Toxicity effect of gentamicin on serum levels of renal functional factors in newborn breast feeding Mice

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Abstract
In this study, it was tried experimentally to investigate the toxic effect of gentamicin on the serum level of renal functional factors in newborn mice through breast milk. This experimental study was conducted on 42 pregnant female mice weighing 20 - 30 g and 24 weeks-old which were purchased from laboratory animal breeding center. After the birth of newborns, the intervention group received intraperitoneal gentamicin at dosage of more than 200 mg/kg every other day from the first day until the end of lactation about of 21 days. The normal group was injected distilled water with the same volume. One day after the last Intraperitoneal injection blood samples were obtained from the hearts of mothers and neonates to study serum levels of renal biochemical factors. The obtained results on the serum level of urea were significantly different between the two groups (P < 0.001). The obtained results on the serum creatinine were significantly different between the two groups (P < 0.001). The obtained results on the serum uric acid level were significantly different between the two groups (P < 0.001). According to the obtained results of this study it seems that serum levels of renal functional factors, including urea, uric acid and creatinine in the gentamicin-treated mother mice are significantly different compared with the normal group.

Keywords : Breast feeding, Gentamicin, Mice and renal functional factors

Introduction
Gentamicin is of aminoglycoside, which is used widely, especially in infancy in humans. One of its important complications is renal toxicity (Ghaznavi et al., 2006). Despite its clinical brilliant effects in humans and animals, the clinical use of Gentamicin, that is an aminoglycoside antibiotic, has been limited due to the side effects of the drug. Free radicals cause peroxidation of membrane phospholipids, as well as breaking and denaturation of proteins; so, some changes occur in membrane fluidity and therefore the membrane will permeable against molecules even as large as enzyme (Ghaznavi et al., 2006). Active species of oxygen, especially hydroxyl radicals, cause lipid peroxidation, cell membrane damage, Protein and nucleic acid oxidation, and tissue damage (Naghizadeh et al., 2006). The use of antibiotics during Pregnancy is common and there is a possibility of their adverse effects on the developing embryo. The potential risk of long-term and high doses treatment of pregnant women with antibiotics, especially in the third month of pregnancy is very important such that causes destroying and losing the leaning of placenta which leads in turn to fetal toxicity and congenital defects (Shahraz and Ghaziani, 2008). Among the side effects of gentamicin it seems that nephrotoxicity is more important (Goodman and Gilman, 1991) such that based on conducted research, 8 to 42 percent of patients who
received gentamicin, have been affected an acute renal failure (Muson et al., 1995; Symmers et al., 1992). Conducted research have shown that pathological damage to renal tissue eventually leads to renal hemorrhage, which then causes the proteins needed fetus and infant reduced in maternal blood and breast milk. Besides the protein, other necessary materials are reduced in maternal blood and breast milk; so, the fetus and infant won’t have the necessary growth (Braulio et al., 2001 and Brzóska et al., 2002).

In this study, it was tried experimentally to investigate the toxic effect of gentamicin on the serum level of renal functional factors in newborn mice through breast milk.

**Methods and Materials**

This experimental study was conducted on 42 pregnant female Bulb/c mice weighing 20-30 g and 24 weeks-old which were purchased from laboratory animal breeding center of Islamic Azad University of Marand branch. The animals were kept in the keeping part of laboratory, animals of the Tabriz Azad University which was standard in terms of light, water, humidity, food and cages flooring. Pregnant female mice were randomly divided into two groups of ten mice. After the birth of newborns, the intervention group received intraperitoneal gentamicin at dosage of more than 200 mg/kg every other day from the first day until the end of lactation about 21 days (Chen et al., 2012), the normal group was injected with distilled water at the same volume. One day after the last Intraperitoneal injection (21 days of lactation), blood samples were obtained from the hearts of mothers and neonates to study serum levels of renal biochemical factors. The serum were isolated by centrifugation of blood at 2500 rpm for 15 min at 30°C. Biochemical factors were evaluated based on JAFFE and TOOS methods. Serum urea was measured using Bertholet quantitative diagnostic kits (Pars Azmoon Company) and colori-metric method. The experiment was based on the formation of a green compound of urea hydrolysis resultant ammonia by urease with sodium hypochlorite and sodium salicylate. The intensity of the color produced is proportional to the amount of urea in the sample (Patton and Crouch, 1977). The serum creatinine level was measured using quantitative diagnostic kits of Ziest Chem Diagnostics as well as JAFFE method. In this method, creatinine forms a complex with alkaline picrate which was measured at a wavelength of 490-510 nm, and the intensity of the color produced is proportional to the amount of creatinine in the sample (Jaffe, 1886). Serum uric acid was measured using Toos quantitative diagnostic kits made by Pars Azmoon Co. (Thomas, 1998). Data were expressed as Mean ± S.E. and t-test was used to statistical analysis of the data, and SPSS 13 was used to compare the differences between the two groups (the normal group and the treatment group using gentamicin). p<0.05 was considered to determine the significant level (p – value) between the groups.

