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Discussion

High-performance liquid chromatographic determination of morphine, morphine-3-glucuronide, morphine-6-glucuronide and codeine in biological samples using multi-wavelength forward optical detection: a reply

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The above mentioned paper [1] touched an extremely important current issue. The reliable and sensitive determination of morphine glucuronides is of great value in various research fields in toxicology and pharmacology. However, the paper stimulates some questions and doubts, which perhaps may be clarified by the authors.

From the three-dimensional chromatogram of plasma extracts, spiked with 5 μg/ml of each drug (Fig. 1), the absorbance of codeine at 220 nm appeared to be *ca.* 0.01 unit. The absorbance of the same drug at the concentration level of 5 ng/ml was only 50 times lower, *i.e.*, *ca.* 0.0002 unit (Fig. 2).

Fig. 2 shows the separated peaks of morphine, its glucuronides and codeine extracted from plasma spiked at the concentration levels of 5–20 ng/ml. The absorbance values for the highest peaks at the highest concentrations never exceeded 0.0025. On the other hand, in Fig. 3 the chromatogram of blank plasma extract is depicted, with matrix peaks with absorbances between 0.0050 and 0.0100. These peaks are located exactly in the elution range of morphine, morphine-3-glucuronide (M-3-G) and M-6-G and should make virtually impossible any reliable detection and determination at this concentration level.

TABLE I

CONCENTRATIONS OF MORPHINE (M), MORPHINE-3-GLUCURONIDE (M-3-G) AND MORPHINE-6-GLUCURONIDE (M-6-G) IN TWO INFANTS FOUND 24 h AFTER SINGLE INTRAVENOUS ADMINISTRATION OF MORPHINE (0.1 mg/kg)

Infant No.	Sample	Concentration (ng/ml)		
		M	M-3-G	M-6-G
1	CSF	500	900	–
(Fig. 4)	Plasma	100	500	500
	Urine	–	5000	–
2	CSF	–	–	2250
(Fig. 5)	Plasma	–	120	1375
	Urine	–	1000	>12 500

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Figs. 4 and 5 show the chromatograms of cerebrospinal fluid, plasma and urine extracts obtained from two infants after administration of morphine. The exact quantitative data are not given in the paper; it was possible, however, to assess roughly the concentration found on the basis of chromatograms from the spiked plasma samples. These concentrations are presented in Table I.

The values in Table I raise very serious doubts, taking into account the applied dose and time of sampling. Other workers, who used more specific electrochemical detection, observed much lower concentrations of morphine, M-3-G and M-6-G after parenteral application of morphine in corresponding conditions [2–4].

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