

## Heroin drugged drivers: Role of morphine and morphine-6-glucuronide in clinical impairment

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**AIMS:** The aim of the present paper was to study psychomotor impairment in heroin abusers during a later stage after heroin intake, when morphine and its glucuronides are the main active substances present in blood. The influence of blood drug concentrations of morphine (M), morphine-6-glucuronide (M6G), morphine-3-glucuronide (M3G) and the pattern of drug use were investigated.

**METHODS:** In cases of suspected drugged driving in Norway, a blood sample is drawn from the suspect shortly after the incident that caused the suspicion. The time delay between driving and blood sampling in our material is on average 1,5 hours. At the same time, a physician performs a Clinical Test for Impairment (CTI) and collects information on pattern of drug use, according to a fixed protocol. All blood samples, CTI results and drug history are together sent to the Norwegian Institute for Public Health (NIPH), Division of Forensic Toxicology and Drug Abuse in Oslo for analysis and further evaluation.

Blood samples from drugged drivers containing solely morphine and information of heroin intake (n=70) were selected from the database. The judgement of impairment from the corresponding CTI and information on pattern of drug use were recorded. For comparison, a group (n=79) of samples thoroughly analysed without any drug detection was selected from the same database ("no drug" cases). Drug concentration measurements were performed with gas chromatography/mass spectrometry for M and 6-AM (blood and urine) and with high pressure liquid chromatography for morphine glucuronides.

**RESULTS:** In the "no drug" cases, 86% were judged as not impaired and 14% as impaired. In the morphine only cases, 20% were judged as not impaired, and 80% as impaired. Median blood M concentration was 0,09  $\mu\text{mol/L}$  (25,7  $\mu\text{g/L}$ ) in the "not impaired" group and 0,15  $\mu\text{mol/L}$  (42,8  $\mu\text{g/L}$ ) in the "impaired" group ( $p=0,067$ ). For M6G, the median blood concentration was 0,09  $\mu\text{mol/L}$  (41,5  $\mu\text{g/L}$ ) in the "not impaired" group and 0,14  $\mu\text{mol/L}$  (64,6  $\mu\text{g/L}$ ) in the "impaired" group ( $p=0,030$ ). A significant correlation between concentration quartiles and number of cases determined as "impaired" was found for M6G ( $p=0,018$ ) and for the sum M+M6G ( $p=0,013$ ), but not for M or M3G (fig1). The proportion of impaired cases was similar for daily users (81%) and non-daily users (82%); and similar to the proportion of impaired subjects in the total material (80%). The mean blood concentrations of all analytes were higher for the daily users than for the non-daily users, but the differences were not significant.

**CONCLUSION:** In our population of heroin-drugged drivers, blood concentrations of M6G and the sum M+M6G appeared to have concentration-dependent effects on the CNS that may lead to impairment as judged from a CTI. The proportion of daily users judged as impaired was not lower than for non-daily users.

**KEYWORDS:** behavioral pharmacology, heroin, morphine, morphine-6-glucuronide, impairment, traffic.

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