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Changing Patterns of Drug and Alcohol Use in Fatally Injured Drivers in Washington State

ABSTRACT: We have previously reported on patterns of drug and alcohol use in fatally injured drivers in Washington State. Here we revisit that population to examine how drug use patterns have changed in the intervening 9 years. Blood and serum specimens from drivers who died within 4 h of a traffic accident between February 1, 2001, and January 31, 2002, were analyzed for illicit and therapeutic drugs and alcohol. Drugs when present were quantitated. Samples suitable for testing were obtained from 370 fatally injured drivers. Alcohol was detected above 0.01 g/100 mL in 41% of cases. The mean alcohol concentration for those cases was 0.17 g/100 mL (range 0.02–0.39 g/100 mL). Central nervous system (CNS) active drugs were detected in 144 (39%) cases. CNS depressants including carisoprodol, diazepam, hydrocodone, diphenhydramine, amitriptyline, and others were detected in 52 cases (14.1%), cannabinoids were detected in 47 cases (12.7%), CNS stimulants (cocaine and amphetamines) were detected in 36 cases (9.7%), and narcotic analgesics (excluding morphine which is often administered iatrogenically in trauma cases) were detected in 12 cases (3.2%). For those cases which tested positive for alcohol *c*. 40% had other drugs present which have the potential to cause or contribute to the driver's impairment. Our report also considers the blood drug concentrations in the context of their interpretability with respect to driving impairment. The data reveal that over the past decade, while alcohol use has declined, some drug use, notably methamphetamine, has increased significantly (from 1.89% to 4.86% of fatally injured drivers) between 1992 and 2002. Combined drug and alcohol use is a very significant pattern in this population and is probably overlooked in DUI enforcement programs.

KEYWORDS: forensic science, toxicology, drug impaired driving, demographics

In 1996, we published a survey of drug use by drivers dying in collisions in Washington State between September 1992 and August 1993 (1). In the intervening years several changes have taken place, which might be expected to impact drug and alcohol use by drivers and their detection by the laboratory. These include the introduction of a drug recognition and evaluation (DRE) program (2), public safety education on drug/driving issues, training for police officers in recognizing drug impaired drivers, increased use of less sedating antidepressant (3) and antihistamine drugs (4), increased drug testing in regulated transportation industries, and the lowering of Washington's *per se* limit for alcohol from 0.10 to 0.08 g/100 mL. Additionally, patterns of recreational drug use have changed in the State since our last report, including a marked increase in the incidence of methamphetamine use (5,6), and the appearance of 3,4-methylenedioxy methamphetamine in the drug using population (7). Analytically, the Washington State Toxicology Laboratory (WSTL) has introduced more sensitive drug testing procedures, which may reveal the presence of lower concentrations of drugs or metabolites (including marijuana metabolites) than were detectable by methods used in our prior study.

To assess the effect of these changes on patterns of drug and alcohol use in fatally injured drivers over the intervening 9-year period, we repeated a survey of 12 months of toxicology data from drivers killed in traffic collisions between February 2001 and January 2002. Additionally, for the purposes of this review, we quantitated any drugs or metabolites identified in the blood of these drivers and we discuss the significance of the blood drug concentrations with respect to assessing impairment. A limitation of this data is that we were unable to perform any responsibility analysis on the collisions that resulted in these deaths, or to separate out causing drivers from noncausing drivers, or make any differentiation of rates of drug use between those two groups.

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Materials and Methods

Study Population

Washington State law requires coroners and medical examiners in the 39 counties of the State to submit samples from drivers who die within 4 h of a traffic accident for drug and alcohol testing. From February 1, 2001, to January 31, 2002, there were 657 traffic fatalities in Washington State. Of these 397 (60%) were drivers, 171 (26%) were passengers, and 75 (11%) were pedestrians. Of the fatally injured drivers, the WSTL received blood samples sufficient for comprehensive drug testing in 370 cases (93%).

