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Postmortem Distribution and Redistribution of Morphine in Man

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ABSTRACT: This study evaluated both site dependent differences and time dependent changes in postmortem morphine concentrations in man. In 32 deaths involving morphine, left ventricular blood, femoral blood, and cisternal cerebrospinal fluid, were collected as soon after death as possible (T1), and collected again together with iliac blood at the time of autopsy (T2). Samples were analyzed for morphine by radioimmunoassay.

No evidence was found for changes in morphine concentration with respect to time at either central or peripheral sites, or in the cerebrospinal fluid. Ventricular blood morphine concentrations were however consistently higher than those in the peripheral compartment, represented by either femoral or iliac blood. This was particularly true when the ventricular morphine concentration exceeded 0.300 mg/L. At peripheral sites, femoral and iliac blood morphine concentrations were well correlated with each other, making either an appropriate site for collection of peripheral blood for toxicological testing.

KEYWORDS: forensic science, forensic toxicology, morphine, postmortem redistribution, drug distribution, toxicology

Two factors believed to exert a significant influence on postmortem blood drug concentrations are the site of sample collection, and the time between death and sample collection. The marked site dependence between the central and peripheral compartments for tricyclic antidepressant drug concentrations has been effectively demonstrated (1–5). This and other work has shown site dependence for other some drugs, and in addition, limited data evaluating temporal changes in drug concentration has been reported (3–6). For most drugs however, much of the information with respect to postmortem drug redistribution is anecdotal, and is based on one or two cases. This is particularly true for morphine (7–9).

Morphine is an opiate narcotic analgesic which is itself abused, but is more frequently found as a metabolite of heroin (diacetyl morphine). After administration, heroin rapidly undergoes deesterification with a half life of 7 minutes, a process which probably continues after death. Morphine is amphoteric and moderately lipid soluble. It has a volume of distribution of 3.3 L/Kg (10), and concentrations of morphine in the brain can be between two and five times greater than those in the blood (11). Elevated concentrations are also found in the lung (11), liver (7,8), muscle (7), bile (8), and myocardium (12). These factors would tend to suggest that tissues could act as a reservoir for morphine, and release the drug from the tissues back into the blood during the postmortem interval thereby elevating postmortem morphine concentrations, and making interpretation of these concentrations complex.

To evaluate the time dependence of morphine concentrations in victims of fatalities involving opiate use, the site dependence of postmortem blood morphine concentrations, and the stability of morphine concentrations in cerebrospinal fluid (CSF), we investigated 32 morphine related deaths, collecting time-series samples of peripheral and central blood, and cisternal CSF.

Methods

Following the report to the authorities of a suspected morphine related death one of us (DS) made immediate contact with the body and drew left ventricular, and femoral blood (10 mL each) using a cut-down procedure to expose the vessel in each case. The vessels were not tied off between sample collection. CSF (~10 mL) was collected by cisternal tap. All samples were collected in tubes containing sodium fluoride and potassium oxalate. The body was then stored at 4°C, and at some later time when the autopsy was performed, samples were collected from the same sites, and in addition an iliac blood sample (10 mL) was collected. The time between death and the collection of the first sample, T1, was estimated from rigor and/or history and witness reports. The interval between the first and second specimen collection was noted. The sum of these, T2, represents the time between death and autopsy. Patient data, the circumstances surrounding the death, the presence of other drugs, the administration of cardiopulmonary resuscitation (CPR), and the determined cause and manner of death were also noted and are discussed.

Following collection, samples were stored at −20°C until analysis. Morphine concentrations were determined by coated tube radioimmunoassay (Coat-a-Count, Diagnostic Products Corp., CA), and were performed in duplicate. Blood and CSF samples were analyzed directly without any prior extraction or hydrolysis. All data reported in Table 1 is means of duplicates. This immunoassay is very specific for free morphine with little cross reactivity (<1%) to most other opiates or morphine metabolites (13) nalorphine and normorphine have cross reactivities of 9 and 26% respectively, but were not believed to be significant in these cases. In our hands, the assay has a limit of quantitation of 0.005 mg/L, and a CV of ±18% at a concentration of 0.050 mg/L, and 12% at concentration of 0.200 mg/L.

Results and Discussion

A consideration that might influence the reliability of results obtained using the radioimmunoassay procedure is the fact that hydrolysis of morphine glucuronides to free morphine during the

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postmortem interval, could not be differentiated from a true redistribution of morphine between tissue and blood. Practically however, this is not a concern, since as discussed as follows, no significant time dependent changes in morphine concentrations were found.

Unfortunately we do not have specific information on which cases, if any, involved the use of morphine or opium as opposed to heroin, however the pattern of opiate use in this population is almost exclusively one of Mexican black tar heroin.

Table 1 lists the morphine concentrations for femoral and left ventricular blood, and CSF at T1 (immediately on receipt of the body), and T2 (at the time of autopsy). Iliac blood morphine concentrations are reported for T2 only. Table 2 summarizes the cause and manner of death, and other decedent information including the presence of other drugs.

The time between death and the collection of the T1 sample ranged from 3 to 144 (mean 17.3) hours, while dT, the interval from T1 to T2 ranged from 3 to 43 (mean 17.4) hours.

Temporal Effects—Femoral Blood

Femoral blood morphine concentrations ranged from 0.006 to 1.280 mg/L at T1, and 0.007 to 1.610 mg/L at T2. Figure 1 shows the femoral blood morphine concentrations in each case with respect to time. There was excellent agreement between the femoral blood morphine concentrations at T1 and T2, implying no time-dependent change. Simple regression over the range 0 to 0.6 mg/L gave a value for R^2 of 0.965, and SEE of 0.023. The slope was 1.09, confirming a lack of significant change in concentration with respect to time. The mean difference between femoral blood concentrations at T1 and T2 in this range was 0.000 mg/L (SD = 0.028). At the highest concentration encountered however, there was an increase from 1.280 to 1.610 mg/L during the 33 hours between the collection of the first and second femoral blood samples (not shown in Fig. 1).

