無機砷化合物對大鼠血壓上升機制之探討

The Mechanism of Inorganic Arsenic Compounds on Elevating Blood Pressure in Rats

中文摘要

本研究以跨世代動物模式探討無機砷化合物是否為引起大白鼠血壓上升的危因，並探討其可能機制，同時亦比較親子二代之間差異。本研究以 48 隻雌雄各半 Wistar 品系大白鼠，隨機分為三組，分別於飲水中長期添加濃度 50 ppm 三價砷、50 ppm 五價砷、正常飲水組三組，於實驗期間定期分析尾靜脈血壓，並採集血液檢體。另外，實驗進行 30 天後將同組雌雄鼠飼養於同一籠中進行交配 10 天，而後母鼠隔離飼養。在分別紀錄受孕母鼠生產時間後，每組隨機取 10 隻之雄性子代共 30 隻，進入跨世代研究。子代於出生第 0 天至 120 天，每 30 天進行一次尾靜脈壓測試，且每 40 天採尾靜脈血。親代於第 200 天犧牲，子代於第 120 天犧牲。於實驗結束收集肝臟、腎臟等組織檢體進行抗氧化酵素及相關分析。結果發現，親代中三價砷及五價砷組血壓皆明顯較正常組升高($p<0.001$)，除了肝臟外，血管張力素轉化?活性於各組織中卻無明顯變化。此外，親代動物血液中氧化壓力增高，於暴露 40 天後超氧化歧化?、麩胱甘?過氧化?活性均顯著下降，而過氧化氫?活性則顯著升高。脂質過氧化物的生成於 160 天時均顯著高於正常組，同時亦發現三價砷及五價砷組動物血中的三酸甘油酯及膽固醇都有偏高的現象。在一氧化氮(Nitric oxide, NO)生成方面，砷飲用組血漿中的濃度則較控制組低。在肝臟結果方面，三價砷飲水組結果則與五價砷組稍有不同，三價砷組肝臟中超氧化歧化?活性顯著較低，而五價砷組麩胱甘?過氧化?活性則較高，但兩者的脂質過氧化物生成均顯著增加，而總 NO 含量則較高。在子代結果方面，並沒有明顯加速高血壓進程的現象產生，但其血壓及抗氧化系統在與親代同時間的砷暴露下也有相同異常現象產生。由上述結果得知，在無機砷化合物長期慢性暴露下會促使大鼠血壓上升，其機轉並非藉由腎素-血管收縮素系統，而可能經由組織中抗氧化酵素的異常致使氧化壓力增加，進一步影響血管內皮細胞 NO 生成量下降，使 NO 鬆弛血管途徑受阻。另一方面，血漿中脂質增加與過多的活性氧屬，亦增加了脂質過氧化物濃度。

英文摘要

The mechanisms of inorganic arsenic compounds on blood pressure regulation and the generation effect were elucidated in the study. Fifty part per million (ppm) arsenate or arsenite in drinking water was given to forty eight animals (Wistar rats) and there offspring for subsequent 200 days ad libitum. Blood and tissue samples were collected for analysis. Results showed arsenic significantly increased blood pressure in Wistar rats at the 80th day. Elevated lipid peroxidation (160th day) and suppressed activity of serum superoxide dismutase (SOD) and glutathione peroxidase (GPx) (40th day) were found during the study. Besides, plasma lipids (triglyceride and cholesterol) increased in both arsenic groups but lowered in the liver. From the nitric oxide (NO) point of view, plasma level of NO was lower in arsenate exposed group but hepatic NO level was significant higher than control group. Furthermore, hepatic SOD and GPx were also imbalanced comparing to controls. Nevertheless, there were no changes in tissue angiotensin converting enzyme activity except in hepatic tissue in both generations and the results. There were no evidences revealed that the development of hypertension or abnormal antioxidative enzyme system accelerated in offspring. In conclusion, the inorganic arsenic compounds may cause elevated blood pressure by increasing oxidative stress, lipid peroxidation and serum lipids but not via renin-angiotensin system. Further studies are needed to clarify the generation effects of chronic arsenic exposure.