphere* **1999**, 38, 3397-3410.
4. Moser A. (Thesis), Absorption und Exkretion persistenter lipophiler Umweltschadstoffe im Gastrointestinaltrakt des Menschen. University of Bayreuth, **1998**.
5. Päpke O.; *Organohalogen Compds* **1997**, 31, 212-214.
6. Päpke O., Ball M., Lis A. and Scheunert K.; *Chemosphere* **1989**, 19, 941-948.