Analysis of excretion of pineal gland hormone melatonin in ex-mercury miners with machine learning methods

Alfred B. Kobal1 Bernard Ženko2 Darja Kobal3 Mladen Krsnik4 Sašo Džeroski2 Milena Horvat5 Joško Osredkar4

1 Idrija Mercury Mine, Slovenia  
2 Department of Knowledge Technologies, Jožef Stefan Institute, Slovenia  
3 Clinical Institute of Occupational, Traffic and Sports Medicine, University Medical Centre, Slovenia  
4 Institute of Clinical Chemistry and Biochemistry, University Medical Centre, Slovenia  
5 Department of Environmental Sciences, Jožef Stefan Institute, Slovenia

Correspondence to: Bernard Ženko, Department of Knowledge Technologies, Jožef Stefan Institute, Jamova 39, SI-1000 Ljubljana, Slovenia, e-mail: bernard.zenko@ijs.si, phone: +386 1 477 3307, fax: +386 1 425 1038

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Introduction. The toxic effects of mercury are well known and in the case of occupational exposure to elemental mercury vapour (Hg\(^{\infty}\)) the most frequent symptoms and signs include erythrom, increased irritability, depression, insomnia, psychotic disturbances, tremor and renal impairment. High Hg and Se retention and co-accumulation have been found in the brain, endocrine glands and also pineal gland, kidney and other body tissues in ex-miners from the Idrija Mercury Mine even several years after exposure. This could be associated with possible health problems or adverse biological effects. The long term effects of mercury toxicity are not well studied. Recently the pineal hormone melatonin was found to have a potent-free-radical scavenging activity and the protective effect of melatonin towards peroxidative damage was found in some in vivo and in vitro studies. High Hg accumulation has been found in the pineal gland in retired miners which could modify the synthesis of melatonin. There are no data available in the scientific literature on the possible effects of Hg on melatonin excretion. The purpose of this study was to investigate the impact of occupational mercury exposure on melatonin excretion in mercury miners.

Data set and methodology. Initially 120 males were examined in the study. After the selection procedure, the study population comprised 53 ex-mercury miners previously exposed to Hg\(^{\infty}\) and 53 workers in the control group. The study group of miners comprised 33 active miners not exposed to Hg\(^{\infty}\) in the preceding 8 to 60 months, and 20 retired miners who had not been exposed to Hg\(^{\infty}\) before the present observations for a period from 32 to 336 months. The miners were employed in the Idrija Mercury Mine. The control workers were taken from "mercury-free" works. They performed jobs in the forests as choppers and transport workers. The medical examination of all subjects included a medical history and lifestyle habits (age, body mass index, smoking, alcohol consumption, dental amalgam score). The examination also included venous blood and urine sampling for determination of blood total (BT-Hg) and methyl mercury (Me-Hg), urine mercury (U-Hg), selected hematological data, selected blood
and urinary data of kidney urinary tract disorders, serum gamma glutamyltransferase (GGT), aminotransferases (ALT, AST), bilirubin, blood glucose, c-reactive protein and finally concentrations of melatonin in blood in urine. Environmental and biological data on the group of miners studied were collected from 1959 onwards from workload records, daily reports on Hg° measurements in the workplace, personal medical records and biological monitoring data. On this basis, several parameters of the duration and level of exposure were calculated for each miner, such as years of work in the mercury mine, cycles of exposure (intervals of work at exposure to Hg°), average time-weighted (ATW) air Hg° concentration expressed in mgHg°/m3 air.

The data were analysed with machine learning methods in order to gain insight in the background of the melatonin excretion process. We have used the algorithm for induction of model trees which can be interpreted by the domain expert. A model tree is similar to a regression tree, except that it has linear equations instead of a single class label in the leaves. The models presented in this study were built with the M5' model tree learning algorithm as implemented in the Weka data mining environment. The default parameters of M5' were used. We have built two models, one for the concentration of melatonin in blood and another for melatonin (melatonin sulfate) in urine, but because of space limitations we only present the latter model in this abstract.

Results and discussion. The following model was built for the concentration of melatonin in urine. The tree has only one node, i.e., one linear equation:

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\begin{align*}
\text{melatonin\_in\_urine} &= -1.1228 \times \text{age} + [25/64/44.6/45/-50.0] \\
&- 0.8144 \times \text{no\_of\_cigarettes\_per\_day} + [0/40/9.4/0/-7.66] \\
&+ 0.5893 \times \text{no\_of\_years\_smoking} + [0/40/9.3/0/5.48] \\
&- 1.8774 \times \text{body\_mass\_index} + [16.8/38.5/26.8/26.0/-50.3] \\
&+ 0.5118 \times \text{sistolic\_blood\_press} + [100/170/129.4/128/66.2] \\
&+ 1.3376 \times \text{se\_in\_urine} + [7.2/41.3/18.4/17.5/24.6] \\
&+ 8.8882 \times \text{cd\_in\_blood} + [0.23/9.51/1.58/11.1/14.0] \\
&- 0.6878 \times \text{pb\_in\_total\_blood} + [14.7/91.3/48.3/49.6/-33.2] \\
&- 29.2923 \times \text{mda} + [0.001/1.26/0.19/0.081/-5.57] \\
&- 0.0026 \times \text{u-hg\_sum\_max} + [0/11365/1831/0/-4.76] \\
&+ 79.6388
\end{align*}
\]

The numbers in the brackets at each attribute are as follows: min value, max value, average value, median value and relative importance factor, where the latter is calculated as a product of the coefficient and the average value. Correlation coefficient of the model (on training data) is 0.60.

Age and body mass index are the most important factors that decrease the concentration of melatonin in urine, which is also known from previous studies. Factors that promote the formation of free radicals (Pb, Cd, Hg, and tobacco smoking) and effect on peroxidative degradation of the lipids and phospholipids of cellular membrane additionally decrease the concentration of melatonin in urine. In accordance with this is the negative influence of a lipid peroxidation product (MDA - malondialdehyde) on the melatonin concentration. This supports some assumptions that melatonin also has antioxidative effect. In the process of antioxidation activity melatonin decomposes and we assume this is the reason for decreased excretion of melatonin in mercury miners.