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Effects of aluminium chloride on some essential elements in pregnant rats and their offspring

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أر الألنيوم اللاي اكلور لى عض اعناصر الأاية ند افران الحوال وأنها

دف تجر ناو إاد لالة ين الحقن دال اصفاق لألنيو م اللاي اكلور و اغير ات اللاز ية و انيية لكاليوم و المغنيز و م و انـاس و از ك و افو فور و الحدد ند افران الحو ال و أنها. قد تم قن افران الحو ال ن ايو م الع إى ايو م الاث شر ن ر ة الحمل بمقادر لفة ن الألنيو م اللاي اكلور (50، 100 و 200 لغ/ لغ/ و م). و للت اعناصر الأاية ي دم و ليي و د و عي الحيو ات و اطة المطياف اضو ئي لاصاص اذر ات. ينت انائج لى أن ناك ار فاا ي ب اكايوم و الحدد و افو فور اكدي، و الحدد و افو فور اكلوي و افاضا ي ب المغنيز و م اكلوي والمعو ي و ي از ك اكدي و انـاس اكدي و اكلوي و ي الحدد المعو ي ند افران الحو ال الخاضعة لر ة، اصة انة لمقادر المر فعة ن الألنيو م اللاي اكلور. و د لاظنا أضا ار فاا ي ب اكايوم و افو فور و از ك ي لاز ا افران الحو ال و افاضا ي ة المغنيز و م ي لاز ا افران الحو ال و أنها و ذك انة لمقادر المر فعة ن الألنيو م اللاي اكلور. هذه انائج ين لى أن الألنيو م يمر لأنة ر المشيمة ا ذك اضطر ات ي اعناصر الأاية.

اكلمات المفاية : الألنيو م اللاي اكلور ـ أض عدي ـ د ـ عي ـ لية ـ افأر

Effets du chlorure d'aluminium sur certains éléments essentiels chez les rates gestantes et leurs fœtus

Le but de notre étude est d'établir une relation de causalité entre l'injection intrapéritonéale d'$AlCl_3$ et les variations plasmatiques et tissulaires des teneurs en calcium, magnésium, cuivre, zinc, phosphore et fer chez les rates gestantes et leurs fœtus. Les rates gestantes sont injectées du 9ème au 13ème jour de la gestation par différentes doses d'$AlCl_3$ (50, 100 et 200 mg/kg.j). Les éléments essentiels sont analysés dans le sang, les reins, le foie et l'intestin des animaux par spectrophotométrie d'absorption atomique. Les résultats montrent, après traitement par $AlCl_3$, une augmentation des concentrations en calcium, fer et phosphore hépatique, aussi bien qu'en fer et phosphore au niveau rénal, et une diminution des concentrations en magnésium rénal et intestinal, en zinc hépatique, en cuivre hépatique et rénal, et en fer intestinal chez les rates gestantes et surtout pour les fortes doses. On a aussi noté une augmentation des concentrations en calcium, en phosphore et en zinc dans le plasma des rates gestantes et une diminution dans la concentration en magnésium dans le plasma des rates gestantes et leurs fœtus pour les doses élevées d'$AlCl_3$. Ces résultats prouvent que le passage de l'aluminium aux fœtus suite au traitement des mères cause des perturbations dans le métabolisme des éléments essentiels.

Mots clés: Chlorure d'aluminium - Métabolisme minéral - Foie - Intestin - Rein - Rat

Effects of aluminium chloride on some essential elements in pregnant rats and their offspring

The aim of this study is to establish a relationship between intraperitoneal $AlCl_3$ injection and variations of plasma and tissue calcium, magnesium, copper, zinc, phosphorus, and iron concentrations in pregnant rats and their offspring. The pregnant rats were injected on gestation days 9-13 with different doses of $AlCl_3$ (50, 100, and 200 mg/kg.day). The essential elements were analyzed in blood, kidney, liver and intestine of the animals by atomic absorption spectrophotometry, before and after $AlCl_3$ injection. The results showed after $AlCl_3$ treatment an increase in hepatic calcium, iron and phosphorus concentrations, as well as in iron and phosphorus in the kidney ; a decrease in renal and intestinal magnesium concentrations. Hepatic zinc, hepatic and renal copper and intestinal iron concentrations of pregnant rats were also decreased. Moreover, we noted an increase in plasma calcium, phosphorus and zinc concentrations with highest doses of $AlCl_3$, and a decrease in magnesium concentration in both pregnant rats and their offspring. These results provide evidence for the passage of aluminium to the fetuses following maternal administration causing some disorders in the metabolism of essential elements.

