TOX/2015/13

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COT)

PAPER FOR INFORMATION

COT response to the EFSA Consultation on a draft scientific opinion on the safety of Caffeine

Secretariat
March 2015

COT Response to the EFSA Consultation on a draft scientific opinion on the safety of caffeine

General Comments

1. Introduction

It would be helpful to clarify further the remit of the opinion. In particular, it is unclear why potentially sensitive subgroups have not been considered, apart from one study looking at people with diagnosed hypertension.

4.2. Pharmacodynamic effects

Section 4.2 on pharmacodynamics seemed incomplete e.g. no mention is made of phosphodiesterase inhibition by caffeine.

Also in this section it is stated that caffeine 'acts, at least in part, by facilitating dopamine D1 receptor transmission. Its mechanism of action appears to be substantially different from that of 'dopaminomimetic' psychostimulants such as cocaine and amphetamine'. This is probably so, but the net result is the same and could lead to potentiation not only of the effects of the drugs mentioned but also of MDMA ('ecstasy') and other psychostimulants. This should be discussed in 4.5.

4.4. Adverse effects of a single dose and of repeated doses of caffeine consumed within a day

In the main text, the opinion describes and discusses studies of acute intakes of caffeine, but their findings are not mentioned in the conclusions. It would be helpful to explain why the health effects of acute exposures have been discounted.

4.4.1. Cardiovascular system

The description of a case-crossover study (page 35, lines 1406-1408) uses incorrect terminology. In a case-crossover study, each person serves as his own control, exposures being compared for different time periods. This apparent lack of understanding leads one to question whether the opinion had the appropriate epidemiological input.

4.4.3. Central nervous system

The reference to the UK COT statement in line 1685 should be (COT, 2012) rather than (Verster, 2012). Moreover, the report cited in the reference section is incorrect – it should not refer to the First Draft statement, but to the final statement, which is available using this link

(http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2012/cotstatement201204).

COT members considered that some of the nuances in the conclusions at the end of each section were lost in the final conclusions. For example, the text includes relevant information about genetic polymorphisms and their effect on caffeine metabolism, but this is hardly mentioned in the conclusions. The Committee considered that caffeine might have a greater effect on the CNS and cardiovascular system in “slow metabolisers” than “fast metabolisers”.

Members noted that there was very little information on behavioural effects of caffeine, which could usefully be expanded, and that the opinion was inconsistent in its consideration of anxiety (pages 39 and 42) with the text stating that caffeine can cause anxiety in normal healthy individuals but the conclusions stating the reverse. The dependency potential and the quite severe withdrawal effects which can occur are not covered in much detail and are somewhat understated.

4.5. Adverse effects of longer-term and habitual caffeine consumption

Members considered that inclusion of data on interactions with other drugs, both prescribed and illicit, would be useful.

In this section, several meta-analyses are discussed, in which extremely low caffeine consumers were used as the reference group. The Committee noted that this might not be the best approach since the group was likely to over-represent people who were more sensitive to caffeine. Members suggested that comparison of high vs. moderate caffeine consumers might be more appropriate.

It was suggested that the effect of genetic differences on caffeine consumption should be brought out more strongly.

4.5.2. Cardiovascular system

The conclusions in lines 1477-1491 state “A single dose of 200 mg of caffeine consumed 1-2 hours pre-exercise significantly increases BP during resistance training in caffeine-naïve subjects as well as in habitual coffee consumers upon 24-48 h of caffeine withdrawal. A single dose of 200 mg of caffeine also decreases myocardial blood flow if consumed approximately one hour prior to endurance exercise (i.e. when the BP-raising effect of caffeine reaches its peak). Whereas such changes could increase the risk of acute cardiovascular events in subjects with an increased risk for CVD (e.g. with underlying hypertension and/or advanced atherosclerosis), the Panel considers them to be of low clinical relevance for healthy individuals in the general population under normal environmental conditions.” Members considered that this should be alluded to in the final conclusions as a significant portion of the “normal adult population” may have underlying cardiovascular problems of which they are unaware.

Conclusions

COT members were generally supportive of EFSA's overall conclusions concerning adults and pregnant women, and considered that the epidemiological studies supported them adequately. With regard to lactating women, members noted that the EFSA conclusions were based on an assessment of the potential exposures of infants through breast milk, but they were concerned that EFSA did not appear to consider that infants might be more susceptible to caffeine than adults because of differences in their metabolism. Members supported EFSA's approach of extrapolating from adults to children and adolescents on a bodyweight basis, which was acceptable given the lack of direct data on toxicity in children and adolescents.

Members suggested that in Appendices F and H, it would be helpful to summarise the results of each study, as well as its design. Similarly in Appendix I, it would be useful to summarise the main findings of each meta-analysis or include some plots.