Autopsy blood was provided in 10 mL tubes containing sodium fluoride and potassium oxalate (Sherwood Medical, St. Louis, MO). In some cases of delayed death, hospital serum collected at the time of admission was submitted. All samples were tested for alcohol using headspace gas chromatography (Agilent® 6890 gas chromatograph (GC)/7694 headspace autosampler; Agilent, Palo Alto, CA). In 214 cases (57.8%), urine was available, and was screened for cocaine, opiates, benzodiazepines, barbiturates, cannabinoids, amphetamines, PCP, methadone, propoxyphene, and tricyclic antidepressants, using enzyme multiplied immunoassay (EMIT, Syva/Dade Behring, Deerfield, IL, on an Olympus AU400® analyzer, Center Valley, PA). Table 1 summarizes the cutoff concentrations used in this study, and highlights methodological changes made since 1993 that would influence the findings of the two studies.

Blood and serum specimens were screened for drugs by EMIT following a protein precipitation with a 4:1 acetonitrile:methanol mixture (8). Analytical cutoff's are listed in Table 1.

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TABLE 1—*Changes in analytical procedures 1992/1993–2001/2002.*

	1992/1993		2001/2002	
Screening assay	Assay	Cutoff (ng/mL)	Assay	Cutoff (ng/mL)
	EMIT (Syva ETS®)		EMIT (Olympus AU400®)	
	Opiates	50	Opiates	20
	Cocaine metabolite	50	Cocaine metabolite	100
	Cannabinoids	50	Cannabinoids	10
	—	—	Benzodiazepines	100
	—	—	Barbiturates	100
	—	—	Amphetamines	200
	—	—	Phencyclidine	10
	—	—	Propoxyphene	100
	—	—	Methadone	100
	—	—	Tricyclic Antidepressants	100
Confirmation	Drug	Method	Drug	Method
	Basic drugs	GC/MS, GC/NPD	Basic drugs	GC/MS, GC/NPD
	Acid and neutral drugs	GC/MS, GC/FID	Acid and neutral drugs	GC/MS, GC/FID
	Benzoylecgonine	HPLC	Benzoylecgonine	GC/MS
	Morphine	RIA	Morphine	GC/MS

EMIT, enzyme multiplied immunoassay; GC/MS, gas chromatography/mass spectroscopy; GC/FID, flame ionization detection; HPLC, high-performance liquid chromatography; RIA, radio immunoassay.

Following immunoassay, and irrespective of the results of the screen, blood or urine samples (1 mL) were extracted at pH 9 (1 mL, 1 N borate buffer) into *n*-butyl chloride (3 mL). Samples were then mixed for 5 min, centrifuged at 2000 r.p.m. for 5 min, then back extracted into 3 N HCl (200 μL). Following basification with ammonium chloride, drugs were back extracted into chloroform (150 μL), and transferred to injection vials. Extracts were analyzed in scan mode by GC/mass spectrometry (GC/MS) (Agilent® 6890 GC/5973MSD). Drugs were quantitated according to three point calibration curves using metycaine as the internal standard. Class-representative controls for the major drugs detected were quantitated alongside the decedent samples, and all agreed within ± 20% of the target. The linear range varied between analytes, however samples exceeding the linear range were diluted and re-extracted. Acidic and neutral drugs in blood or serum were extracted at neutral pH onto *c.* 1 g of XAD resin (Supelco®, Bellefonte, PA). After vortex mixing for 1 min the aqueous portion was aspirated, and ethyl acetate (6 mL) was added. The mixture was vortex mixed, the ethyl acetate aspirated into conical centrifuge tubes, and evaporated to dryness under air. The residue was reconstituted in acetonitrile (75 μL) and washed with *N*-heptane (500 μL), and centrifuged. The acetonitrile layer was transferred to injection vials for chromatographic analysis. Extracts were analyzed by GC with flame ionization detection (Agilent® 6890 GC/FID), and confirmation by GC/MS (Agilent® 6890 GC/5972MSD) (9). Delta-9-tetrahydrocannabinol (THC) and carboxy-THC and deuterated internal standards in blood or serum (2 mL) were extracted into hexane:ethyl acetate 4:1 (8 mL) at pH 4.5 using phosphate buffer. The organic layer was then transferred to a conical centrifuge tube and evaporated to dryness under air. Extracts were derivatized using BSTFA/TMCS/acetonitrile 1:1 (50 μL), and analyzed by GC/MS (Agilent® 6890 GC/5973 MSD) using selected ion monitoring. Benzoylecgonine, ecgonine methylester, and morphine were confirmed and quantitated by GC/MS using selected ion monitoring. The analytes and deuterated internal standards were extracted from blood or serum (1 mL) into chloroform:isopropanol 4:1 (8 mL) at pH 9 using 1 N borate buffer (2 mL), back extracted into 0.2 N HCl (4 mL), re-extracted into chloroform:isopropanol (8 mL), and evaporated to dryness under air. Following evaporation, samples were derivatized using BSTFA (60 μL) and transferred to injection vials for GC/MS analysis.