Key words: Aluminium chloride - Mineral metabolism - Liver - Intestine - Kidney - Rat

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INTRODUCTION

Aluminium is an abundant element in the earth's crust and is widely dispersed throughout the environment. Nowadays, aluminum salts are included in cosmetics, food processing and storage and also used in various nonprescription drugs. However, aluminum toxicity was initially recognized as a neurological and/or skeletal disease (Alfrey, 1986). On the other hand, aluminium sulfate is extensively added as a coagulant agent during the drinking water-purification process in order to flocculate the organic matter and so clarify the water (Domingo, 1993; Greger, 1993). The knowledge of aluminium toxicity has markedly improved in recent years, information concerning the reproductive toxicity of this element is still very limited. A number of investigations have suggested that pregnancy could be a time of enhanced susceptibility to aluminium toxicity (Golub & Domingo, 1996); and a competition for transport with essential trace elements is one of the possible mechanisms that explains aluminium toxicity (Chmielnicka & Nasiadek, 1991). It seems particularly relevant during periods of rapid growth in late gestation and early infancy when heavy demands are made on trace element metabolism (Golub & Domingo, 1996). However, an important issue that has not been addressed yet is the possible mobilization of maternal aluminium stores in bone and other tissues and a transfer to the fetus along with calcium and other essential elements (Golub & Domingo, 1996). A phenomenon that was already demonstrated for lead (Silbergeld, 1991).

It was previously shown that $AlCl_3$ affects significantly hematocrit and hepatic, kidney and intestinal proteins during rat pregnancy especially for the highest $AlCl_3$ dose used (200 mg/kg.day) (Mestaghanmi *et al.*, 2001).

However, there is relatively little information about the effect of intraperitoneal injection of aluminium chloride to the pregnant rats and their fetuses on related mineral status, and also the possible interactions of aluminum with essential elements.

The aim of our study is to elucidate some effects of intraperitoneal $AlCl_3$ treatment of pregnant rats on their offspring especially in terms of calcium, magnesium, phosphorus, zinc, copper, iron concentrations in plasma and different tissues of the rats exposed to $AlCl_3$ on gestation days 9-13.

MATERIALS AND METHODS

The experiments were performed on white female Wistar rats of 230-260 g body weight. Female rats were mated with male (3:1) overnight and examined the following morning for copulatory plugs. Day 1 was defined as the day when the vaginal plug was found. The animals were maintained on commercial pelleted chow, and tap water *ad libitum* in a room equipped with automatic light cycles (12 h light/dark), maintained at 22 ± 2°C with relative humidity of 40-60 %. The diet (N° GPF 81, from INAAM, Casablanca, Morocco) contained average amounts of: 160 g of protein, 20 g of fat, 70 g of mineral supplements, 9 g of calcium, 3.5 g of phosphorus per kilogram of diet. It also contained vitamin A, D_3 and E at relatively 10000, 1500, and 10 UI respectively. Aluminum concentration in water was 0.013 mg/l.

The animals were divided into two groups. The first group was subdivided in three sub groups (each subgroup contained 6 rats) which received intra peritoneal injections of 50, 100 and 200 mg of $AlCl_3$/kg each day from the 9 th to the 13 th of the pregnancy days. Aluminium chloride ($AlCl_3$) was administered in physiological saline solutions at doses 50, 100 and 200 mg/kg.day. The choice of these doses was based on previous studies concerning the developmental toxicity of aluminum in mice, rats and rabbits (Bennet *et al.*, 1975; Cranmer *et al.*, 1986; Yokel *et al.*, 1989; Chmielnicka *et al.*, 1996; Sanchez *et al.*, 1997). The $AlCl_3$ used for intraperitoneal injection was taken from 20 sterile solution of $AlCl_3$ (pH 2.4). The second control group also received intraperitoneal injections, but with only sterile physiological saline for all gestation days from 9 to 13.

