Evaluation of the effect of Molybdenum nanoparticles on the incidence of pregnancy in *Mus musculus*

Radwa H. El-Atawy, Hanan R.H Mohamed, Ahmed M. Ghoneim, Akmal El Ghor

Abstract— Molybdenum nanoparticles (Mo-NPs) are extensively used in huge applications. However, limited studies investigated their effect on the pregnancy incidence. This study aimed to evaluate the effect of Mo-NPs on the incidence of pregnancy in mice. Female mice were divided into different groups and treated with different doses of Mo-NPs. Administration of Mo-NPs caused significant decreases in the number of pregnant female mice during the experimental period. Conclusion: Mo-NPs administration decreased the incidence of pregnancy in mice.

Keywords— Mo-NPs, oral administration, pregnancy, female mice

1 Introduction

Over the past few years, there has been a rapid development in the field of nanotechnology around the world due to its wide applications in the industry and biomedicine. Nanotechnology deals with materials in the size range of 0.1 to 100 nm. As a result of their small size, these materials are characterized by different properties such as electrical conductance, chemical reactivity, magnetism, optical effects, and physical strength, from bulk materials. Nano medicines are used for drug delivery and can improve drug bioavailability. Nanotechnology devices are being developed for diagnosis of cancer and infectious diseases which can help in early detection of the disease [4].

Molybdenum (Mo) is an essential trace element in the human and plant nutrition. Molybdenum is considered the key component of several important enzymes, including nitrate reductases (NAR), nitrogenase, aldehyde oxidase, sulfite oxidase, and xanthine oxidase in human and other mammals [12]. Human can be exposed to molybdenum via many ways like diet, drinking water, or inhalation from occupational exposure from mining operations and various industrial uses. Highly dietary intake of Mo causes damage to humans and animals such as renal tubule degeneration, glomerular atrophy, nuclei deformation, and fracture in goat kidney [7].

Molybdenum nanoparticles (Mo-NPs) are widely used in various industries including magnetic materials, optical materials, chemical catalysis and sensing as well as Mo-NPs are used as additives to plastic, oils [18]. Additionally, Mo-NPs are intensively used in cutting tools and hard alloys and also they are used as smoke inhibitors [1]. In spite of all these uses that increase human exposure to Mo-NPs, no studies are available on the effect of Mo-NPs administration on the rate of pregnancy. Thus, the current study evaluated the effect of Mo-NPs administration on the incidence of pregnancy in female mice.

2 Materials and methods

2.1 Animals

Mice were purchased from the animal house of the National Organization for Drug Control and Research, Egypt (NODCAR). They were housed in plastic cages under standard lighting conditions and supplied with standard diet and water. Mice were left for one week for accommodation before beginnig the experiment.

2.2 Chemicals

Molybdenum nanoparticles (Mo-NPs) were purchased in the form of black powder from Sigma Company (St. Louis, MO) and suspended in deionized distilled water for oral administration in mice.

2.3 Treatment schedule

For pregnancy, female mice were housed with healthy males overnight under controlled conditions. Then, females were examined in the next morning and considered pregnant if were positive for vaginal plug or theough vaginal smears, and the day of detection was defined as the first day (E1) of pregnancy or gestation. Females were then transferred to plastic cages and randomly divided into five groups of (5-6) animals: the 1st group is the negative control group and was administered deionized distilled water from the 1st day up to the 17th day of gestation, the 2nd (G1) and the 3rd (G2) groups were orally administered Mo-NPs at the dose level 500 mg/kg.bw from the 1st day up to the 17th day or from the 9th day up to the 17th day of pregnancy, respectively. While the 4th (G3) and the 5th (G4) groups were orally administered Mo-NPs at 750 mg/kg.bw from the 1st day up to the 17th day or from the 9th day up to the 17th day of pregnancy, respectively.

2.4 Detection of pregnancy rate

Females were followed up throughout the whole gestation period and the number of pregnant females was recorded in each group.

2.5 Statistical analysis

Statistical Package for the Social science software (SPSS-20) was used to compare between the five different groups using One way Analysis of Variance (ANOVA) followed by Duncan's test at the level of significance $p<0.05$.

3 Results

Oral administration of Mo-NPs at the two different doses 500 and 750 mg/kg. b.w during the two time intervals from 0 to 17th day and from 9 to 17th day of pregnancy affected the pregnancy incidence as revealed by the recorded significant decreases in number of pregnant mice in the first three treated groups (G1-G3) while no significant change was observed in the pregnancy rate in the fifth group (G4) as shown in Fig 1.