Temporal Effects—Ventricular Blood

The left ventricular blood morphine concentrations ranged from 0.008 to 0.836 mg/L at T1, and 0.010 to 0.732 mg/L at T2. Figure 2 shows the relative ventricular blood morphine concentrations in each case, with respect to time. Compared to the data for femoral morphine, there was greater variability, particularly at higher concentrations between the ventricular concentrations at T1 and T2. Simple regression over the range 0 to 0.6 mg/L gave a value for R^2 of 0.92, and SEE of 0.032. The slope was 0.920, again suggesting no significant change in concentration with respect to time. Within this range, the mean difference between ventricular blood concentrations at T1 and T2 was 0.000 mg/L (SD = 0.089). At

TABLE 1—*Morphine concentrations at postmortem intervals T1 and T2 for femoral, and ventricular blood and cerebrospinal fluid and at T2 for iliac blood.*

		Morphine concentrations (mg/L)				Morphine concentrations (mg/L)			
Case #	T1 (hrs)	Femoral blood T1	Ventricular blood T1	Cerebrospinal fluid T1	T2(hrs)	Femoral blood T2	Ventricular blood T2	Cerebrospinal fluid T2	Iliac blood T2
1	4.3	0.081	0.490	0.019	17.8	0.078	0.440	0.047	0.065
7	3.5	0.038	0.020	0.027	46.8	0.042	0.069	0.038	0.052
9	8	0.052	0.083	0.020	10.5	0.064	0.119	0.028	0.041
10	4	0.049	0.045	0.033	17.5	0.040	0.047	0.033	0.050
11	5.5	0.044	0.115	0.013	37.5	0.042	0.096	0.022	0.070
14	25	0.314	0.686	0.180	31.1	0.376	0.612	0.182	0.250
15	6.5	0.035	0.038	0.014	9.6	0.031	0.035	0.019	0.040
16	5.3	0.018	0.015	0.025	9.25	0.018	0.015	0.016	0*
17	8.9	0.127	0.181	0.044	35.7	0.116	0.209	0.086	0.144
19	9	0.108	0.188	0.037	17	0.160	0.484	0.042	0.140
20	144	0.240	0.222	0.202	154	0.232	0.214	0.290	0.200
21	32	0.085	0.013	0*	44.3	0.007	0.010	0*	0*
23	3.3	0.070	0.108	0.013	26.5	0.068	0.180	0.051	0.080
24	24	0.009	0.011	0.010	32.8	0.009	0.012	0.008	0.011
26	11	0.154	0.173	0.047	43	0.116	0.165	0.032	0.131
27	23	1.280	—	0.246	55.5	1.610	—	1.620	—
28	28	0.038	0.031	0.024	31.5	0.036	0.038	0.023	0.070
31	3	0.125	0.138	0.046	12.5	0.135	0.195	0.060	0.160
32	14	0.082	0.742	0.018	33	0.083	0.482	0.070	0.085
33	26	0.028	0.022	0.014	56	0.046	0.029	0.024	0.100
34	3.5	0.006	0.008	0*	16.8	0.007	0.011	0.004	0*
36	8.5	0.133	0.163	0.031	30.5	0.122	0.158	0.081	0.150
40	11	0.130	0.836	0.060	42.3	0.116	0.722	0.009	0.134
41	18	0.044	0.225	0.156	21.3	0.042	0.310	0.168	0.350
42	17	0.218	0.732	0.425	56	0.165	0.732	0.188	0.198
43	3	0.068	0.073	0.023	35	0.065	0.070	0.019	0.072
44	9.5	0.171	0.606	0.094	18.8	0.172	0.460	0.054	0.126
45	27	0.161	0.198	0.017	35.3	0.154	0.177	0.048	0.125
46	37	0.514	0.590	0.118	55	0.584	0.684	0.180	0.400
47	7.3	0.086	0.143	0.026	19.3	0.095	0.123	0.026	0.064
48	7.5	0.014	0.012	0.028	19.8	0.014	0.012	0.033	0.030

— no sample available
0* concentration less than 0.005 mg/L

TABLE 2—*Circumstances surrounding the morphine related deaths reviewed in this study.*