For the purposes of this study, the presence of caffeine, nicotine, lidocaine, and atropine were not considered significant, and are not reported. Lidocaine and atropine are used almost exclusively for resuscitation and when encountered can be attributed to that source with some confidence. Morphine and diazepam are often used as an analgesic and a muscle relaxant respectively in trauma or emergency care, and their administration postcollision cannot be ruled out in our cases based on the information we had access to. Subsequent sections in this manuscript make reference to "impairing drugs," which for the purposes of this discussion, excludes selective serotonin reuptake inhibitors (SSRIs), acetaminophen, ibuprofen, naproxen, salicylates, diltiazem, bupropion, laudanosine (an atracurium metabolite), and bupivacaine, for which there is currently no good evidence of impairment in driving.

Results and Discussion

The size of the population, the age distribution, and gender breakdown of the fatally injured drivers are shown in Table 2. These characteristics were notably similar to those of the fatally injured driver population described in our earlier study (1), consequently, changes in patterns of drug use and driving observed cannot be ascribed to changing demographics.

Alcohol Use

Of 370 cases tested, 150 blood samples (41%) were positive for ethanol, with a mean ethanol concentration of 0.17 g/100 mL (see Table 3). This was not significantly different ($p < 0.05$) from the mean of 0.18 g/100 mL reported in the 1992 study, suggesting that levels of consumption in those individuals who continued to drink and drive has not changed. The *per se* legal limit for alcohol in Washington was lowered to 0.08 g/100 mL from 0.10 g/100 mL in 1999.

The rate of alcohol use in this population had dropped from 47% in 1992/1993 to 41% in 2001/2002. Using a test of confidence interval for proportions shows a significant reduction ($p < 0.07$) in the rate of alcohol use by fatally injured drivers. Many factors likely contributed to this positive trend including public safety education, strict enforcement, and widespread post-

TABLE 2—*Study demographics.*

	1992/1993 ($n = 347$)	2001/2002 ($n = 370$)
Men	257 (74%)	277 (75%)
Mean age	39	38
Range	15–92	15–87
Women	90 (26%)	93 (25%)
Mean age	44	47
Range	17–83	16–91

ing of the lower legal limit. Other assessments of the effectiveness of lowering the *per se* limit for alcohol related driving offenses have shown similar positive benefits (10,11).

Our findings are comparable with rates of alcohol use by fatally injured drivers reported by other workers including Mercer and Jeffery (12) who reported the presence of alcohol in 48% of fatally injured drivers in British Columbia (Canada), del Rio and Alvarez (13), reporting a rate of 50.5% in Spain, and Drummer et al. (14), reporting alcohol in $\sim$ 31% of cases in Australia. Drummer et al. also summarizes rates of alcohol use in fatally injured drivers from several other studies, varying between 12.5% (fatally injured truck drivers in eight U.S. states, 1993) to 79% (single vehicle accidents in North Carolina, U.S.A. in 1978).

