Validation of biomarkers for improved assessment of exposure and early effect from exposure to crystalline silica.

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Abstract:

This is the third phase of a project to identify, confirm, and operationalise biomarkers for crystalline silica dust exposure that could be used for surveillance of dust exposure levels in South African mines. The first phase of the project involved a comprehensive review of the relevant literature [Gulumian *et al*., 2006] from which ten potential biomarkers of effect were identified as being worthy of further investigation. The second phase of the project examined the ten identified biomarkers in silica dust-exposed and unexposed black male subjects [Murray *et al*., 2006]. Two of the ten short listed biomarkers, namely erythrocyte glutathione peroxidase (GPx) and serum Clara cell protein 16 (CC16), were found to have significantly reduced levels in the silica dust-exposed versus unexposed subjects. In addition, the biomarkers were found to be unaffected by HIV sero-status, smoking, age and the presence of silicosis. As a result, this third phase of the project aimed to confirm the levels of and further analyze GPx and CC16 in miners exposed to crystalline silica dust.

This third phase involved the measurement of the levels of erythrocyte GPx and serum CC16 in 80 adult male gold miners upon their return from leave and then again two to six months after they had returned to work (involving exposure to crystalline silica). Before

the field work was conducted, however, the optimal operational parameters for the biomarkers (namely storage temperature, delay in time between blood collection and separation, laboratory temperature and storage duration) were established. The results of these optimization experiments were used to develop Standard Operating Procedures (SOPs) for biomarker specimen handling and storage under field conditions, and for laboratory assays.

In this phase, the findings of the second phase were confirmed in that the levels of GPx and CC16 were lowered in miners exposed to crystalline silica dust and were unaffected by age, race and cigarette smoking. In addition, while CC16 was unaffected by the presence of radiological silicosis, GPx may have been affected. Finally, the decrease in the levels of GPx activity and CC16 concentration observed in the study were unaffected by the level of silica dust exposure (high or low) as determined by job category or by the duration of crystalline silica exposure.

Regarding the levels of GPx activity, the results suggested that GPx levels decrease after two to six months of chronic exposure to crystalline silica dust and remain decreased (throughout the working week and over a weekend) and then increase or even recover to normal levels during a period of leave. It was therefore concluded that GPx activity levels rise and fall, in response to silica dust exposure, gradually and over periods of some time, possibly months.

The CC16 results were, however, less promising. After two to six months of chronic exposure to crystalline silica dust there was a significant change in CC16 on a Wednesday afternoon following an 8-hour shift and during the duration of a shift. In addition, there is the possibility that the observed changes were due to a time-dependent diurnal variation in the CC16 levels.

It was concluded that the results of the current phase warrant further research into the use of erythrocyte GPx and serum CC16 as biomarkers of early effect from crystalline silica exposure.