Case #	Sex	Age	Height	Weight	Scene death?	CPR	Paraphenalia	Iliac Morphine (mg/L)	Other drugs present	Conc. (mg/L) (ethanol g/100mL)	Cause of Death	Manner of Death
1	M	41	—	—	Yes	No	Syringes and pipe	0.065	Ethanol	0.22	Acute intoxication due to ethanol and opiates	Probable accident
7	M	37	5′10″	167	Yes	No	None	0.052	Cocaine Cocaethylene Benzoylecgonine Ethanol	0.06 0.16 1.46 0.09	Acute intoxication due to opiates and cocaine	Probable accident
9	M	35	6′1″	176	Yes	Yes	None	0.041	Ethanol	0.26	Acute intoxication due to ethanol and opiates	Probable accident
10	M	38	5′7″	193	Yes	No	Syringe at scene	0.050	Cocaine Cocaethylene Benzoylecgonine Ethanol	0.60 0.20 2.00 0.12	Acute intoxication due to ethanol, opiates and cocaine	Probable accident
11	M	35	—	—	Yes	Yes	None, witnessed collapse shortly after injection	0.070	Ethanol	0.21	Acute intoxication due to opiates and cocaine	Probable accident
14	M	43	5′6″	144	Yes	No	Syringe and cooker	0.270	Ethanol Carbamazepine	0.17 2.00	Acute intoxication due to ethanol and opiates	Probable accident
15	M	35	5′10″	165	Yes	No	Syringes	0.040	Cocaine Benzoylecgonine	1.60 2.70	Acute intoxication due to cocaine and opiates	Probable accident
16	M	39	5′5″	165	Yes	Yes	none	<0.025	Cocaine Cocaethylene Benzoyleconine Ethanol	<0.10 <0.10 0.30 0.07	Acute intoxication due to ethanol, opiates and cocaine	Probable accident
17	M	42	6′1″	187	Yes	No	Suffocation with plastic bag	0.144	Cocaine Benzoylecgonine Diazepam Nordiazepam Doxepin Nordoxepin Fluoxetine Norfluoxetine	0.05 0.91 0.10 0.09 0.09 0.03 0.48 0.44	Acute intoxication due to opiates, cocaine, diazepam, fluoxetine and doxepin secondary to suffocation with a plastic bag	Suicide
19	M	45	5′7″	178	Yes	Yes	Syringe	0.140	Ethanol	0.10	Acute intoxication due to ethanol and opiates	Accident
20	M	44	5′9″	154	Yes	No	Syringe cap and cooker	0.200			Acute intoxication due to opiates	Accident
21	M	41	5′9″	146	Yes	No	Syringes, spoon	0.010	Cocaine Benzoylecgonine Cocaethylene Methadone Ethanol	0.12 2.50 0.07 0.29 0.06	Acute intoxication due to opiates and cocaine	Probable accident

TABLE 2—*Continued.*

Case #	Sex	Age	Height	Weight	Scene death?	CPR	Paraphenalia	Iliac Morphine (mg/L)	Other drugs present	Conc. (mg/L) (ethanol g/100mL)	Cause of Death	Manner of Death
23	M	31	5′7″	151	Yes	Yes	Drug and syringe Witnessed collapse	0.080	Ethanol	0.19	Acute intoxication due to ethanol and opiates	Accident
24	M	38	6′3″	194	Yes	No	Syringes and drug	0.011	Cocaine Benzoylecgonine	0.74 1.93	Acute intoxication due to cocaine and opiates	Probable accident
26	F	38	5′7″	262	Yes	Yes	Syringes and drug	0.131	Amitriptyline Nortriptyline	1.70 4.20	Acute intoxication due to opiates and amitriptyline	Probable accident
27	M	20	5′9″	203	Yes	No	None	>1.0			Acute intoxication due to opiates	Undetermined
28	M	35	5′8″	212	Hospital	Yes	Died live hours after injection	0.070	Benzoylecgonine	4.10	Acute intoxication due to cocaine and opiates	Probable accident
31	M	47	6′3″	195	Yes	No	Died clutching syringe	0.160	Cocaine Benzoylecgonine	<0.05 0.50	Acute intoxication due to cocaine and opiates	Probable accident
32	F	40	5′3″	149	Yes	No	Syringe cap	0.090	Cocaine Cocaethylene Benzoylecgonine Ethanol Diazepam Nordiazepam	0.27 0.17 0.69 0.18 0.03 0.30	Acute intoxication due to cocaine, opiates and ethanol	Probable accident
33	F	29	5′6″	136	Yes	No	Syringe	0.100	Benzoylecgonine	0.60	Acute intoxication due to opiates and cocaine	Undetermined
34	F	34	5′5″	148	Yes	Yes	None	0.030	Imipramine Desipramine Carbamazepine Chlordiazepoxide Nordiazepam	0.22 0.10 4.70 15.60 0.45	Acute intoxication due to chlordiazepoxide, carbamazepine, nordiazepam, imipramine and desipramine	Undetermined
36	M	41	5′11″	216	Yes	Yes	None	0.150	Cocaine Cocaethylene	0.30 <0.1	Acute intoxication due to cocaine, opiates and ethanol	Probable accident
40	M	33	5′9″	130	Yes	No	Syringes	0.134	Cocaine Benzoylecgonine	0.38 1.55	Acute intoxication due to opiates and cocaine	Probable accident
41	F	29	5′4″	128	Yes	No	Drug, syringes	0.350	Meprobamate Carisoprodol	3.00 3.70	Acute intoxication due to cocaine, opiates and meprobamate	Probable accident

TABLE 2—*Continued.*

Case #	Sex	Age	Height	Weight	Scene death?	CPR	Paraphenalia	Iliac Morphine (mg/L)	Other drugs present	Conc. (mg/L) (ethanol g/100mL)	Cause of Death	Manner of Death
42	M	40	5'9"	163	Yes	No	Syringe, tourniquet in place	0.198	Acetaminophen Codeine	19.00 0.12	Acute intoxication due to opiates	Probable accident
43	F	24	5'1"	124	Yes	Yes	Syringe and spoon	0.072	Ethanol Fluoxetine Norfluoxetine	0.08 0.74 0.32	Acute intoxication due to cocaine, opiates and fluoxetine	Probable accident
44	M	43	5'11"	196	Hospital	Yes	None	0.126	Nordiazepam Irazodone	0.12 0.66	Acute intoxication due to opiates	Probable accident
45	M	27	6'0"	224	Yes	Yes	None	0.125	Cocaine Benzoylecgonine	<0.1 0.53	Acute intoxication due to opiates and cocaine	Probable accident
46	M	37	5'11"	242	Yes	No	Syringes	0.400	Meperidine	0.08	Acute intoxication due to opiates and meperidine	Probable accident
47	M	35	5'9"	190	Yes	Yes	Syringes and spoon	0.064	Cocaine Cocaethylene Benzoylecgonine Diazepam Nordiazepam	0.16 0.06 4.24 0.29 0.33	Acute intoxication due to opiates and cocaine	Probable accident
48	M	28	5'10"	196	Yes	Yes	None	0.030	Benzoylecgonine	0.20	Acute intoxication due to opiates and cocaine	Probable accident
49	M	41	5'9"	186	Yes	No	Syringes	0.070	Diazepam Nordiazepam Ethanol	0.17 0.32 0.07	Acute intoxication due to opiates	Probable accident

concentrations greater than 0.6 mg/L however, there was greater variability, and the concentration at T2 was generally lower than that at T1 (mean difference = 0.09 mg/L, n = 7). Those cases displaying large changes in concentration between T1 and T2, were those with the highest initial concentrations, not those with the longest postmortem interval.