Of the 150 cases positive for alcohol, 63 (42%) were positive for one or more impairing drugs. Combined drug and alcohol use was common, and is one of the most significant findings from this study. The significance of this lies in the fact that in DUI enforcement, the investigation as to the impairing agents responsible typically ends with a positive blood or breath alcohol result. These data suggest, that even among individuals with impairing amounts of alcohol in their systems, drug use—either recreational or therapeutic—may be contributing to their impairment. Table 3 shows that for those cases which tested positive for alcohol, above and below 0.08 g/100 mL, and in aggregate, that *c*. 40% had other drugs present which have the potential to cause or contribute to the driver's impairment.

The principle drugs detected were cannabinoids, cocaine, diphenhydramine, methamphetamine, and methadone. If these patterns of combined drug and alcohol use carry over into the general impaired driving (DUI) population, as many as 40% of all individuals arrested for alcohol related driving offenses could be at least partially under the influence of drugs. Failing to identify this group by appropriate toxicological testing and to have their drug use or abuse addressed through education or intervention within the courts is likely to contribute to recidivism.

A corollary to this is to consider the rates of combined drug and alcohol use among drivers testing positive for the most frequently encountered classes of drugs. Table 4 lists the numbers of cases in which various drugs were detected, and corresponding rates at which cases testing positive for these drugs were also positive for alcohol. For the most frequently identified drugs the rate of combined drug and alcohol use included: cannabinoids 53%; cocaine 38%; methamphetamine 33%; diazepam 53%; diphenhydramine 50%. These figures demonstrate again that users of these recreational drugs will combine their patterns of drug and alcohol use to fine-tune the desired effect, or to offset negative side effects, placing them at greater risk for traffic accident involvement.

Drugs Other than Alcohol

Table 4 shows all drugs and metabolites encountered in the specimens tested, the frequency with which they were detected, and the mean, median, and ranges of concentrations detected.

It is informative to compare the patterns of most frequently detected drugs in the current population to that studied in our earlier publication (Table 5).

Overall, there was a significant increase in rates of positivity for impairing drugs, rising from 25% in 1991/1992 to 35% in 2001/2002. The positivity rates for individual drugs were compared using a confidence interval for proportions, and there were significant ($p < 0.07$) differences in the frequency of positives for amphetamines, benzodiazepines, diphenhydramine, hydrocodone, and phenytoin. As noted elsewhere, there are contributions to these differences from changing drug use demographics (both licit and illicit), and improved laboratory procedures.

Marijuana

After alcohol, marijuana (THC or its metabolite 11-carboxy-THC) continued to be the most frequently detected drug, being present in 47 of the 370 cases tested (12.7%). This compares with 10% of cases in 1992, indicating no significant change in marijuana use by fatally injured drivers. This is in spite of an improvement in the sensitivity of the screening method (10 ng/mL in 2002 relative to 50 ng/mL in 1992). Other studies have demonstrated similar rates of detection of THC or its metabolites in fatally injured drivers of 13% in British Columbia, Canada (12), and 13.5% in Australia (14). Lower rates were reported in Spain, 1.4% (15), and in Norway, 5% (16).

The mean concentration of THC in the fatally injured drivers in this study was 8 ng/mL (median 6 ng/mL; range 2–32 ng/mL; $n = 13$). Drummer et al. (14) reported a mean THC concentration of 12 ng/mL (median 10 ng/mL; range 0.7–100 ng/mL) in fatally injured drivers in Australia between 1990 and 1999. For 11-

