IS THERE A CORRELATION BETWEEN CAFFEINE ELIMINATION RATE FROM SALIVA AND DIOXIN CONCENTRATION IN BLOOD OF CHILDREN?

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1. Introduction

In humans caffeine is mainly metabolized to paraxanthine (1,7-dimethyl-xanthine) by the cytochrome P 450 (CYP 1 A2) dependent monooxygenase system [1]. This enzyme system is closely related to CYP 1 A1, which is inducible by several xenobiotics like polycyclic aromatic hydrocarbons (PAH) or polychlorinated dibenzodioxins and dibenzofurans (PCDD/PCDF). There exists a cross linked relationship of both monooxygenase systems, CYP 1 A1 and CYP 1 A2, respectively, regarding the inducibility of both systems by PAH or PCDD/PCDF. The normal burden with these xenobiotics may already increase the activity of CYP 1 A1 and CYP 1 A2, thus leading to a shortening of the caffeine elimination rate. It is well known from literature as well as from studies in our laboratory that cigarette smoking shortens the half life ($t_{0.5}$) of caffeine elimination.
In adults, cigarette smoking shortens $t_{0.5}$ of caffeine from about 5.0 hours (non smokers) to about 2.5 hours (smokers). It is suggested that this increase in the caffeine elimination rate is mainly caused by PAH in cigarette smoke, which are known as strong inducers of CYP 1 A1 and CYP 1 A2 monooxygenases. In the present work the influences of PCDD/PCDF on $t_{0.5}$ of caffeine was studied. Only few persons were available for participation in this study. These persons lived on a PCDD/PCDF contaminated ground and it was supposed that this contamination would lead to higher blood levels of PCDD/PCDF than in controls living on an uncontaminated ground.
We got the chance and permission for the determination of the caffeine elimination rate and to correlate the $t_{0.5}$ values of caffeine with the corresponding PCDD/PCDF values (I-TEQ) in blood of these persons. The aim of this study was to find out, whether higher I-TEQ of PCDD/PCDF correlate with shorter $t_{0.5}$ of caffeine indicating an enzyme induction of CYP 1 A1 and CYP 1 A2 monooxygenases.

2. Methods

2.1 Characteristics of the collectives

In this study participated 8 adults (3 women, 5 men) and 9 children (4 girls, 5 boys). The PCDD/PCDF analysis was performed by ERGO scientific group, Hamburg. All persons were interviewed by a questionaire. The data were made anonymous and controlled regarding possible confounding factors on the hepatic metabolizing enzymes.

2.2 Caffeine application and analysis

Adult men and women received caffeine tablets by oral route: generally 200 mg caffeine for men and 100 mg caffeine for women. Children got 400 ml Coca Cola, which contained about 50 mg caffeine.
Caffeine was determined in saliva. For this purpose a cotton-wool ball was put into the mouth and the ball was chewed as long as saturation with saliva was reached. The cotton-wool balls were centrifuged in special vials (Salivetten®) in a minifuge T (Haereus) taking 3.500 rev/min for 5 min. 0.5 ml saliva were mixed with 1.0 ml methanol. The mixture was centrifuged again using 3.500 rev/min for 5 min. The methanol phase was filtered and used for caffeine determination by HPLC equipment: Column containing spherisorb ODS II, 5 µm (Bischoff 25461725), precolumn (Bischoff 63021725), pump (Gynkothec 300 C), gradient former (Gynkothec 250 B), automtic injection system (Waters Millipore Wisp 710 B), UV detector (Spectroflow 783 T 119/68), integrator (Gynkothec C-R 317).
Caffeine was detected at a wavelength of 254 nm, and the caffeine concentration was evaluated using the integral of the peak area and a defined retention time of the caffeine peak in the chromatogram.

3. Results

The results are presented in the following tables:

Tab. 1: Non smoking adults

Sex f=female m=male	**Age** years	**Body weight** kg	**Body size** cm	**PCDD/PCDF I-TEQ** ng/kg fat	**Caffeine elimination rate** $t_{0.5}$ min
f	40	65	166	44,8	280
f	63	50	151	62,1	248
m	40	76	181	33,1	279
m	33	81	180	30,3	420
m	42	90	175	31,8	173

Tab. 2: Smoking adults

Sex f=femal m=male	**Age** years	**Body weight** kg	**Body size** cm	**PCDD/PCDF I-TEQ** ng/kg fat	**Caffeine elimination rate** $t_{0.5}$ min
f	39	80	165	22,0	117
m	34	90	190	29,6	167
m	35	85	183	30,6	177

Tab. 3: Non smoking children

Sex f=femal m=male	Age years	Body weight kg	Body size cm	PCDD/PCDF I-TEQ ng/kg fat	Caffeine elimination rate $t_{0.5}$ min
f	8	35	130	14,6	141
f	9	25	139	16,9	178
f	9	43	144	10,7	199
f	9	37	150	8,6	262
m	13	62	175	9,6	184
m	11	48	164	13,5	157
m	9	40	139	7,3	244
m	10	34	145	8,6	119
m	9	29	140	15,4	150

In children the $t_{0.5}$ of the caffeine elimination rate correlates with the I-TEQ of the PCDD/PCDF found in the blood. The correlation coefficient was -0.78.

4. Summary

Although the number of persons participating in this study was very small the following general conclusions may be drawn: The I-TEQs of PCDD/PCDF found in blood of adults and children were in a normal range. In this respect there were no differences in non smoking and smoking adults (ng/kg fat): lowest value: 22.0, highest value: 62,1. In adults we did not find any correlation between the $t_{0.5}$ of caffeine and the I-TEQ of PCDD/PCDF. However, as expected from literature smoking adults had shorter $t_{0.5}$ of caffeine than non smoking adults.
In children the I-TEQ of PCDD/PCDF found in the blood was similarly in a normal range (ng/kg fat): lowest value: 7,3; highest value: 16,9. However, in contrast to the results obtained from adults, a correlation between the $t_{0.5}$ of caffeine and I-TEQ of PCDD/PCDF was seen in children with a negative correlation coefficient of 0.78 suggesting that in children the CYP 1 A1 and CYP 1 A2 monooxygenase systems may be very sensitive to increasing concentrations of PCDD/PCDF.

5. Conclusion

Our results deserve cautious interpretation, because of the very small the number of investigated persons. However, the results obtained from the correlation analysis in children should stimulate further investigations proofing the hypothesis that PCDD/PCDF burdens already in the so-called normal range may induce the CYP 1 A1 and Cyp 1 A2 monooxygenases. This may be the reason for impaired biochemical pathways found to a higher degree in breast fed babies by KOPPE and her coworkers[2].

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6. References

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