Temporal Effects—Cerebrospinal Fluid

The CSF morphine concentrations also appeared to be stable with respect to time, ranging from 0 to 0.425 mg/L at T1 and 0 to 1.62 at T2. Four of the CSF samples were badly contaminated with blood and so were not used. Simple regression for 26 paired T1 and T2 samples gave an R^2 value of 0.82, with an SEE of 0.032, and a slope of 1.14. Some other CSF samples had some contamination with blood, which may account for the poorer correlation between CSF samples than observed for femoral or ventricular blood. The mean CSF to femoral blood ratio at T1 was 0.67 (SD = 0.74), values in good agreement with our earlier study (14), which showed a CSF to iliac blood morphine ratio of 0.56 (SD = 0.47). At T2 this ratio was to 0.77 (SD = 0.74). Because the average central blood morphine concentration was higher than that in the peripheral blood, the CSF to blood morphine ratio for the ventricular blood was lower, 0.50 (SD = 0.54) at T1 and 0.49 (SD = 0.53 at T2). The large relative standard deviation makes the use of a CSF morphine concentration for the prediction of a peripheral blood morphine concentration inadvisable. We have proposed elsewhere that CSF morphine concentrations of greater than 0.020 mg/L are consistent with morphine caused death (14). In this group of 31 patients, 9 had CSF morphine concentrations at T1 less than 0.02, however, alcohol or other drugs, notably cocaine, were also present in all those cases (Table 2). The reliability of CSF morphine concentrations in assessing the role of morphine in drug related deaths, assumes a stable concentration in the CSF with respect to time. In the above cases, we found no marked change in CSF morphine concentration between T1 and T2. This supports the use of elevated postmortem CSF morphine concentrations as a marker in opiate death.

Site Dependence

Figure 3 illustrates all the paired femoral and ventricular blood samples analyzed at T1 and T2, arranged in order of increasing postmortem interval. The concentrations of morphine in the femo-

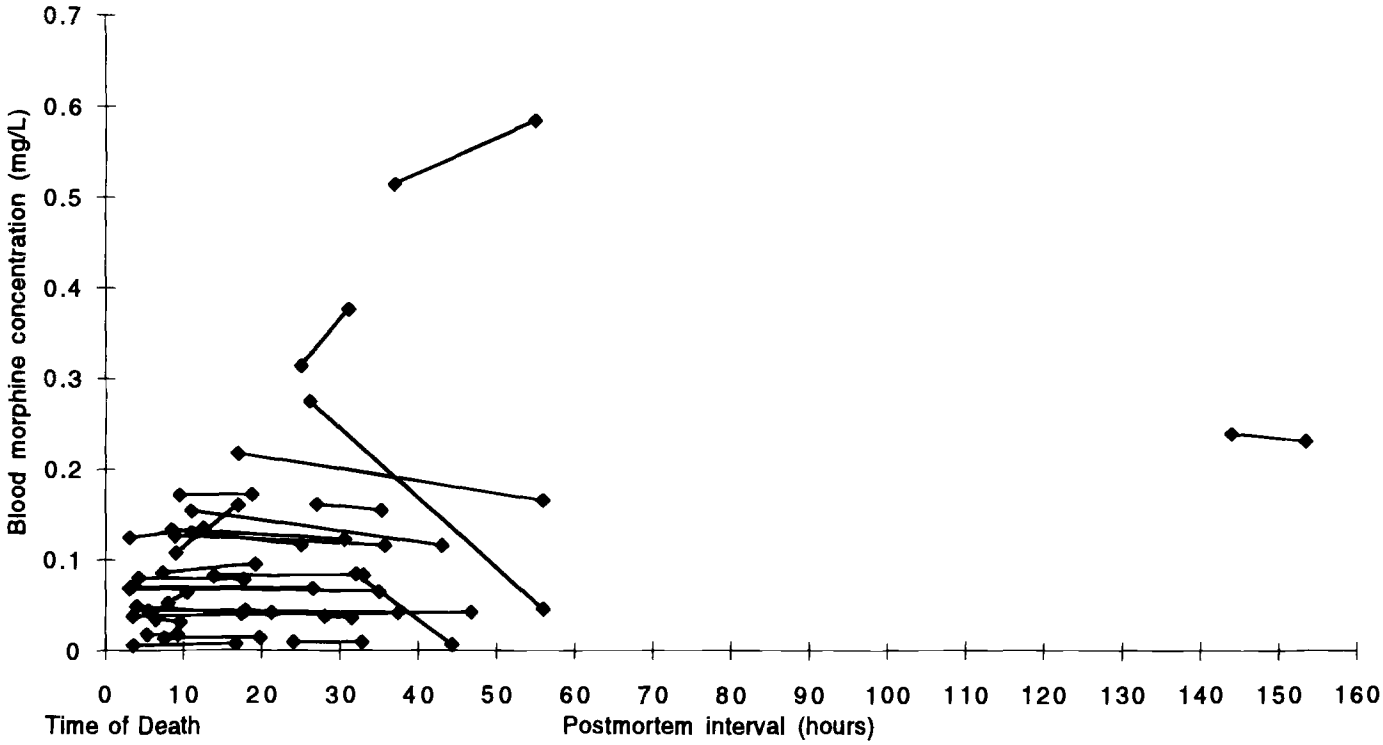

FIG. 1—*Postmortem femoral blood morphine concentrations in 32 human subjects as a function of postmortem interval.*

