THE ROUTES OF CONTAMINANT'S PASSAGE FROM MOTHER TO CHILD: IN VITRO AND IN VIVO STUDIES OF PRE AND POSTNATAL EXPOSURE IN LIVESTOCK MODELS

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Food and feed contaminants have different routes of mother-to-child passage and their direct effects on reproductive cells/tissues, due to pre or postnatal exposure, must be analysed. To this aim, livestock models of accepted translational relevance are needed, also because many contaminants have widespread occurrence in food and feed. Ochratoxin A (OTA) is a mycotoxin produced by some toxigenic fungal species of the genera *Aspergillus* and *Penicillium* [1] and induces nephrotoxic, immunotoxic, reprotoxic, embryotoxic and teratogenic effects [2]. The sheep is a relevant model for human reproductive medicine, particularly for mechanisms controlling ovarian follicle development [3]. As a ruminant, it is known to be relatively resistant to toxic effects of OTA, due to its degradation to the less toxic metabolite ochratoxin alpha by rumen microbiota. However, in ewes fed with OTA-contaminated feed, undegraded OTA was detected in serum where it accumulates with exposure time and administered dose [2]. The donkey is a monogastric species, thus with high sensitivity to OTA, and is a suitable model to follow, like human, the route of natural exposure from feed to jennies during pregnancy and in foals after delivery. Moreover, donkey milk is of high interest for its nutritional value and its industry uses. Thus, the aims of the present study were to determine: 1) as on an *in vitro* pre-natal exposure model, the effects of ovine oocyte exposure to OTA on oocyte and embryo development; 2) as on an *in vivo* post-natal exposure model, OTA levels in the spinneret feed, blood and milk samples of jennies and related foals. Ovine cumulus-oocyte complexes (COCs) were exposed to 1μM, 5μM and 10μM OTA during in vitro maturation (IVM) [4]. After IVM, part of the oocytes were analyzed for meiotic sMetaphase II (MII) rate whereas another part underwent in vitro fertilization (IVF) and embryo culture up to day 7 [4]. At any tested concentration, OTA reduced MII rates ($P<0.05$). No apparent effects were noticed on total cleavage and blastocyst formation rates but normal fertilization rates were reduced ($P<0.05$) with corresponding increase of polyspermy. Feed and blood samples were collected from 7 jennies and their foals, two months before and three months after delivery, and analyzed [5]. In feed, toxin concentrations were far below the guidance values of OTA in feed materials reported by the EU Commission Recommendation 2016/1319. In jennies, the incidence of positive (with OTA levels higher than the detection limit) blood samples was 73%, (median value=114 ng/L; range 51 to 6,000 ng/L). In foals, the incidence of positive blood samples was 50% (median value= 136 ng/L, range 79 to 4030 ng/L). No placental transfer of OTA was observed in all tested jennies and no influence on pregnancy length and health of foals was observed. In milk, the incidence of positive samples was 36% (range 17 to 82 ng/L). In conclusion, in sheep, in vitro exposure to OTA affected oocyte function and, in jennies, in which no placental passage was observed, OTA passed from feed to milk through blood. Effects on female fertility and offspring health will be further investigated.

1, Malir et al., Toxins 2016; 8:191 doi:10.3390/toxins8070191; 2. Gallo et al., Toxins 2015; 7:3057-3111; 3 Mastrorocco et., Mol Reprod Dev. 2019;1–14; 4. Asif et al., Proc. ECAR Vienna July 2019 (a); 5. Asif et al., Proc. ECAR Vienna July 2019; 5. Asif et al, World Mycotoxin Forum, Belfast, October 2019. Study funded by the Rep-Eat - H2020 MSCA-COFUND 2015 program; G.A. n. 713714.

Domande

Quale specie animale è sensibile agli effetti tossici dell'Ocratossina?

a) tutti gli animali compreso l'uomo

b) solo l'uomo

c) *solo i monogastrici*

d) solo i poligastrici

2) Perchè si è studiato l'effetto dell'Ocratossina sulla riproduzione/sviluppo embrionale?

a) perchè il feto è sempre esposto all'Ocratossina durante tutta la gravidanza

b) perchè il tutti gli animali c'è passaggio placentare

c) perchè induce aborto

d) *perchè è embriotossica e teratogena*

3) Nell'asina quali sono le vie di esposizione dei nati?

a) solo con passaggio placentare

b) *solo con il latte *

c) con passaggio placentare e con il latte

d) i nati non sono esposti all'Ocratossina.

4) Cosa ha determinato l'OTA nell'ovocita del modello ovino?

a) *Riduzione delle percentuali di meiosi 2*

b) Incremento delle percentuali di meiosi 2

c) Inibizione delle percentuali di ovociti allo stadio di vescicola germinale

d) Aumento dell'atresia follicolare.