On the 20 th gestation day, the animals were killed by decapitation. Blood was collected rapidly in heparinized polypropylene tube from pregnant rats and fetuses. Blood samples from same litter fetuses were pooled, cooled at 4°C, centrifuged at 3000 g for 10 min. Liver, kidney and intestine were quickly removed from pregnant rats and fetuses, rinsed with sterile physiological saline, then mineralized according to Cossa and Bourguet (1980) for calcium, magnesium, copper, zinc, iron and phosphorus determinations. Each tissue was dried under 100°C, until the weight did not change. Then, 0.2 g of the organ powder was put in polypropylene tube with 4 ml of nitric acid (Merk, 70). The tubes were plugged for 12 h at room

temperature (22 ± 2°C) then heated at 90°C for 3 h. After cooling, the volume was completed to 50 ml with bidistilled water filtered and stored at 4°C. The blanks were prepared simultaneously to prevent contamination.

For serum mineral components determination, we have used the methods described by Willis (1959, 1960) for magnesium and calcium, Sprague & Slavin (1965) for copper and zinc, Olson & Hamlin (1969) for iron. The mineral phosphorus was determined using the Biotrol Kit (Merk). Copper concentrations were determined using graphite furnace atomic absorption spectrophotometer (Perkin-Elmer, 3030, equipped with HGA 600 graphite furnace and AS-60 automatic runner samples). Other elements were determined by flameless atomic absorption spectrophotometer (GBC, Scientific Equipment, Victoria, Australia).

Statistical evaluations

Results (of the quantitative continuous variables) were compared by analysis of variance (ANOVA-MANOVA). Newman Keuls and Duncan's multiple-range tests were also used to evaluate statistical significance among groups. A probability value of p 0.05 was considered as significant.

RESULTS

In the present study, increases of calcium, phosphorus and zinc concentrations in plasma were noted (p0.05) for $AlCl_3$ injection at a dose of 200 mg/kg.day in pregnant rats (Table 1). The magnesium and iron concentrations decrease significantly in the plasma of pregnant rats and their offspring at the highest $AlCl_3$ dose used, decrease in trends (n.s.) the plasma copper content were also noted for both $AlCl_3$-treated pregnant rats and their offspring.

Tissue mineral concentrations of calcium, iron, magnesium are summarized in table 2. There were increases in calcium and iron concentrations in pregnant rats treated by $AlCl_3$ at the highest dose. A decrease of magnesium was observed in kidney and intestine of pregnant rats treated with $AlCl_3$, and to a lesser extent also in the offspring.

The concentrations of phosphorus, copper and zinc in liver kidney and intestine are presented in table 3. The $AlCl_3$ treatment of pregnant rats induced an increase in the hepatic and renal phosphorus content but had no effects on their offspring. We have also observed a decrease in zinc and copper tissue concentrations in liver and kidney from pregnant rats treated by $AlCl_3$ ($p < 0,05$), with no changes in fetuses. We noted a decrease in hepatic and renal copper ($p < 0,05$) concentrations in $AlCl_3$-treated pregnant rats but there was no variation in their offspring for any tissue.

Table 1. Ca, P, Fe, Mg, Zn, and Cu mineral concentrations in plasma (µ/ml) of pregnant rats and their offspring exposed to $AlCl_3$ at a dose of 50, 100 and 200 mg/kg.day from day 9 to day 13 of gestation