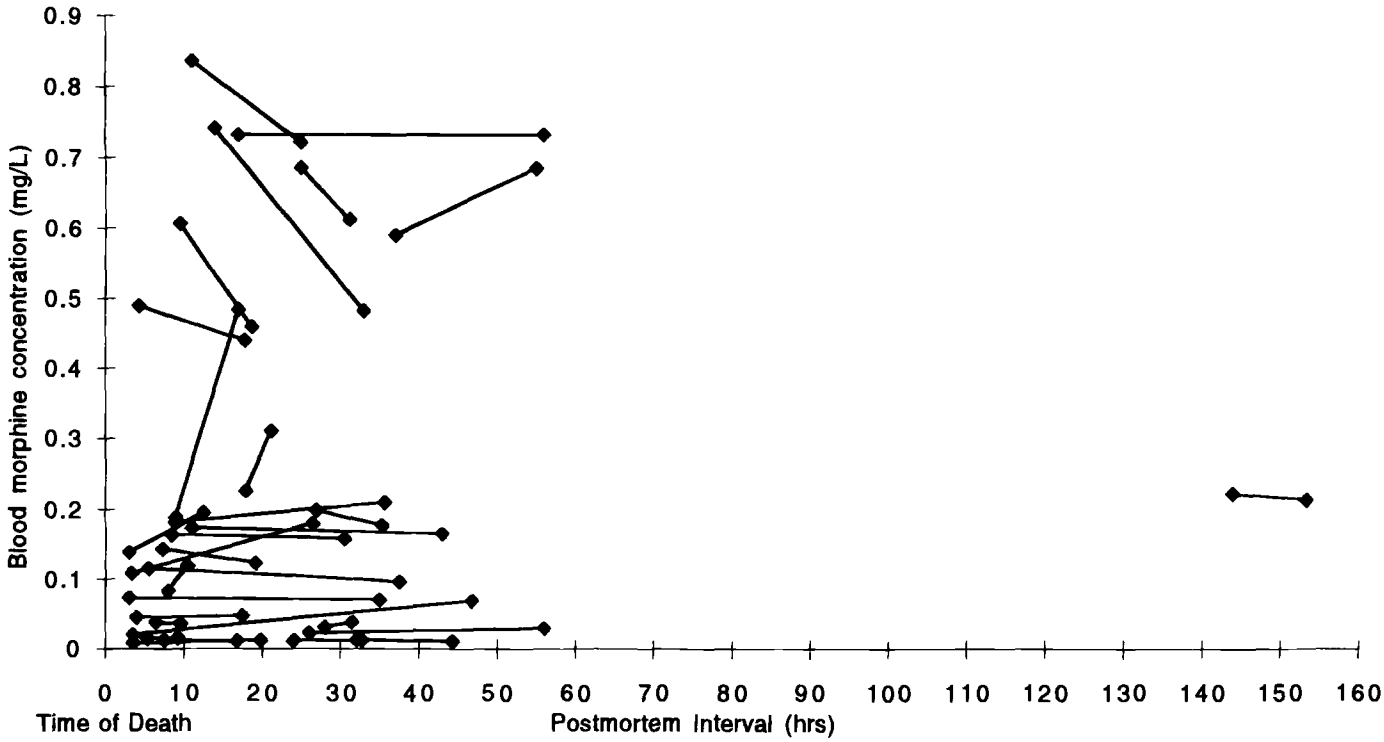

FIG. 2—*Postmortem ventricular blood morphine concentrations in 32 human subjects as a function of postmortem interval.*