TABLE 3—*Alcohol-positive drivers testing positive for drugs.*

	BAC $<$ 0.08 ($n = 23$)		BAC $\geq$ 0.08 ($n = 127$)		BAC $>$ 0.00 ($n = 150$)	
	n	%	*n*	%	*n*	%
Cannabinoids	5	21.74	22	17.32	27	17.33
Cocaine	3	13.04	9	7.09	12	8.00
Diphenhydramine	1	4.35	6	4.72	7	4.67
Methamphetamine	0	0.00	6	4.72	6	4.00
Methadone	3	13.04	1	0.79	4	2.67
Nordiazepam	1	4.35	3	2.36	4	2.67
Hydrocodone	0	0.00	3	2.36	3	2.00
Midazolam	1	4.35	1	0.79	2	1.33
MDMA	0	0.00	1	0.79	1	0.67
Potentially impairing drug	10	43.48	52	40.94	62	41.33

BAC, blood alcohol concentration; MDMA, methylenedioxy methamphetamine.

TABLE 4—*Drug and alcohol levels in fatally injured drivers.*

	n	Mean (mg/L)	Median (mg/L)	Range (mg/L)	EtOH Positive (%)
Ethanol*	150	0.174	0.174	0.020–0.388	100
Carboxy-THC	47	0.018	0.011	0.002–0.163	53
THC	13	0.008	0.006	0.002–0.032	38
Cocaine	13	0.15	0.11	<0.01–0.23	69
Benzoylecgonine	18	0.72	0.31	0.03–3.30	67
Ecgonine methyl ester	12	0.34	0.19	0.07–0.99	58
Cocaethylene	7	0.02	0.01	0.01–0.04	100
Methamphetamine	18	0.73	0.26	<0.01–1.08	33
Amphetamine	9	0.20	0.09	<0.05–0.93	11
Diazepam	15	0.15	0.09	<0.05–0.44	53
Nordiazepam	7	0.20	0.11	0.02–0.47	43
Citalopram	10	0.71	0.36	<0.01–2.27	50
Desmethylcitalopram	4	0.21	0.15	0.11–0.37	50
Diphenhydramine	10	0.09	0.08	<0.01–0.19	70
Hydrocodone	7	0.01	0.01	<0.05	43
Phenytoin	7	9.03	9.45	<2.5–12.38	14
Morphine	6	0.06	0.04	0.02–0.17	0
Sertraline	5	0.27	0.13	0.02–0.80	20
Desmethylsertraline	5	0.16	0.13	0.07–0.27	20
Amitriptyline	4	0.06	0.06	0.02–0.09	25
Nortriptyline	2	0.09	0.09	0.07–0.10	0
Methadone	4	1.19	1.60	0.01–1.96	75
EDDP—methadone met.†	2	—	—	NA	50
Midazolam	4	0.06	0.07	0.02–0.08	50
Codeine	3	0.07	0.07	<0.05–0.11	0
Dextromethorphan	3	0.19	0.19	<0.05–0.25	100
Diltiazem	3	0.97	0.48	0.23–2.19	0
Venlafaxine	3	0.05	0.03	0.01–0.10	0
O-desmethyl venlafaxine	3	0.20	0.22	0.15–0.22	0
Oxycodone	3	0.15	0.08	0.05–0.33	0
Acetaminophen	2	>10.30	>10.30	<12.5	0
Bupropion	2	0.10	0.10	0.07–0.13	0
Bupropion met.	2	2.45	2.45	0.80–4.09	0
Chlorpheniramine	2	0.03	0.03	0.02–0.03	100
Fluoxetine	2	0.15	0.15	0.05–0.24	50
Norfluoxetine	2	0.14	0.14	0.09–0.19	50
Laudanosine	2	0.15	0.15	NA‡	0
Methanol	2	0.35	0.35	0.29–0.40	0
Paroxetine	2	0.53	0.53	NA‡	50
Phenobarbital	2	8.89	8.89	<2.5–8.89	0
Pseudo/ephedrine	2	0.74	0.74	<0.25–0.74	50
Bupivacaine	1	0.87	0.87	NA	0
Butalbital	1	3.57	3.57	NA	0
Carbamazepine	1	4.10	4.10	NA	0
Cyclobenzaprine	1	0.02	0.02	NA	0
Desipramine	1	0.06	0.06	NA	0
Fluvoxamine	1	5.00	5.00	NA	0
Hydroxyzine	1	0.23	0.23	NA	0
Hydroxyzine metabolite†	1	—	—	NA	0
Ibuprofen†	1	—	—	NA	0
Trazodone	1	1.20	1.20	NA	0
mCCP—trazadone metabolite	1	0.09	0.09	NA	0
MDMA	1	0.26	0.26	NA	0
Meperidine	1	0.80	0.80	NA	0
Meprobamate	1	3.37	3.37	NA	0
Metoclopramide	1	0.06	0.06	NA	0
Naproxen	1	44.1	44.10	NA	0
Olanzapine	1	0.20	0.20	NA	0
Phentermine	1	0.11	0.11	NA	0
Primidone	1	8.98	8.98	NA	0
Salicylates	1	<100	<100	NA	100
Toluene	1	<4.0	<4.00	NA	0
Verapamil	1	0.15	0.15	NA	0
Norverapamil	1	0.25	0.25	NA	0
Zolpidem	1	<0.05	<0.05	NA	0

