Reviewer’s report

Title: Urinary Mycoestrogens and Age and Height at Menarche in New Jersey Girls

Version: 0 Date: 27 Nov 2018

Reviewer: Gisela Degen

Reviewer's report:

General comments

The manuscript reports results from a 'follow-up' of the New Jersey girl cohort: The authors examined subsequent growth and age at menarche in relation to previous data on an analysis of the mycoestrogen zearalenone and its congeners in spot urine samples (n=163) which had been taken at the time when the cohort was enrolled (at 'baseline', i.e. at the age of 9-10 years). Urinary analyte levels of the free (unconjugated) forms were inversely associated with height and weight z-scores at menarche, in accordance with findings from the previous study (Bandera et al. 2011) which suggested that exposure to zearalenone, zeranol, and their main metabolites is associated with slower growth and pubertal development in this cohort.

In short, exposure information based on urine samples collected at the age of 9-10 years has been re-used and related to data gathered in subsequent years by mail questionnaire on age, weight and height at menarche (which occurred ≤ 11.8 years or > 11.8 years). It is highly regrettable that no further urine samples were collected from the study participants for additional exposure analysis (see below).

Specific remarks and questions

It is unclear why the authors have not made efforts to collect additional urine samples from study participants to assess their exposure to zearalenone, zeranol and their metabolites for several reasons.

(1) In the previous urine analysis the authors have only analyzed the unconjugated forms, omitting enzymatic hydrolysis of conjugates. But, these are known to comprise a large fraction of the excreted mycoestrogen and its reduced forms (see Mally et al. 2016; Metzler et al. 2011 and references cited in these reviews).

(2) Moreover, recent studies on the analyte pattern in human urines from several cohorts by state-of-the art methods vary considerably from the pattern found in the New Jersey girls: Whilst zearalenone was the predominant analyte in the latter, other studies found that urine levels of alpha-zearalenone exceeded those of the parent mycoestrogen (Shepard et al. 2013; Solfrizzo et al. 2014; Fleck et al. 2016; Ali & Degen, 2018; Sarkanj et al. 2018). These studies (not yet...
included) are of interest and the apparent discrepancy in analyte pattern requires a comment, also in light of the strong differences in estrogenic potency for ZEN, alpha-/ and beta-ZEL.

(3) Human biomonitoring studies in spot urines shed a light on exposure at a given point in time, but should be repeated if possible to gain also insight on variability as dietary exposure may change within a given period (e.g. Ali & Degen, 2018). In the present study this would have been particularly important in light of the controversial findings on the impact of mycoestrogen exposure on puberty in girls (Asci et al. 2014; Massart et al. 2008; Szuets et al. 1997).

Several other aspects in the present manuscript require amendments:

(4) In the Methods section, several references are mentioned by author and year whilst numbering is used in other sections.

(5) In addition to the EFSA opinion mentioned (of 2011) there is a more recent one (EFSA 2016) which deals with the rational for setting a group value for ZEN and its reduced forms.

(6) The analytical method described a bit more detailed in the previous paper (Bandera et al. 2011) may have been fit for purpose, but chromatograms of a real sample (and standards) would be useful, perhaps as supplementary information.

(7) Table 1 contains (in the first column, characteristics) also the category 'missing'; this should be explained in a footnote.

(8) The acronyms used here for zearalenone, zeranol (alpha-zearalanol) and its congeners are outdated and should follow better nomenclature (Metzler M, 2011; Mycotoxin Res. 27:1-3).

References cited in the above text (in alphabetical order)


For further reading the review by Lorenz N et al. published recently (2018) in Mycotoxin Research; DOI: 10.1007/s12550-018-0328-z is also recommended.

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