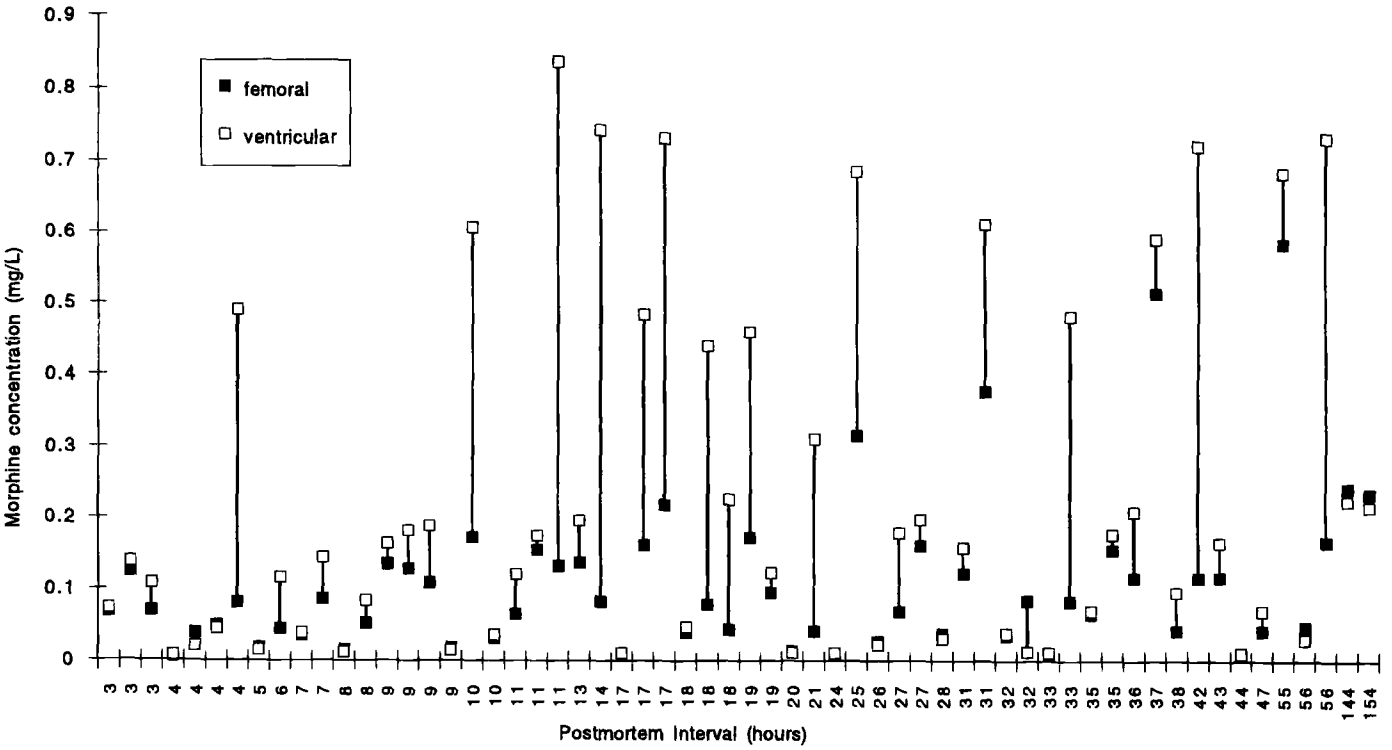

FIG. 3—*Paired postmortem femoral and ventricular blood morphine concentrations arranged in order of increasing postmortem interval.*

ral and ventricular blood were generally not well correlated (R^2 = 0.40), with the ventricular morphine concentration consistently exceeding the femoral morphine concentration by as much as 0.700 mg/L. Based on 60 paired ventricular and femoral samples from 30 cases, the average ventricular to femoral blood morphine ratio was 2.16 (range 0.15 to 9.21). Considering only those cases with morphine concentrations below 0.300 mg/L (n = 44), there was a much better correlation (R^2 = 0.68), with differences typically no greater than 0.100 mg/L, and a mean ventricular to femoral blood morphine ratio of 1.36 (range 0.15 to 5.14). There was no relationship between the difference and the postmortem interval.

Figure 4 shows the same paired femoral and ventricular concentrations with respect to the concentration of the ventricular blood morphine. This clearly shows that femoral—ventricular differences are concentration dependent, and that ventricular blood morphine concentrations greater than 0.300 mg/L are likely to be significantly elevated over the corresponding femoral concentration.

Comparison of Iliac and Femoral Blood Morphine Concentrations

Figure 5 shows the morphine concentrations at the two peripheral sites, iliac and femoral blood, at the time of autopsy. Morphine concentrations were well correlated, at concentrations of up to 0.300 mg/L (R^2 = 0.85, SEE 0.024) with a slope of 0.89. In the two cases where the femoral blood concentration exceeded 0.300 mg/L, it tended to overestimate the iliac blood by about 50%. Similarly, in the one case where the iliac blood concentration exceeded 0.300 mg/L, it overestimated the femoral blood morphine concentration at both T1 and T2 by 700%, agreeing well with the ventricular concentration. This data substantiates the observations made with respect to femoral—ventricular concentration differences, that as the body burden of morphine increases, particularly at concentrations above 0.300 mg/L, significant and sometimes unpredictable site-dependent differences in morphine concentration can develop.

Since these site dependent differences are apparently concentration dependent and not time dependent, it is likely that factors other than simply tissue release are involved. Other authors (3,4) have reviewed some of the potential causes of site dependent differences in drug concentration, including postmortem recirculation, pH and temperature dependent release of tissue bound drug, postmortem circulation resulting from gas buildup, the positioning and movement of the body postmortem, and the application of CPR. In the cases we evaluated we did note that when site dependent differences were present, they were not related to whether or not CPR had been performed.

In those cases where there was a femoral—ventricular difference in morphine concentration, it is possible that the higher ventricular concentration reflects incomplete distribution of the drug into the periphery following intravenous administration, in deaths occurring very soon after injection. However, there was no consistent pattern in these cases suggesting instantaneous death following injection. Nor were there consistent pathological findings; for example, pulmonary edema was present in only a few of the cases displaying these differences. It is also possible that in these cases, there was some morphine release from the myocardium immediately after death (that is to say within the first three hours, an interval not investigated in this study), followed by subsequent equilibration as described above. In either event, these large site dependent differences, in our subjects were only significant when the ventricular blood morphine concentration was above 0.300 mg/L.

Studies on the postmortem distribution of morphine in man are typically limited to a few cases, and one or two tissues (4,7–9,12,14). Furthermore they often have not documented the site of collection of the blood. Despite their limitations, these studies

