



K2 Urinary Fentanyl and Norfentanyl During Application of Duragesic® Transdermal Patches

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After attending this presentation, attendees will have data concerning the urinary concentration of fentanyl and its major metabolite norfentanyl in patients treated with "Duragesic®" transdermal patches.

Toxicologist will be aware that urine concentrations of fentanyl and norfentanyl in patients on Duragesic® transdermal patches for control of chronic pain will far exceed previously reported values from overdose cases or patients receiving fentanyl for control of acute pain.

This poster presents the urinary concentration of fentanyl (F) and its major metabolite norfentanyl (NF) in chronic pain patients treated with "Duragesic" transdermal patches. The Duragesic® continuous release transdermal patch is designed to release 25 µg/h per 10 cm² of surface area. The patches are available in 10, 20, 30 and 40 cm² sizes releasing 25, 50, 75 and 100 µg/hr F, respectively. Desired therapeutic blood concentrations are obtained 8 to 12 hours after patch application. F is rapidly and extensively metabolized, with NF as the major metabolite. Little data is available on expected urine F concentrations in therapeutic situations, while urine concentrations in overdose cases have been reported to range from 5-93 ng/ml (Baselt, 1995).

Random urine specimens were collected from 200 chronic pain patients wearing 25, 50, 75 or 100 ug F transdermal patches. Urine specimens were collected from hours after application to several days later after continuous F release. Each specimen was analyzed for F, NF, creatinine and pH. Additionally, each was screened by enzyme immunoassay for the following: amphetamines, barbiturates, benzodiazepines, cocaine metabolite, methadone, phencyclidine, d-propoxyphene, opiates and marijuana metabolites. All positive screening results were confirmed by GC/MS. F and NF were isolated from urine by solid phase extraction (Biochemical Diagnostics GV-65), then identified and quantified by GC/MS in SIM mode. Mass to charge ions monitored were: F, 245, 146, 246; d5-F, 250, 251; NF-acetyl derivative, 231, 158, 132; and d5-NFacetyl derivative 236. Quantification of F and NF was by comparing ions 250/245 and 236/231, respectively. The LODs and LOQs for both F and NF were 3 ng/mL. The ULL for F and NF were 250 and 400 ng/mL, respectively. The results of F and NF analysis are presented below:

Dose, ug/hr		Fentanyl ng/mL		Norfentanyl ng/mL	
Patch	No.	mean	range	mean	range
25	46	48	0 - 474	161	0 - 800
50	71	78	0 - 569	222	0 - 931
75	29	75	0 - 444	245	0 - 820
100	51	159	0 - 631	220	0 - 722

The incidence of other drugs detected as a percentage the 200 specimens were: opiates, 48% (incidence: Codeine 1, Hydrocodone 41, Hydromorphone 7, morphine 12, oxycodone 36); benzodiazepines, 43%; barbiturates, 3%; methadone, 4%; marijuana metabolite, 3%; amphetamines, 2% and cocaine metabolite, 1%. Other than F and/or NF no drugs were detected in only 25% of the specimens.

Conclusion: These data demonstrate the wide variation in concentrations of F and NF in random urine specimens following application of Duragesic® patches. However, these values obtained during therapeutic use far exceeded concentrations previously reported in fatal poisoning. In general, one may expect to find urine NF concentrations 3 to 4 times higher than those of F. Also, in addition to fentanyl therapy, chronic pain patients routinely are prescribed other opiates and benzodiazepines.

Fentanyl, Norfentanyl, Urine Drug Testing