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ARTICLE ORIGINAL

Dimethoate effects on thyroid function in suckling rats

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Effets du diméthoaste sur la fonction thyroïdienne chez le rat en période d'allaitement

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L'objectif de notre travail est d'étudier l'effet du diméthoate sur la fonction thyroïdienne chez le rat en période d'allaitement. Le produit a été administré dans la boisson des mères, de la mise bas jusqu'au 10e jour postnatal, à une dose de 40 mg/kg de poids corporel, soit 0,2 g/L. Les jeunes et leurs mères ont été sacrifiés le dixième jour après la mise bas. Comparés au groupe des témoins, les jeunes rats traités au diméthoate, présentent une réduction de 48 % de leur poids corporel qui pourrait être attribuée à une déficience en hormones thyroïdiennes. En effet les taux plasmatiques en FT_4 et FT_3 ont diminué chez les jeunes de 56 % et 40 % et chez les mères de 27 % et de 15 % respectivement.

La chute de l'hormonémie thyroïdienne est la conséquence d'une réduction en iode thyroïdien qui a diminué de 75 % chez les jeunes et de 24 % chez les mères. Cette diminution de l'hormonémie thyroïdienne après traitement au diméthoate a des répercussions sur les taux plasmatiques en TSH en exerçant un feed-back positif sur les cellules thyréotropes adénohypophysaires. En effet ces taux ont été multipliés par des facteurs de 2,31 chez les mères et de 1,96 chez leur progéniture.

Ces modifications biochimiques confirment l'aspect histologique des thyroïdes des jeunes rats et de leurs mères. En effet, chez les rats traités au diméthoate, certains follicules thyroïdiens présentent des cavités vésiculaires vidées de leur contenu; d'autres renferment un peu de colloïde. Par contre, chez les mères, les follicules thyroïdiens présentent des cellules épithéliales cubiques entourant des cavités vésiculaires vidées de leur contenu colloïdal.

Mots-clés : Diméthoate, rats, fonction thyroïdienne, T_3, T_4, iode thyroïdien, follicules thyroïdiens, contenu colloïdal.

Dimethoate effects on thyroid function in suckling rats

The aim of our work is to study dimethoate effects on thyroid function given in drinking water (40 mg/kg body weight, equivalent to 0.2 g/L) to mothers from day zero until the 10th day after delivery. Pups and their mothers were sacrificed on day ten after parturition. Compared to a control group, dimethoate-treated pups showed a 48% decrease in body weight which could be attributed to a defect in thyroid hormones. Indeed, after treatment by dimethoate, plasma rates of free T_4 and T_3 decreased by 56% and 40% in the young and by 27% and 15% in dams respectively. We can attribute the reduction in plasma thyroxine and triiodothyronine rates to a decrease in thyroid iodine levels (–75%) in the young and (–24%) in their mothers. The decrease in production of thyroid hormones after dimethoate treatment affect thyroid stimulating hormone (TSH) levels. In fact, plasma TSH levels were multiplied in dimethoate-treated group by factors of 2.31 in dams and 1.96 in their offspring.

These biochemical modifications confirmed the histological thyroid aspects of pups and dams. In fact, in dimethoate-treated rats, some thyroid follicles of pups presented vesicular cavities without colloid; others contained colloid. However in dams, thyroid follicles presented cubical epithelial cells which surrounded empty vesicular cavities.

Key words: Dimethoate, rats, thyroid function, T_3, T_4, thyroid iodine, follicular cells, colloid space.

INTRODUCTION

Organophosphorus dimethoate is widely used in agriculture and plant protection. The application and frequent use of this insecticide and other organophosphorus compounds have resulted in their widespread distribution in the environment and have been shown to exert deleterious effects on the biological system [10].

Organophosphorus exposure can produce long term changes in brain function, affect the human immune system, cardiac and reproductive functions.

Changes may occur in the metabolism and the endocrine activity after organophosphorus exposure [2, 17].

In previous studies, the thyroid inhibitory nature of organophosphate pesticides was reported [20, 21, 32, 33]. However, the reports were made on non mammalian-models (fish and cockerel).

Despite well-documented information on the neurotoxicity of dimethoate in laboratory animals, reports concerning the effects of this insecticide on endocrine activity in mice and rats remain scarce in adults [22, 32, 35] or completely absent in young.