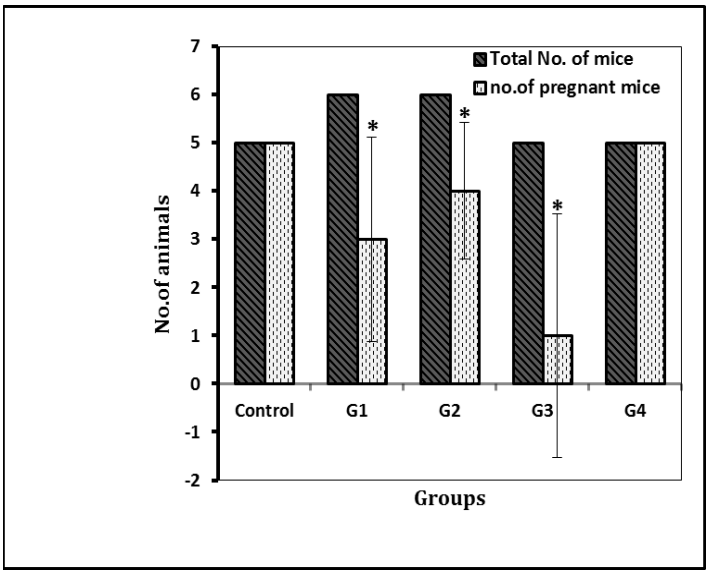

Fig. 1: Incidence of pregnancy in mice groups (G1-G4) administered Mo-NPs compared to that in the negative control.

4 Discussion

Although Mo-NPs are intensively used in many industrial food and medicine applications, their effect on the rate of pregnancy has not been well investigated. Therefore, this study evaluated the effect of Mo-NPs administration on the incidence of pregnancy in female mice.

Results of the current study showed that oral administrations of Mo-NPs decreased the incidence of pregnancy as revealed by the significant decreases observed in the number of pregnant mice at the two studied time intervals. These results confirmed the previously reported embryo-toxic effects of Mo in several studies [2], [13], [14], [15], [17] that demonstrated that excessive ingestion of Mo affected male reproductive efficiency in animals and humans.

Also, Fungwe et al. [6] found prolonged estrous cycle and abnormal embryogenesis in rats as a result of a high ingestion level of Mo. Similarly, Howell et al. [8] indicated that exposure of human to high dose of Mo during pregnancy was related to the increased risk of neural tube defects. In contrast, other studies showed no effects on the reproduction in rats

- Radwa H. El_Atawy , Zoology Department; faculty of science, Damietta University, Egypt, radwaelatawy@gmail.com
- Hanan R.H Mohamed,Assistant professor of Genetics, Zoology Department; faculty of science, Cairo University, Egypt, hananesresm@yahoo.com
- Ahmed M. Ghoneim,Assistant professor of Molecular Biology, Zoology Department; faculty of science, Damietta University, Egypt, am_ghoneim@du.edu.eg
- Akmal El Ghor, professor of Genetics, Zoology Department; faculty of science, Cairo University, Egypt, akmalelghor@gmail.com

and Guinea pigs [7], [11]. But the mechanisms that affect female reproduction are not well defined until now.

High dietary intake of Mo induced oxidative stress, histopathological changes in rabbit testes and decreased antioxidant enzymatic activities in rabbits [2].

Oxidative stress affected the ovarian efficiency that may result in female infertility [9], [14]. Several studies have studied the bio-distribution of nanoparticles to the fetuses across the placenta. Normal placenta is required for successful development of embryos. Some studies have warned about the potential adverse effects of nanoparticles on fetuses and showed that the Mo compounds have the ability to cross the placental barriers more easily and affect the embryos [3], [10].

5 Conclusion

In conclusion, oral administration of Mo-NPs caused significant decreases in the incidence of pregnancy that threatens human life and requires further studies to investigate its teratogenic effects.

References

[1] Asadi Fardin ; Mehran Mohseni ; Karim Dadashi Noshahr ; Fariba Haj Soleymani; Ahmad Jalilvand; Azam Heidari (2017): Effect of Molybdenum Nanoparticles on Blood Cells, Liver Enzymes, and Sexual Hormones in Male Rats. Biol. Trace Elem. Res., 175:50–56.