*Concentrations reported are in g/100 mL.
†Drug not quantitated.
‡Only one case reported drug concentration.
MDMA, methylenedioxy methamphetamine; THC, tetrahydrocannabinol.

TABLE 5—*Rates of drug positives 1992/1993–2001/2002.*

	1992/1993 (% Positive)	2001/2002 (% Positive)
Cannabinoids	11.01	12.7
Amphetamines**	1.89	4.86
Benzodiazepines**	1.26	5.14
Cocaine/met**	3.14	4.86
Diphenhydramine**	0.63	2.7
Hydrocodone**	0.31	1.89
Phenytoin**	0	1.89
Morphine	1.26	1.62
Doxylamine	0.63	0
Amitriptyline	0.31	1.08

**Significant difference ($p > 0.07$).

carboxy-THC the mean concentration was 18 ng/mL (median 11 ng/mL; range 2–163 ng/mL; $n = 47$). The level of detection/level of quantitation (LOD/LOQ) for this assay was 2 ng/mL.

Most studies of smoked marijuana administration report plasma concentrations, however whole-blood concentrations are expected to be about 55% of the corresponding plasma value. Based on plasma concentrations reported following single acute administration of 15.8 mg of smoked THC (17) blood THC concentrations would be expected to peak at around 8 min at concentrations of 46 ng/mL (28–71 ng/mL), declining to 0.7 ng/mL by 3 h. 11-Carboxy THC concentrations in blood would be expected to peak at 2.4 h, at a mean concentration of 13.8 ng/mL (range 8–29.7 ng/mL), declining more slowly to 4.8 ng/mL by 8 h). There is general consensus among toxicologists that blood THC concentrations cannot be related to a specific degree of impairment, and it is universally accepted that the 11-carboxy THC metabolite is inactive. Detection of parent THC in blood however is generally indicative of recent use, and the period of effect following the smoking of marijuana is typically 2–4 h. Effects on driving associated with recent marijuana use may include decreased car handling performance, increased reaction time, impaired time and distance estimation, inability to maintain headway, lateral travel, and impaired sustained vigilance (18).

Combined marijuana and alcohol use are a concern in the driving population because of the marked synergism demonstrated between these two drugs, particularly in inexperienced users (19). Of 150 alcohol-positive drivers, 26 (17%) were also positive for cannabinoids. Out of all deceased drivers who tested positive for cannabinoids ($n = 47$), 25 (53%) had been drinking (mean = median BAC = 0.15 g/100 mL).

Marijuana was also found frequently with other sedating or stimulant drugs including methamphetamine, cocaine, methadone, and midazolam, and would be expected to compound the impairing effects of these drugs.