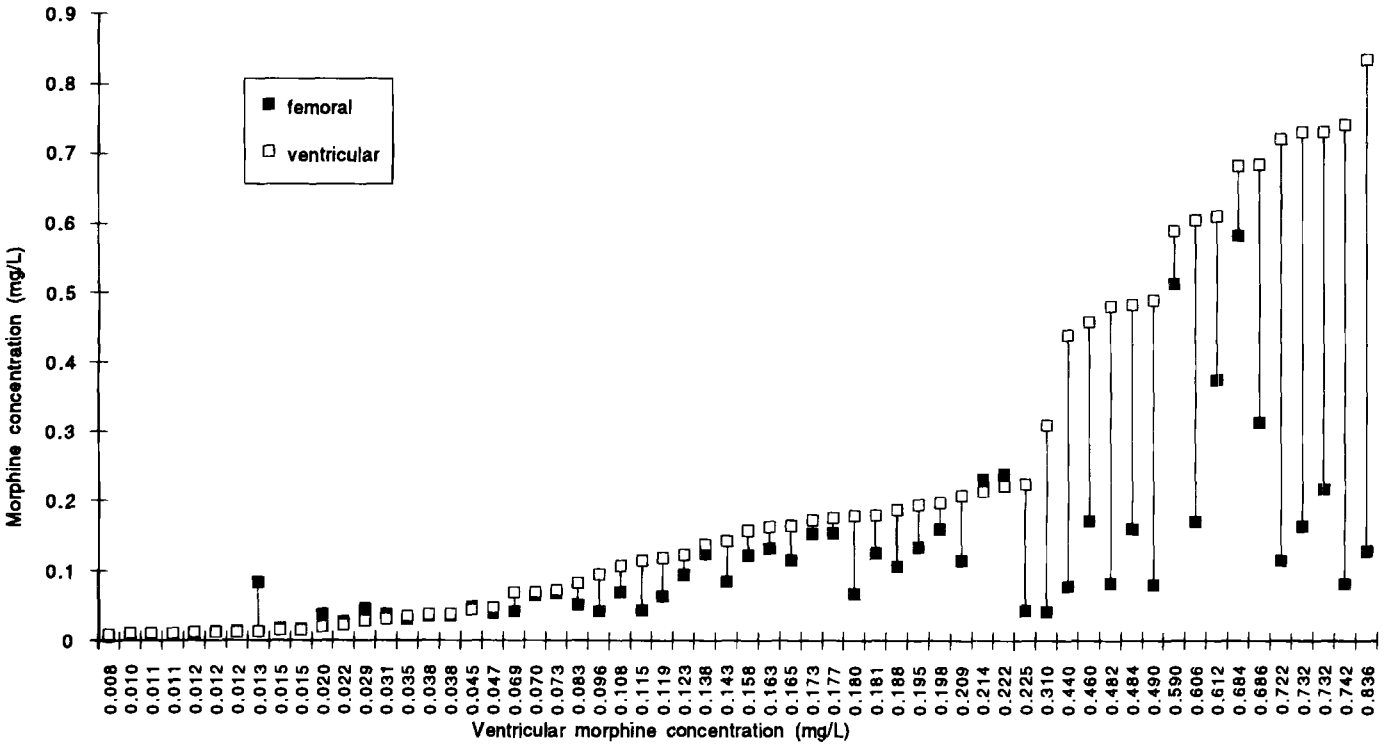

FIG. 4—*Paired postmortem femoral and ventricular blood morphine concentrations arranged in order of ventricular blood morphine concentration.*

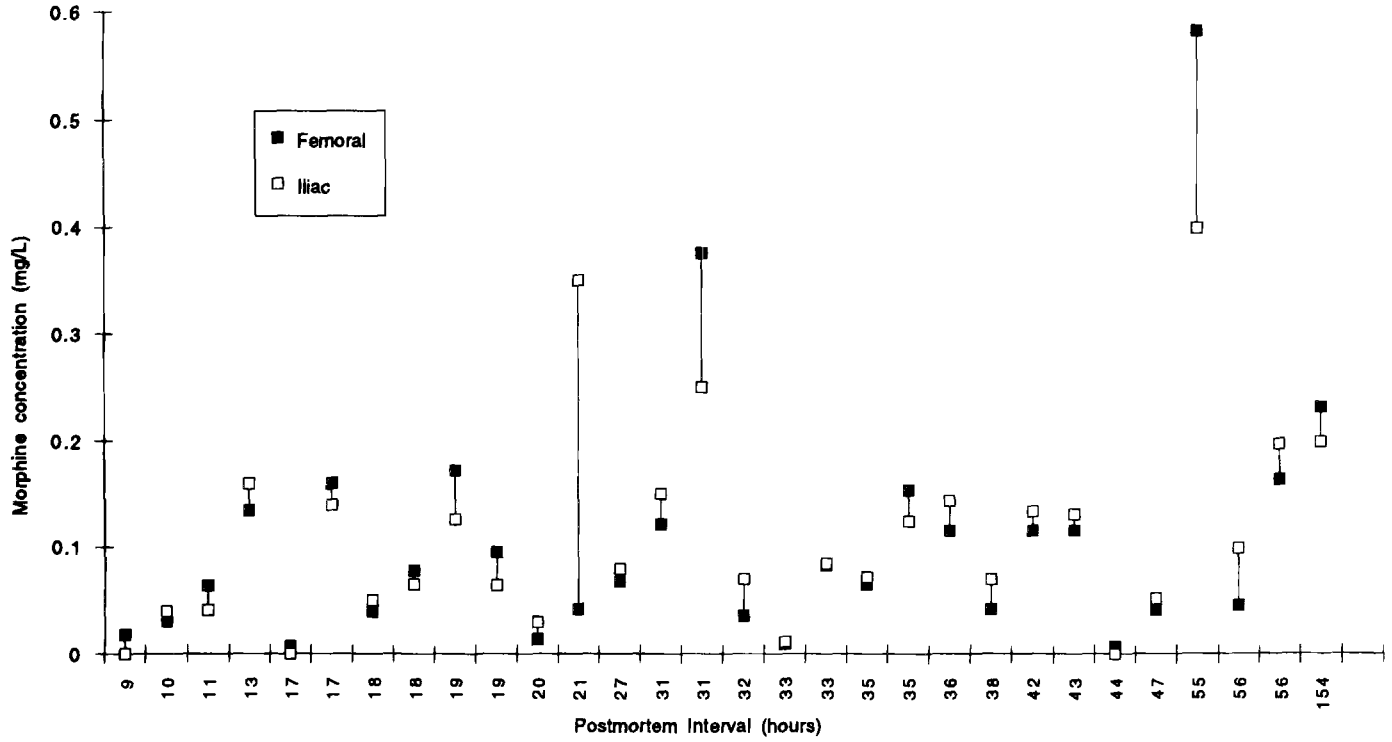

FIG. 5—*Paired postmortem femoral and iliac blood morphine concentrations arranged in order of increasing postmortem interval.*