Min.	$AlCl_3$ dose mg/kg.day	50	100	200
Ca	Mothers			
	Controls	1,801±0,223	1,837±0,215	1,900±1,128
	Treated	1,713±0,321	1,800±0,091	2,299±0,199*
	Fetuses			
	Controls	1,805±1,550	1,830±0,140	1,795±0,091
	Treated	1,780±0,119	1,607±0,129	1,910±0,091
P	Mothers			
	Controls	106,560±4,815	103,452±3,215	104,000±2,903
	Treated	104,27±4,829	106,155±0,630	112,035±1,583 *
	Fetuses			
	Controls	92,882±2,756	92,338±3,541	91,939±3,186
	Treated	92,875±1,361	91,992±0,979	91,482±0,703
Fe	Mothers			
	Controls	9,089±1,591	9,098±1,113	9,077±0,436
	Treated	9,095±0,277	9,057±0,307	8,265±0,230*
	Fetuses			
	Controls	10,410±1,072	10,390±0,770	10,477±0,566
	Treated	10,247±1,224	9,938±0,851	9,700±0,806
Mg	Mothers			
	Controls	2,881±0,134	2,951±0,102	2,862±0,161
	Treated	2,900±0,129	2,740±0,141	2,527±0,168 *
	Fetuses			
	Controls	3,075±0,125	3,108±0,126	3,045±0,149
	Treated	3,122±0,116	2,930±0,123	2,727±0,068 *
Zn	Mothers			
	Controls	1,164±0,065	1,189±0,791	1,133±0,898
	Treated	1,147±0,240	1,559±0,099	1,776±0,304 *
	Fetuses			
	Controls	1,496±0,120	1,419±0,098	1,398±0,083
	Treated	1,753±0,113	1,720±0,265	1,865±0,084
Cu	Mothers			
	Controls	0,885±0,166	0,914±0,205	0,885±0,218
	Treated	0,881±0,171	0,855±0,096	0,765±0,088
	Fetuses			
	Controls	0,632±0,009	0,625±0,026	0,614±0,058
	Treated	0,642± 0,009	0,609± 0,067	0,551±0,051

Min. : Minerals ; *: p 0.05

Table 2. Concentrations of Ca, Mg, Fe (µg/g dry weight of tissue) in liver, kidney and intestine from pregnant rats and their offspring exposed to $AlCl_3$ at a dose of 50, 100, and 200 mg/kg.day from day 9 to day 13 of gestation

Min.	Tissues	Liver	Kidney	Intestine
Ca	Mothers			
	Controls 50	218,13±7,79	358,80±1,62	403,10±2,92
	Treated 50	219,56±7,46	358,67±2,21	402,86±3,95
	Controls 100	222,39±5,21	358,89±1,86	402,63±2,76
	Treated 100	217,82±2,04	356,52± 4,03	403,93±4,19
	Controls 200	220,50±7,69	357,77± 0,98	402,81±3,44
Ca	Treated 200	230,77±0,14 *	350,62±0,542	495,99±1,242 *
	Fetuses			
	Controls 50	267,92±4,39	394,97± 6,67	408,33± 2,65
	Treated 50	266,71± 4,75	393,25± 1,70	408,48± 2,93
	Controls 100	269,78±1,56	393,68± 3,64	407,36± 1,48
	Treated 100	265,36±4,60	394,62± 3,16	407,90± 4,04
	Controls 200	269,25±2,31	392,75± 4,04	406,90± 1,85
	Treated 200	272,41±0,73	398,37± 1,29	410,20± 1,25
Mg	Mothers			
	Controls 50	331,26±5,03	533,20± 3,62	601,86± 3,06
	Treated 50	331,44±6,92	535,94± 2,78	602,77± 3,65
	Controls 100	331,04±1,12	534,39± 3,92	598,69± 6,91
	Treated 100	332,31±3,00	534,15± 3,27	596,75± 1,17 *
	Controls 200	330,98±7,96	538,01±1,59	602,65±3,22
	Treated 200	336,41±3,18	528,06±1,26 *	583,58±2,11 **
	Fetuses			
	Controls 50	361,04±4,97	542,92±1,61	585,56±4,20
	Treated 50	362,73±5,92	542,90±1,76	586,57±3,37
	Controls 100	361,55±0,93	543,25±1,27	588,22±1,1,69
	Treated 100	361,20±2,49	541,88±1,00	582,11±1,33
	Controls 200	362,35±7,76	542,83±2,72	587,87±1,88
	Treated 200	361,12±1,79	538,40±1,67	576,69±2,40
Fe	Mothers			
	Controls 50	399,22±9,41	131,30±1, 42	117,55±1,75
	Treated 50	396,41±3,96	131,20±1,76	116,12±3,49
	Controls 100	402,01±6,04	129,75±2,68	116,61±1,77
	Treated 100	392,00±9,84	136,85±2,61	117,49±4,42
	Controls 200	399,90±3,68	129,85± 2,61	115,35±2,11
	Treated 200	414,94±11,24*	142,54±0,46*	125,07±2,55 *
	Fetuses			
	Controls 50	420,05±1,26	117,25±1,37	122,65±3,07
	Treated 50	420,35±1,28	117,38±2,17	120,05±1,26
	Controls 100	419,29±2,19	116,63±1,62	121,10±1,18
	Treated 100	416,77±3,48	115,16±1,11	119,25±1,50
	Controls 200	420,27±3,14	118,36±1,64	121,84±2,51
	Treated 200	414,40±1,56	114,27±1,67	119,15±1,24