**Results**

**The effect on serum levels of urea**

In postpartum female mice of the normal and gentamicin groups the mean serum urea was 31.14 ± 1.342 and 54.6 ± 2.459 mg/dl, respectively. The obtained results were significantly different between the two groups (p<0.001).

In newborn mice of the normal and gentamicin groups the mean serum level of urea was 38.55 ± 1.369 and 49.68 ± 2.424 mg/dl, respectively. The obtained results were significantly different between the two groups (p<0.001).

**The effect on serum creatinine**

In postpartum female mice of the normal and gentamicin groups the mean serum creatinine was 1.72± 0.102 and 2.14 ± 0.128 mg/dl, respectively. The
obtained results were significantly different between the two groups (P < 0.05).

In newborn mice of the normal and gentamicin groups the mean serum level of creatinine was 1.34 ± 0.636 and 2.84 ± 0.748 mg/dl, respectively. The obtained results were significantly different between the two groups (p<0.001).

The effect on serum uric acid levels

In postpartum female mice of the normal and gentamicin groups the mean serum uric acid was 4.86 ± 0.307 and 5.66 ± 0.256 mg/dl, respectively. The obtained results were significantly different between the two groups (P < 0.05).

In newborn mice of the normal and gentamicin groups the mean serum level of uric acid was 4.18 ± 0.328 and 5.23 ± 0.256 mg/dl, respectively. The obtained results were significantly different between the two groups (p<0.001).

**Discussion**

Gentamicin crosses the placenta and its amount in the umbilical Cord Blood was reported by separate studies as 34% and in postpartum female as 42% (Chow and Jewesson, 1985; Philipson et al, 1973; Santschi and Papich, 2000). The antibiotic enters breast milk, but its absorption in the intestine is minimal such that its traces can be found only in half of breast feeding newborns. No signs of clinical symptoms in newborns feeding with gentamicin-treated mothers (Salil-oghlu et al, 1994; Schaefer et al, 1996; Ayatollahi et al, 2008).

According to the obtained results of this study it seems that serum levels of renal functional factors, including urea, uric acid and creatinine in the gentamicin-treated mother mice are significantly different compared with the normal group. Furthermore, in the evaluations conducted on the mentioned biochemical factors, it was found that there is a significant difference among the newborns feeding by the milk of gentamicin-treated mothers which is related to the digestion rate of the drug in milk and its impressionability during lactation.

Silanefit et al. (1991) in their study on the effect of cadmium chloride on newborns’ kidney have explained
that cadmium chloride causes some important changes in the renal biochemistry of rats during early after birth, which was limited to the neonatal period and occurs in the absence of other toxicity symptoms.

**Conclusion**

Based on the findings of this study, the role of the direct toxic effects of gentamicin on the newborn mice which received the drug via breastfeeding is a certain issue. In any case, it is better to administrate the drug as a treatment for infectious disease in lactating mothers with caution. In addition, significant changes in serum levels of renal function of newborn mice can suggest the effect of gentamicin on breast milk during lactation at concentrations used in this study. The results of the survey can provide settings for more comprehensive investigations and studies with different concentrations and durations.

**References**


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