suggest that the cerebrospinal fluid (CSF) morphine concentration is about half that in the blood, concentrations in the muscle tissue are similar to those in the blood, concentrations in the liver are elevated, and those in the bile can be between one and two orders of magnitude higher than in the blood. With respect to differences in blood morphine concentration between the central and peripheral compartments, Prouty and Anderson (4) cite a single case which suggests that heart blood and femoral blood morphine concentrations are very similar (ratio = 1.2). They did not however, have access to any cases involving morphine where time-series blood samples were collected. Bailey and Shaw (12) conducted a study to evaluate myocardium and blood concentrations of various drugs,

and while lacking any data for morphine, they noted for codeine only a small difference between myocardium and heart blood morphine concentrations (ratio = 1.7, n = 35). This is in contrast to their findings for the tricyclic antidepressants, which showed a four to seven fold difference between myocardium and blood concentrations. These ratios suggest a relatively lower risk of postmortem release of morphine into the ventricular blood compared to that for tricyclic antidepressants. A study of postmortem distribution and redistribution of morphine in rats (10) suggests that morphine is subject to significant postmortem drug redistribution because of its large volume of distribution (3.3 L/Kg). These authors demonstrated that rats with an initial mean postmortem heart blood morphine concentration of 0.041 mg/L experienced a consistent increase (3-fold) over the initial 24 hour postmortem interval. The authors suggest that similar changes may take place in man. One potential concern in working with a small animal model however, is the increased risk of transfer of blood between the major vessels, and accelerated release of fluids from tissue to replace the abstracted volume. Contrary to the experience of these authors we found no significant change in either the femoral or peripheral blood morphine concentrations with respect to time when the morphine concentration was 0.300 mg/L or less. In none of our cases however, were we able to evaluate changes or differences in morphine concentration which develop during the three hours immediately following death.

Although both site dependent differences and time dependent changes have been shown to affect the concentration of some drugs in postmortem samples, neither appears to be the case with morphine. The exception to this occurs when the morphine concentration in ventricular blood is elevated (greater than 0.300 mg/L in the cases we evaluated), in which case it was likely to be significantly higher than that in the peripheral compartment, in either femoral or iliac blood. Femoral and iliac blood morphine concentrations are well correlated, making either an appropriate site for collection of peripheral blood for toxicological testing. Morphine concentrations in CSF, and central and peripheral blood appear to be stable over time, and any significant changes observed between T1 and T2 were closely associated with elevated concentrations and not postmortem interval. Because of the known propensity for postmortem redistribution of other drugs, and the likelihood of elevated ventricular morphine concentrations in massive acute overdoses, we strongly recommend the collection of femoral or iliac blood for routine drug screening, and advise caution in the interpretation of central blood morphine concentrations, when this is the only sample available.

Acknowledgments

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References

(1) Bailey DN, Shaw RF. Interpretation of blood and tissue concentrations in fatal self ingested overdose involving amitriptyline: an update (1978–1979). J Anal Toxicol 1980;4:232–36.
(2) Hebb JH, Caplan YH, Crooks CR, Mergner WJ. Blood and tissue concentrations of tricyclic antidepressant drugs in postmortem cases: literature survey and a study of forty deaths. J Anal Toxicol 1982;6:209–16.
(3) Anderson WH, Prouty RW. Postmortem redistribution of drugs. In: Baselt RC, editor. Advances in Analytical Toxicology, Volume II. Boca Raton FL, Yearbook Medical Publishers, 1989:71–102.
(4) Prouty RW, Anderson WH. The forensic science implications of site and temporal influences on postmortem blood-drug concentrations. J Forensic Sci 1990;35(2):243–70.
(5) Pounder DJ, Owen V, Quigley C. Postmortem changes in blood amitriptyline concentration. Am J Forensic Med Pathol 1994;15(3): 224–30.
(6) Pounder DJ, Hartley, AK, Watmough PJ. Postmortem redistribution and degradation of dothiepin. Human case studies and an animal model. Am J Forensic Med Pathol 1994;15(3):231–35.
(7) Felby S, Christensen H, Lund A. Morphine concentrations in blood and organs in cases of fatal poisoning. J Forensic Sci 1974;3:77–81.
(8) Chan SC, Chan EM, Kaliciak HA. Distribution of morphine in body fluids and tissues in fatal overdose. J Forensic Sci 1986;31(4): 1487–91.
(9) Robinson A, Williams F. Postmortem distribution of morphine in heroin addicts. Med Sci Law 1971;11:135–38.
(10) Koren G, Klein J. Postmortem redistribution of morphine in rats. Therapeutic Drug Monitoring 1992;14:461–63.
(11) Spiehler VR, Cravey RH, Richards RG, Elliott HW. The distribution of morphine in the brain in fatal cases due to the intravenous administration of heroin. J Anal Toxicol 1978;2:62–7.
(12) Bailey DN, Shaw RF. Concentration of basic drugs in postmortem human myocardium. J Toxicol Clin Toxicol 1982;19(2):197–202.
(13) Coat-a-Count Serum Morphine Radioimmunoassay, Package insert. Diagnostic Products Inc., Los Angeles CA, September 7, 1990.
(14) Logan BK, Lüthi R. The significance of morphine concentrations in the cerebrospinal fluid in morphine caused deaths. J Forensic Sci 1994;39(3):699–706.

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