[2] Bersényi, A.; Berta, E.; Kádár, I.; Glávits, R.; Szilágyi, M.; Fekete, S.G. (2008): Effects of high dietary molybdenum in rabbits. Acta. Vet. Hung, 56 (1):41–55.

[3] Bougle, D.; Voirin, J.; Bureau, F.; Voirin, J. (1989): Molybdenum normal plasma values at delivery in mothers and newborns. Acta Paediatr Scand, 78:319–320.

[4] Burke, A. R.; Singh, R. N.; Carroll, D. L.; Wood, J. C.;D'Agostino, R. B., Jr.; Ajayan, P. M.; Torti, F. M.; Torti, S. V. (2012): Biomaterials, 33: 2961−2970.

[5]Fardin Asadi; Mehran Mohseni; Karim Dadashi Noshahr; Fariba Haj Soleymani;Ahmad Jalilvand; Azam Heidari; (2017): Effect of Molybdenum Nanoparticles on Blood Cells, Liver Enzymes, and Sexual Hormones in Male Rats. Biol Trace Elem Res., 175:50–56.

[6] Fungwe, T.V.; Buddingh, F.; Demick, D.S.; Lox, C.D.; Yang, M.T.; Yang, S.P. (1990): The Role of Dietary Molybdenum on Estrous Activity, Fertility, Reproduction and Molybdenum and Copper Enzyme-Activities of Female Rats. Nutr. Res., 10:515–524.

[7] Gu, X.; Ali. T.; Chen, R.; Hu, G.; Zhuang, Y.; Luo, J.; Cao, H.; Han, B. (2015): In vivo studies of molybdenum induced apoptosis in kidney cells of caprine. Biol.Trace Elem. Res., 165: 51-58.13.

[8] Howell, J.M.; Shunxiang, Y.; Gawthorne, J.M. (1993): Effect of thiomolybdate and ammonium molybdate in pregnant guinea pigs and their offspring. Res. Vet. Sci., 55:224–230.

[9] Huang, J.; Wu, J.L.; Li, T.J.; Song, X.M.; Zhang, B.Z.; Zhang, P.W.; ZHENG, XiaoYing. (2011) :Effect of exposure to trace elements in the soil on the prevalence of neural tube defects in a high-risk area of China. Biomed. Environ. Sci., 24:94–101.

[10] Hussain, S.M.;Hess, K.L.; Gearhart, J.M.; Geiss, K.T.; Schlager,J.J.(2005): In vitro toxicity of nanoparticles in BRL 3A rat liver cells. Toxicol. In. Vitro.; 19: 975-83.

[11] Keelan, J. A. (2011): Nanotoxicology : nanoparticles versus the placenta. Nat. Nanotechnol., 6: 263–264.

[12]Kisker, C.; Schindelin, H.; Rees, D.C. (1997): Molybdenum cofactor containing enzymes:structure and mechanism. Annu. Rev. Biochem ,66:233–67.

[13] Lyubimov, A.V.; Smith, J.A.; Rousselle, S.D.; Mercieca, M.D.; Tomaszewski, J.E.; Madhumitha, G.; Fowsiya, J.; Roopan, S.M. (2016): Nanoparticles for Agriculture: Synthesis, Classification and Characterization. In: Ranjan S., Dasgupta N., Lichtfouse E. (eds) Nanoscience in Food and Agriculture 3. Sustainable Agriculture Reviews, vol 23. Springer, Cham.

[14] Meeker, J.D.; Rossano, M.G.; Protas, B.; Diamond, M.P.; Puscheck, E.; Daly, D.; Paneth, N.; Wirth, J.J. (2008): Cadmium, Lead, and Other Metals in Relation to Semen Quality: Human Evidence for molybdenum as a male reproductive toxicant. Environ Health Perspect,116(11):1473-9.

[15] Pandey, R.; Singh, S.P. (2002): Effects of molybdenum on fertility of male rats. Biometals, 15: 65-72.

[16] Wang, W.; Craig, Z.R.; Basavarajappa, M.S.; Hafner, K.S.; Flaws, J. A. (2013): Mono-(2- ethylhexyl) phthalate induces oxidative stress and inhibits growth of mouse ovarian antral follicles. Biol. Reprod., 27: 87-152.

[17] Wirth, J.J.; Mijal, R.S. (2010): Adverse effects of low level heavy metal exposure on male reproductive function. Syst. Biol. Reprod. Med., 56:147–167.

[18] Yadav, T. (2006): Molybdenum Comprising Nanomaterials and Related Nanotechnology.US Patent 20060079410A1.