The purpose of our study is to investigate thyroid function in suckling rats and their mothers given dimethoate.

MATERIALS AND METHODS

Animals

Wistar strain rats (Central Pharmacy, Tunisia), weighing about 180g, were

housed at 22±3 °C, with light-dark periods of 12 hours (light between 8 a. m and 20 p. m), relative humidity of 40%, free access to water and a commercial diet (SICO, Sfax Tunisia) containing 0.720±0.012 µg of iodine/g of diet.

After acclimatization to laboratory conditions for one week, female rats were kept overnight in separate cages containing five females with one male. Mating dates were established from the appearance of vaginal plugs. The presence of spermatozoa in the vaginal smear was taken as an indicator of day zero of pregnancy.

Experimental procedures

Twenty pregnant rats were allowed to deliver spontaneously three weeks after coitus. At birth, the litters were reduced to eight pups each and the day of birth was considered as postnatal day zero.

Lactating rats were divided into two groups of ten each. The first group represented control group. The second group was treated with dimethoate (40 mg/kg body weight, equivalent to 0.2 g/L) administered in their drinking water from the day of birth until the 10^{th} day after delivery. This dose represented one quarter of DL50.

Since the birth, daily food, drink consumption and dimethoate quantities ingested by lactating rats were measured during ten days *(table I)*.

Suckling pups (n=160) and their mothers were studied on day 10 after parturition. Each lactating rat treated by dimethoate ingested 5.601 mg of this organophosphorus compound and 18 µg of iodine daily *(table I)*.

They were anaesthetized with chloral hydrate by intra-abdominal way. Body weights of all animals were measured. Blood samples were collected by the brachial artery of pups and by the aortic puncture of their mothers. Plasma was obtained by centrifugation at 2200 g of all blood samples and stored at –20° C until FT_3, FT_4 and TSH analysis by radio-immunoassay, using kits from Immunotech for $FT_3$and FT_4 (references: 1579 and 1363 respectively) and kit from Biocode-Hycel for TSH (rat TSH, reference: AH R001).

Some thyroid glands were taken from pups and dams. They were weighed and preserved at –20° C until their acid mineralization and analysis of their iodine contents by Sandell and Kolthoff method [30]. Others were taken with a piece of trachea, fixed in Bouin solution, embedded in paraffin and serially sectioned at 5 micrometer. The sections were stained with hematoxylin-eosine [13].

Statistical analysis

Significance among groups was determined by using Student's t- test or Man and Whitney test [31] when the means of two groups were compared.

RESULTS

Compared with the control group, the ten-day-old rats whose mothers had been treated with dimethoate (40 mg/kg of body weight) had a 48% decrease in body weight (p≤0.001) *(fig. 1)*, a 18% decrease in femur length, a 34% decrease in femur weight (p≤0.001) *(table II)* and a decrease in all organs weights, among which thyroid glands were reduced by 45%. Their weights were

Table I
Daily food and water intake (g or ml/day/mother), dimethoate (mg/day/mother) and iodine (µg/day/mother) quantities ingested by lactating rats: controls and treated with dimethoate (0.2 g/L) from the day zero until day ten after delivery.
Treated vs controls ***: p≤0.001.

Tableau I
Consommations quotidiennes d'aliment solide et de boisson (g ou ml/jour/mère); quantités de diméthoate (mg/jour/mère) et d'iode (µg/jour/mère) ingérées par des rates allaitantes témoins et traitées au diméthoate (0,2 g/L) de la mise bas jusqu'au 10e jour après la parturition.
*Traités vs témoins ***: p ≤ 0,001.*

Parameters and treatments	Food consumption (g/day/mother)	Drink consumption (ml/day/mother)	Quantities of dimethoate ingested (mg/day/mother)	Quantities of iodine ingested (mg/day/mother)
Controls	33.214 ± 3.068	34.600 ± 2.524	—	23.914 ± 2.208
	(n = 14)	(n = 15)		(n = 14)
Treated with	25.000± 2.662	28.055 ± 2.622	5.601 ± 1.049	18.000 ± 1.917
dimethoate	(n = 12)	(n = 18)	(n = 18)	(n = 12)
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