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Title: GTn heme oxygenase-1 polymorphism in beryllium-exposed dental technicians

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Body: Background: Dental technicians (DTs) are exposed to Beryllium (Be) and other substances capable of inducing lung disease. Heme oxygenase -1 (HO-1) play a protective antioxidant role in the lung. The guanine-thymidine (GT) n repeats in the HO-1 promoter determine HO-1 induction level. Short (GT) n repeats (n = <25; S genotype) is considered as protective since HO-1 is induced more rapidly than in long (GT) n repeats (n = \geq 25; L genotype). Aims To evaluate the correlation of HO-1 polymorphisms to functional and exposure parameters in DTs and the protective role of HO-1 on Be Oxide (BeO) exposed A549 epithelial cells apoptosis. Methods 65 DTs were followed-up for 2 years by questionnaires, induced sputum (IS) particles size distribution laser analysis (Dapi 2000 Donner Tech and Pulmonary Function Tests. HO-1 genotyping was done by PCR DNA sequencer (AB prism 310). A549 epithelial cell line was cultured with BeO and pretreated with Hemin and Znpp (for stimulation and inhibition of HO-1 respectively), HO-1 gene expression was evaluated in IS and A549 cells by quantitative PCR and apoptosis by TUNEL staining. Results: Association was found between GTn and HO-1 gene expression in IS (r=-0.35 p=0.017), the GTn<25 group had higher HO1 expression than the GTn>25 group (0.18±0.16 Vs 0.07±0.06 p= 0.007 respectively). Decrease in DLCO (Diffusion Lung CO) was associate with GTn >25. Hemin increases the HO-1 gene expression and decreases the apoptosis levels in A549 epithelial cells while is increased by ZnPP. Conclusions: DLCO decrease is associated with L genotype. Decrease apoptosis in BeO-exposed A549 epithelial cells by hemin may indicate a protective role of HO-1. Supported by USA-Israel Bi National Science Foundation.