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INCREASED SUSCEPTIBILITY OF PLATELETS BY ARSENIC IN DRINKING WATER: A CONTRIBUTING FACTOR TO CARDIOVASCULAR DISEASE

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Arsenic (As) is a ubiquitous element found in several forms in foods and environmental media, such as soil, air, and water. The primary route of human exposure is through ingestion of arsenic-contaminated food and drinking water. The predominant form of arsenic in drinking water is inorganic arsenic, which is both highly toxic and readily bioavailable. Chronic ingestion of arsenic-contaminated drinking water is therefore considered the major pathway that drives risk to human health. Chronic arsenic exposure has been associated with diverse health effects including cancer, hyperkeratosis, hyperpigmentation, reproductive toxicity, diabetes, and cardiovascular disease. Cardiovascular effects associated with high arsenic levels in drinking water include Blackfoot disease (BFD), peripheral vascular disease, atherosclerosis, hypertension and ischemic heart disease. This suggests the possibility that long term ingestion of inorganic arsenic may alter hemostasis and normal blood vessel function. Blood platelets play a major role in hemostasis, thrombosis and initiation of various vascular diseases. Certain chronic diseases such as diabetes or exposure to exogenous chemicals and drugs can alter the normal hemostatic balance, thereby causing excessive platelet aggregation and ultimately lead to various cardiovascular diseases (CVD), such as thrombosis.

The present study investigated the effects of arsenic on platelet aggregation to determine if arsenic-induced alteration of hemostasis could be a causative factor in the cardiovascular disease observed following chronic ingestion of arsenic-contaminated drinking water. Sodium arsenite (iAsⅢ) enhanced in vitro platelet aggregation induced by several agonists (thrombin, collagen, ADP and arachidonic acid) in a concentration- and time-dependent manner, but was not directly toxic to platelets and did not directly induce platelet aggregation. The relative potency of various forms of arsenic to enhance thrombin-induced platelet aggregation was iAsIII > iAs V>MMA>>DMA. Treatment of iAsⅢ with thrombin also resulted in a concentration-dependent

significant increase of serotonin secretion from platelets. Formation of thromboxane B2 (TXB2) from platelets followed the same general trend, but was not statistically significant. In vivo, iv infusion of iAsIII increased thrombus formation by thromboplastin. Ingestion of iAsIII-contaminated drinking water elevated the plasma serotonin levels, which was consistent with the in vitro serotonin secretion from platelets. These results suggest that arsenic exposure renders platelets more susceptible to aggregatory stimulus and readily enhances serotonin secretion from platelets, two effects which may contribute to arsenic-associated cardiovascular diseases.

keyword : Arsenic, Platelets, Cardiovascular disease, Drinking water