Stimulants—Methamphetamine

Methamphetamine detections increased from six cases in 1992 (1.89%) to 18 cases in 2002 (4.9%) an increase of 200%, and reflective of the general trend in popularity of the drug. Amphetamine was detected in nine cases, but was present along with (and most likely a metabolite of) methamphetamine in each instance. Other measures of methamphetamine consumption have increased over the same time period in Washington State. In 1993, there were 16 driving under the influence of drugs (DUID) cases involving methamphetamine submitted to the WSTL (0.7% of all DUIs). In 2001, methamphetamine was detected in 256 DUID cases (7.9% of all DUIs), representing an increase of 1500%. A significant component of this increase however reflects additional enforcement efforts, and the incidence of methamphetamine in fatally injured drivers is probably a more reliable indicator of increased rates of use.

Couper et al. (6) reported on drugs in voluntary urine samples from truck drivers in Washington State. The study had a compliance rate of 81%, and found methamphetamine in 1.7% of the drivers tested ($n = 822$). Crouch et al. (20) reported on drug findings in fatally injured truck drivers and found a methamphetamine-positive rate of 7%. Drummer et al. (14) reported an incidence of methamphetamine use in fatally injured drivers in Australia of 1.5% between 1990 and 1999. del Rio and Alvarez (15) reported finding methamphetamine in 1.4% of fatally injured drivers in Spain.

Fatally injured drivers in this study had a mean methamphetamine concentration of 0.73 mg/L (median 0.26 mg/L; range < 0.01–1.08 mg/L; $n = 18$). This concentration compares to a mean of 0.61 mg/L (median 0.47 mg/L; range < 0.05–2.48 mg/L; $n = 27$) in a group of drivers suspected of driving under the influence of drugs (5) and a mean of 0.39 mg/L (median 0.20 mg/L; range 0.01–3.6 mg/L; $n = 51$) in fatally injured Australian drivers (14). Other studies have also reported on blood concentrations of methamphetamine in traffic fatalities. In a report of mortality associated with methamphetamine use (21), the mean concentration in deceased drivers was 0.89 mg/L (median 0.35 mg/L; range 0.05–2.6 mg/L; $n = 17$), very comparable with this report. The wide range of adverse affects on driving associated with recreational methamphetamine use is now well accepted (5,14, 18,22,23). Furthermore, the concentrations are consistent with patterns of drug use in other methamphetamine abusers dying from nondrug causes, again suggesting typical recreational patterns of use (24).

In spite of the fact that blood concentrations cannot be reliably linked to a specific degree of effect for stimulants due to tolerance and hysteresis issues (5) the significance of these concentrations should not be underestimated. For example, they can be assessed in terms of whether they are within the normal therapeutic range, consistent with overdose, or consistent with ranges reported for recreational use or abuse, or in other impaired drivers. In addition, parent to metabolite ratios may offer insight into chronic versus acute use, or recency of use. With this information, a range of possible effects associated with different doses and patterns of use can be presented to the trier of fact for consideration along with other objective information in a given case, such as observations of the subject, their performance in field sobriety tests or a structured evaluation such as a DRE exam.

Stimulants—Cocaine

The inactive cocaine metabolite benzoylecgonine was present in 18 cases (4.9%), indicating cocaine consumption. This represents a significant increase from eight cases (2.0%) in 1992. This increase occurred in spite of the fact that the immunoassay screening cutoff was increased to 100 ng/mL in 1996. Cocaine itself was present in 13 cases (3.5%), and benzoylecgonine was present in each instance. Within the state, the number of cocaine-positive DUID cases increased from 39 (1.7% of DUI cases) in 1993 to 127 (3.9% of DIUI cases) in 2001. This increase of 225% falls far short of the 1500% increase observed for methamphetamine, and more closely reflects the increase resulting from enforcement as opposed to increased rates of use. A study of the incidence of cocaine use in fatally injured drivers in Quebec (25), reported

finding cocaine in 6.9% of blood samples, and in 1% of saliva samples from a large ($n = 8177$) control group.