Min. : Minerals ; *: p 0.05 ; **: p 0.005

Table 3. Mineral concentrations of P (mg/g dry weigh of tissue), Zn, and Cu (g/g dry weigh of tissue) in liver, kidney and intestine from pregnant rats and their offspring exposed to $AlCl_3$ at a dose of 50, 100, and 200 mg/kg.day from day 9 to day 13 of gestation

Min.	Tissues	Liver	Kidney	Intestine
Cu	Mothers			
	Controls 50	20,74± 1,24	27,97±0,80	17,99±0,44
	Treated 50	20,55±0,81	27,68±0,56	17,70±0,42
	Controls 100	21,53±0,93	28,84±0,57	18,08±0,31
	Treated 100	18,99±0,36	19,80±0,46*	18,30±0,48
	Controls 200	20,82±1,22	28,84±0,60	18,23±0,50
	Treated 200	17,27±0,76 *	13,97±0,46 **	18,45±0,84
	Fetuses			
	Controls 50	19,00± 0,42	27,38±0,86	16,87±0,26
	Treated 50	18,92±0,32	27,27±0,89	16,78±0,45
	Controls 100	18,84± 0,61	27,40±0,59	16,80±0,40
	Treated 100	18,60±0,33	26,58±0,88	17,00±0,18
	Controls 200	18,97±0,41	27,09±0,57	16,95± 0,33
	Treated 200	18,25±0,28	26,23±0,94	17,16±0,36
Zn	Mothers			
	Controls 50	126,46± 3,21	87,80±1,41	76,25±0,81
	Treated 50	124,50±2,94	86,58±1,07	76,60±1,42
	Controls 100	126,00±3,81	87,16±1,26	75,95±1,28
	Treated 100	126,40±4,49	87,72±0,55	78,02±1,25
	Controls 200	126,77±2,53	87,47±1,41	76,51±0,83
	Treated 200	119,31 0,74 *	83,84±0,95*	78,35±2,19
	Fetuses			
	Controls 50	133,77± 1,37	88,22±1,17	78,35±0,94
	Treated 50	134,10±2,653	87,94±0,61	78,18±0,94
	Controls 100	133,55±1,71	87,58±0,75	78,52±0,53
	Treated 100	133,47±0,81	87,17±1,18	78,81±0,37
	Controls 200	134,115±1,945	87,39±1,67	78,57±0,78
	Treated 200	132,86±0,68	87,30±1,65	79,50±0,71
P	Mothers			
	Controls 50	17,99±0,45	13,90±0,56	10,93± 0,16
	Treated 50	17,60±0,41	13,85±0,45	10,90±0,29
	Controls 100	18,30±0,38	13,75±0,22	11,02±0,06
	Treated 100	16,17±0,24	13,73±0,62	11,20±0,35
	Controls 200	18,22±0,38	13,70±0,21	11,05±0,19
	Treated 200	20,00±0,45 *	15,52±0,36*	11,13±0,75
	Fetuses			
	Controls 50	18,32±0,23	15,34±0,31	10,41±0,07
	Treated 50	18,49±0,47	15,21± 0,16	10,41±0,22
	Controls 100	18,33±0,14	15,25±0,21	10,45±0,14
	Treated 100	17,89±0,58	15,01±0,43	10,47±0,09
	Controls 200	18,24±0,38	15,20±0,29	10,46±0,15
	Treated 200	18,81±0,38	14,52±0,13	10,41±0,20

Min. : Minerals ; * : p 0.05 ; ** : p 0.005

DISCUSSION

In the present study, we observed that $AlCl_3$ induced some modifications in the plasmatic and tissue mineral element concentrations of pregnant rats and their offspring at the highest dose used. These variations were mainly characterized by decreases in renal and intestinal magnesium concentrations, hepatic and renal copper contents, increases in renal, hepatic and intestinal iron and calcium, renal and hepatic phosphorus concentrations and decreases in renal and hepatic zinc concentrations.

