

Heartburns, Aluminum Containing Antacids and Pregnancy

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In order to determine short-term and long-term effect of aluminum containing antacids, pregnant mice were given a daily i.p dose of 0.7mg/100gm of aluminium sulphate for various periods according to the grouping. This dose was equivalent to a 70kg person ingesting 5000mg Al/day. Short-term exposure did show increased respiratory activity and decreased locomotor activity but all these symptoms disappeared within 24 hours of stoppage of drug. Long-term exposure showed cholergic signs and typical scaly dermatitis of dorsal skin. Recovery of mothers from these toxic effects varied from 100% in few groups to 50% in others. However mothers of all treated groups showed a very slow weight gain and negative response towards drug by decreased locomotor, respiratory and other physical activities. Fetal development was found to be arrested in the groups exposed to drug for longer periods.

Key Words: Antacid, Aluminum, Pregnancy.

Heartburn is a burning sensation felt behind the sternum when acid from the stomach's digestive juices splashes up into the esophagus. Most people experience heartburn from time to time; in pregnancy it can become frequent and over half of all pregnant women experience symptoms. There are a number of reasons why heartburn is more common in pregnancy; the baby is growing which puts some extra pressure on the stomach but more importantly the hormonal changes of pregnancy relax the muscle at the top of the stomach that usually stops the acid from splashing up^{1,2}

Pregnant women commonly use medications for their hyperacidity. Although most of the antacids have an excellent safety profile, some have unproven safety and may adversely affect the fetus. The safety profile of some medications may change according to the gestational age of the fetus. An estimated 10 percent or more of birth defects result from maternal drug exposure. Acetaminophen, chlorpheniramine, kaolin and pectin preparations, and most antacids have a good safety record. Several antacids are available including preparations that contain alginic acid, aluminum, magnesium, and calcium. These medications can be very effective in relieving heartburn and acid indigestion during pregnancy. All of these preparations generally are regarded as safe in pregnancy³. There have been sporadic reports of fetal maldevelopment and injury associated with prolonged use of high dosages of aluminum-containing antacids during pregnancy⁴. Data are insufficient to determine if these associations are significant.

Aluminum is a trivalent cation found in its ionic form in most kinds of animal and plant tissues and in natural waters everywhere. It is the third most prevalent element and the most abundant metal in the earth's crust. Dietary aluminum is ubiquitous, but in such small quantities it is not a significant source of concern in persons with normal elimination capacity. Urban water supplies may contain a greater concentration because water is usually treated with the element before becoming part of the supply. Subsequent purification processes that remove

organic compounds take away many of the same compounds that bind the element in its free state, further increasing aluminum concentration⁵.

All metals can cause disease through excess, deficiency, or imbalance. Malabsorption through diarrhea can result in essential metal and trace element deficiencies. Toxic effects are dependent upon the amount of metal ingested, entry rate, tissue distribution, concentration achieved, and excretion rate. Mechanisms of toxicity include inhibition of enzyme activity and protein synthesis, alterations in nucleic acid function, and changes in cell membrane permeability⁶. No known physiologic need exists for aluminum; however, because of its atomic size and electric charge (0.051 nm and 3+, respectively), it is sometimes a competitive inhibitor of several essential elements of similar characteristics, such as magnesium (0.066 nm, 2+), calcium (0.099 nm, 2+), and iron (0.064 nm, 3+). Approximately 95% of an aluminum load binds to transferrin and albumin intravascularly and is then eliminated through kidneys⁷.

Aluminum is absorbed from the GI tract in the form of oral phosphate-binding agents (aluminum hydroxide) and parenterally via dialysate or total parenteral nutrition (TPN) contamination. It is also absorbed during peritoneal dialysis. Lactate, citrate, and ascorbate all facilitate GI absorption⁸. If a significant load exceeds the body's excretory capacity, the excess is deposited in various tissues, including bone, brain, liver, heart, spleen, and muscle. This accumulation causes morbidity and mortality through various mechanisms⁹. Aluminum causes an oxidative stress within brain tissue, leading to the formation of Alzheimer like neurofibrillary tangles^{10, 11}. Aluminum also has a direct effect on hematopoiesis. Excess aluminum has been shown to induce anemia through decreased heme synthesis, decreased globulin synthesis, and increased hemolysis¹². Aluminum may also have a direct effect on iron metabolism. Patients with anemia from aluminum toxicity often have increased reticulocyte counts. Other organic manifestations of aluminum intoxication have been proposed, but the

