中文摘要

本研究主要目的為預測及評估孩童因暴露於含砷飲用水而誘導皮膚損害之風險，並探討 18 歲以下孩童各年齡層之飲用水安全含砷量。皮膚損害之色素沉著症 (Hyperpigmentation) 及角化症 (Keratosis) 與慢性砷暴露有著密不可分之關係。本研究以印度西孟加拉 (West Bengal, India) 砷流行疫區之流行病學調查資料為基礎，利用韋伯 (Weibull) 模式建立砷暴露劑量、年齡及孩童皮膚損害效應之關係，評估孩童飲用水安全含砷量，再結合以生理為基礎之藥理動力學 (Physiologically Based Pharmacokinetic, PBPK) 模式模擬孩童不同生理狀況及代謝機制，以探討飲水量變異所造成體內濃度之變化。生命階段之 PBPK 模式描述孩童對主要代謝物種砷 As(III)、As(V)、MMA(III)、MMA(V)、DMA(III) 及 DMA(V)之吸收、分佈、代謝及排除，並評估孩童體內各器官物種砷濃度之動態變化。本研究利用勝算比 (Odds Ratio, OR) 推估孩童暴露於砷所造成皮膚損害之不利健康效應之相對危險性大小，主要利用 PBPK 模式模擬暴露組及控制組孩童尿液中 MMA(III) 之濃度，結合韋伯模式模擬不同年齡及不同砷濃度之盛行率，計算暴露組及控制組累積盛行率之比值。結果顯示，砷暴露濃度與皮膚損害之累積盛行率呈正相關 (R^2=0.91−0.96)，因男性皮膚損害最為嚴重，故以男性皮膚損害為基準，並設其最高可接受風險為 10^{-3}，可得 0−6 歲男性及女性之飲用水安全含砷量分別為 2.2 及 6 μg/L，而 7−18 歲男性及女性則分別為 1 及 2.8 μg/L。本研究以勝算比 (95%信賴區間) 評估印度西孟加拉、孟加拉以及台灣西南部之平均飲用水砷濃度分別為 283.19、282.65 及 468.61 μg/L 時，18 歲以下孩童之 OR 分別為 1.38−5.20、2.03−20.97 及 3.50−21.10。本研究建議尿液 MMA(III) 濃度之增加與砷誘導孩童皮膚損害風險之增加有關。本論文提供環境風險管理之架構並整合流行病學做為政府訂定規範之建議。

關鍵詞：砷暴露；孩童；皮膚損害；甲基化；韋伯模式；藥理動力學；風險評估；印度西孟加拉

Abstract

The purpose of this study was to predict and assess the arsenic-related children skin lesions risk from drinking water and estimate the safe drinking water arsenic standard below 18 years old children. Chronic arsenic exposure and skin lesions (such as hyperpigmentation and keratosis) are inextricably linked. We established the relationship among arsenic exposure dose, age and effects of children skin lesions with Weibull model based on arsenic epidemiological data in West Bengal, India. We assessed the safe drinking water arsenic standard for children with Weibull model and linked Physiologically Based Pharmacokinetic (PBPK) model to estimate children organ-specific arsenic concentrations varied with methylating activity and drinking water consumption rates. This study present an integrated approach by using Weibull model-based framework on the basis of gender/age-specific epidemiological data on arsenic exposure, skin lesions prevalence, and using PBPK model to predict monomethylarsonous acid (MMA(III)) levels in urine to estimate the likelihood risk obtained from studies conducted in arseiasis-endemic in West Bengal, India. A life-stage PBPK model is used to describe the absorption, distribution, metabolism, and excretion of the metabolites: arsenate (As(V)), arsenite (As(III)), monomethylarsonic acid (MMA(V)), monomethylarsonous acid (MMA(III)), dimethylarsinic acid (DMA(V)), and dimethylarsinous acid (DMA(III)) in target tissue groups, considering the potential impact by physiologically life-stage differences. We calculated odds ratio (OR) to assess the relative magnitude of the effect of the arsenic exposure on the likelihood of the prevalence of children skin lesions. The results show that arsenic exposure dose, age and cumulative prevalence ratio of the hyperpigmentation and keratosis are correlated significantly (R2=0.91-0.96). On the other hands, arsenic exposure dose raised followed

cumulative prevalence ratio. The safe arsenic drinking water standards were estimated to be 2.2, 6 respectively for 0-6 years males and females as well as 1, and 2.8 μg/L respectively for 7-18 years males and females based on the index skin lesions of male hyperpigmentation with cumulative prevalence ratio equals 10-3. Risk predictions indicate that estimated ORs have 95% confidence intervals of 1.83−5.20, 2.03−20.97, and 3.50−21.10 based on mean drinking water arsenic concentrations of 283.65, 282.65, and 468.81 μg/L, respectively, in West Bengal, Bangladesh, and southwestern Taiwan. Our finding also suggests that increasing urinary MMA(III) levels are associated with an increase in risks of arsenic-induced children skin lesions. This study offers an environmental risk management framework to suggest regulations and administrating process by linking arsenic epidemiological data.

***Keyword*:** Arsenic Exposure; Children; Skin lesions; Methylation Capacity; Weibull; PBPK; Risk assessment; West Bengal (India)