First of all, in pregnant Al-induced rats, the plasmatic mineral elements show an hypercalcaemia. This may be explained by a loss of bone mineral elements because the calcium plays an important role in homeostasis (Jackson *et al.*,1985). Thus, $AlCl_3$ treatment alters bone mineralization and activates calcium transit toward blood. A decrease in renal calcium excretion may also explain the hypercalcaemia. This nephrotoxicity has been observed in rats by Liu & Nordberg (1995) after intraperitoneal injections of $AlCl_3$. Muller *et al.* (1993) have observed a significant rise of calcium in serum and spleen of adult rats, as well as in newborns whose mother received oral aluminium lactate. A slight hypercalcaemia (but n.s.) was observed in fetuses whose mothers were treated by $AlCl_3$.

This agrees with the results of Muller *et al.* (1993). They have demonstrated in rats that aluminum lactate treatment induces, an increase in plasma calcium accompanied by a decrease in magnesium concentration because magnesium serves as a substitute for calcium in bone mineralization when there is an alteration of calcium bone fixation. The hyperphosphatemia observed in pregnant rats treated with $AlCl_3$ (but not in their offspring) likely occurs when an increase in phospholipids happens because all HDL fractions increased (Mahieu & Calvo, 1998).

In pregnant rats treated with $AlCl_3$ the hyperzincemia and the lower decrease (n.s.) in copper content (especially with highest doses of $AlCl_3$) may be explained by the relationship between copper and zinc which are competitive for protein intestinal (metallothionein) site fixation. Indeed, zinc inhibits the copper intestine absorption (O'Neil Cutting *et al.*, 1981). This suggests that zinc is an antagonist to copper absorption because it induces intestinal metallothionein synthesis. Thionein fixes copper in intestinal cells which become inapt for plasma transfer.

We have noted an alteration in calcium, phosphorus and zinc concentrations of pregnant rats without any perturbations for their offspring mineral components. This suggests that the placenta plays an important role to palliate the toxic effects of $AlCl_3$ and the young age of the animal is also a good criteria for reduction of toxic effects of $AlCl_3$ (Sanchez *et al.*, 1997).

We have observed a decrease in serum iron concentration. This decrease can be explained by the fact that aluminium can be carried by transferrin (the protein that transport Fe) or albumin (Van Ginkel *et al.*, 1990) in tissue. Chmielnicka *et al.*, (1994) have studied effect of $AlCl_3$ (100 mg/kg for 21 days in rats Wistar), they caused normocytic anemia. They have also observed (Chmielnicka *et al.*, 1996; Mahieu *et al.*, 2000) a significant decrease in serum iron concentration after each week of exposure of 4 mg/kg.day. Chmielnicka & Nasiadek (1991) have also observed a decrease in blood iron accompanied by an increase in plasmatic calcium. Han *et al.*, (2000) have observed that aluminium exposure alters tissue iron and ferritin, the protein that stores Fe, concentrations in chick. Vittori *et al.* (2002) have observed that anemia is associated with aluminium, erythrocyte morphological changes were induced by aluminium during in vitro ageing. The cells lost their typical biconcave shape. Aluminium was found within the cells and attached to the membrane. They suggest that aluminum may disturb human erythropoiesis through combined effects on mature erythrocytes and cellular metabolism in late erythroid progenitors.