mechanism by which it exerts its effect is complex and multifactorial but Aluminum toxicity has no predilection for any race, sex or age. Work in animal models (rats, mice, and rabbits) demonstrates that Al is distributed transplacentally and is present in milk¹³. Oral Al administration during pregnancy produces a syndrome including growth retardation, delayed ossification, and malformations at doses that also lead to reduced maternal weight gain. The severity of the effects is highly dependent on the form of Al administered¹⁴. In the postnatal period, reduced pup weight gain and effects on neuromotor development have been described as a result of developmental exposures. The significance of these findings for human health requires better understanding of the amount and bioavailability of Al in food, drinking water, and medications and from sources unique to infants and children such as breast milk, soil ingestion, and medications used specifically by pregnant women and children. We also need a better understanding of the unique biological actions of Al that may occur during developmental periods, and unique aspects of the developing organism that make it more or less susceptible to Al toxicity.

Aims & Objectives:

Since normal pregnancy is characterized by critical periods of protein synthesis during cell division and differentiation, it is obvious that these periods represent a time of optimal enzymatic activity, and it is not surprising that many of these enzymes may be sensitive to toxic levels of aluminum. Thus the purpose of this study was to formulate guidelines for precautionary measures to be taken by the mothers during pregnancy.

Material & Method:

72 non-pregnant female and 30 male albino mice were used for the present research. Dryness and bluish discoloration of external genitalia revealed the state of estrus cycle in female mice. Vaginal smear study was not done in order to avoid pseudopregnancy. Mating was allowed in estrus period. Presence of vaginal plug was considered as sign of initiation of pregnancy.

The pregnant female mice were then divided into experimental and control groups of 6 animals each. A sterilized solution of commonly available aluminum sulphate was made in distilled water. 0.7mg/100gm of this solution was injected daily intraperitoneally for various periods according to the grouping, starting from day 1 of pregnancy (Table-1). The control group animals were injected with the distilled water for the same period as the corresponding experimental group.

Results:

The results of present research work have revealed it quite clearly that the aluminum compounds are not only teratogenic and embryotoxic but detrimental for the pregnant

mothers as well especially when exposure is prolonged. Weight gain of mothers of all experimental groups was very slow as compared to control groups.

Table 1: Experimental Design

Control Group	Dose	Experimental			
		Period*		Group	Dose period*
A	0.25nk of dust, water	1-6	A ₁	0.25ml of Al ₂ (SO ₄) ₃ Solution	1-6
B	-do-	7-12	B ₁	-do-	7-12
C	-do-	13-18	C ₁	-do-	13-18
D	-do-	1-12	D ₁	-do-	1-12
E	-do-	7-18	E ₁	-do-	7-18
F	-do-	1-18	F ₁	-do-	1-18

*Days of gestation

Results of short-term exposure: When drug was administered for small periods (GpA₁, B₁ & C₁) it did not produce any toxic symptoms in mothers but the embryos recovered from these mothers showed dwarfism, reduced body weight and intrauterine growth retardation. Mothers of these groups did show increased respiratory activity and decreased locomotor activity during the period of exposure to the drug. All these symptoms disappeared within 24 hours of stoppage of drug.

Results of long-term exposure: The mothers of group D₁, E₁ & F₁ were all listless, weak and exhausted on day 20 of gestation. They showed cholenergic signs and typical scaly dermatitis of dorsal skin. Dermatitis was more marked in F₁ as exposure was longest. The cholenergic signs, which appeared in mothers of group D₁, E₁, and F₁, indicated toxicity of aluminum sulphate. Recovery of mothers from these toxic effects was 100% in-group D₁, 90% in-group E₁, and only 50% in-group F₁.

Conclusion:

These results revealed that aluminium is a type of heavy metal that is non-toxic to the adults when used for short periods but prolonged usage especially in stressful conditions like pregnancy may produce toxic signs & symptoms. So these compounds should be used under strict medical supervision.

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