We have also noted a decrease in plasmatic magnesium in $AlCl_3$-treated pregnant rats and their offspring. This decrease may be related to calcium and phosphorus concentration variations or to an hyperparathyroidism as observed by Alfrey (1985) and Felsenfel *et al.* (1993). This can be explained by a change in the relationship between calcium and phosphorus and between calcium and the parathyroids secretion. The hyperparathyroidism protects the bone against demineralization when there is an aluminium toxic effect. In other respects the decrease in plasmatic magnesium can be related to a nephrotoxicity caused by aluminum causing a

decrease in renal magnesium reabsorption. A negative effect of aluminium on magnesium levels in serum, bones and kidney was observed in sheep after oral exposure. Lower magnesium concentration in bones is probably not only a result of its lower concentration in blood, but also points to disturbances of magnesium metabolism (Allen, 1985, Muller *et al.*, 1993). It was also noted that magnesium level is lower in carcasses of newborn offspring of rat fed aluminium compounds, as these rats also showed lower magnesium level in blood (Muller *et al.*, 1993).

About tissue mineral components, we have observed an increase in hepatic and intestinal calcium concentrations in pregnant rats treated by 200 mg of $AlCl_3$/kg.day as well as in their offspring. These data are in good agreement with those of Chmielnicka & Nasiadek (1991) and Dlugaszek *et al.* (2000) who have observed a perturbation in hepatic calcium metabolism. They have also noted an increase in urinary calcium excretion. After aluminium treatment, there is a calcium bone loss which causes an hypercalcaemia and an increase in hepatic calcium concentration. This should be a protective effect for homeostasis. In fetuses, aluminum passes through the placenta from pregnant rats and modifies the calcium content.

Phosphorus is an important element for the skeleton. Its absorption occurs in the different parts of the intestinal tract. In duodenum, the phosphorus is widely absorbed in presence of vitamin D (Moya, 1987). The plasmatic phosphorus level is controlled by parathyroid hormone. In fact, this hormone favors the absorption of phosphorus in the intestine when calcium is also absorbed. This leads, to an increase in the quantity of phosphorus and calcium which are elimined in feces (Mahieu & Calvo, 1998).

In $AlCl_3$-treated pregnant rats, we have only observed a decrease in hepatic and kidney zinc concentration which probably causes toxic effects in liver. Zhang *et al.* (1998) have reported that gavage or "underskin" injection of aluminum induces metallothionein in the rat. This induction reflects the response to stress caused by aluminum. Thus, the detoxication effect is uncertain and the metallothionein induction in liver sites may influence zinc metabolism. The decrease observed in renal and hepatic copper concentrations may be explained by the interaction between zinc and copper which are competitors for the protein sites fixation. Zinc inhibits copper absorption (O'Neill Cutting *et al.*, 1981), by induction of intestinal methallothionein synthesis that retens copper. Yang *et al.* (1998) showed that aluminium could alter copper homeostasis in brain of mice after prolonged administration of $AlCl_3$.

When pregnant rats are treated with $AlCl_3$, there is a decrease in renal and intestinal magnesium concentrations, but not in liver magnesium content. This can be attributed to a nephrotoxicity, thus magnesium is not reabsorbed by kidney (Liu & Nordberg, 1991).

The increase in intestinal, renal and hepatic iron concentrations in $AlCl_3$-treated pregnant rats can be explained by a decrease in intestinal proteins concentration after an aluminum treatment (Mestaghanmi *et al.*, 2001) which causes a perturbation in the absorption of amino-acids (Dlugaszek *et al.*, 2000). Morgan & Redgrave (1998) have shown a relationship between intestinal absorption, transit in plasma and induction of lipid peroxidation with cell damages related to aluminum treatment. The increase in tissue iron content may be attributed to the promotion of transferrin receptor synthesis while blocking ferritin synthesis (Ward *et al.*, 2001). In cells, transferrin receptors are able to bind transferrin, which may carry iron Fe^{3+} or aluminium, with similar affinity

Perez *et al.* (2001) and Han *et al.* (2000) have suggested that aluminum inhibits iron absorption and disrups the regulation of tissue ferritin levels.

$AlCl_3$ injected into pregnant rats causes some metabolic perturbations in mothers and fetuses especially in regard to plasmatic calcium, phosphorus and magnesium concentrations and in their tissue mineral component.

This disturbances of essential element induces disturbances on skeleton, neurological functions and erythropoietic system in human. To prevent the potential disturbances caused by aluminium ingestion during pregnancy we must avoid the consumption of Al-containing antacids, as well as other Al-containing products, which can be easily replaced by other compounds.

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