In our population, mean benzoylecgonine concentrations of 0.72 mg/L (median 0.31 mg/L; range 0.03–3.30 mg/L; $n = 18$), and mean cocaine concentrations of 0.15 mg/L (median 0.11 mg/L; range <0.01–0.23 mg/L; $n = 13$) were noted. Cocaine concentrations vary as a function of dose, route of administration, storage conditions and many other factors, making them difficult to interpret. For example, following smoking of 50 mg of cocaine base, peak plasma concentrations of cocaine of 0.23 mg/L were achieved in about 45 min, while benzoylecgonine peaked at 1.5 h at a concentration of 0.15 mg/L (26). The typical benzoylecgonine concentrations found in these fatally injured drivers represent substantially greater levels of consumption most likely over a longer period of time. Impairment resulting from cocaine use has been attributed to the distracting nature of its stimulant and euphoric effects, and to adverse withdrawal effects of sleepiness, fatigue, intense depression, anxiety associated with the "crash" following binge use. Consequently, as with methamphetamine, it is difficult to predict the phase of intoxication from blood drug concentrations.

Benzodiazepines

The data showed a significant increase ($p > 0.07$) in the rate of benzodiazepine detection, from four cases (1%) in 1992/1993, to 19 cases (5%) in 2001/2002, an increase of 275%. These rates however may underestimate the total number of benzodiazepine-positive cases within the data set. Clonazepam and lorazepam, two drugs with known effects on driving, are not detected by the EMIT reagents, and thus would have gone undetected in our study population. Consequently, the true rate of benzodiazepine use in fatally injured drivers could be higher than our data reflects. Other evidence points to increasing rates of lorazepam detection in drivers arrested for DUI in Washington State over the past 8 years (27). Identifying this trend has prompted more thorough testing in DUI and DRE cases, particularly for those cases where our primary assays (EMIT, basic, and acid/neutral drug screens) fail to detect impairing drugs while roadside tests for impairment indicate central nervous system (CNS) depression.

Similar detection rates for benzodiazepines in fatally injured drivers have been reported by other investigators. Drummer et al. (14) report a detection rate of 4%, and Mercer and Jeffery (12) report a detection rate of 5% for diazepam alone. In this study diazepam and nordiazepam were the most frequently detected benzodiazepines, with diazepam being detected in 15 cases and nordiazepam being detected in seven cases. Additionally, four cases were positive for midazolam, a drug not encountered in our previous report. Analytical changes in our laboratory that are likely to have influenced this increase include the addition of benzodiazepines in our blood immunoassay panel (cutoff 100 ng/mL) and a more sensitive benzodiazepine GC/MS confirmatory assay.

As noted earlier, interpretation of the diazepam positivity is complicated by the use of diazepam iatrogenically by emergency personnel responding to trauma scenes, and we were not able to definitively distinguish post- versus preaccident administration. The presence of nordiazepam in seven cases however would suggest that these at least represent use by the driver before driving. The mean diazepam concentration was 0.15 mg/L (median 0.09 mg/L; range <0.05–0.44 mg/L; $n = 15$), and the mean nordiazepam concentration was 0.2 mg/L (median 0.11 mg/L; range 0.02–0.47 mg/L; $n = 7$). The mean midazolam concentration was 0.06 mg/L (median 0.07 mg/L; range 0.02–0.08 mg/L; $n = 4$).

The literature reflects that prescribed doses of 5–40 mg of diazepam can produce blood concentrations from 0.1 to 1.0 mg/L, and doses of 5–15 mg midazolam correspond to blood concentrations of 0.005–0.20 mg/L (28). This suggests that benzodiazepine concentrations encountered in this study represent therapeutic use of these drugs. Nevertheless, the sedative hypnotic, and psychomotor effects of benzodiazepines, such as poor coordination, increased reaction time, poor visual perception and tracking, render them a liability to driving performance (29). Furthermore, the synergistic effects of benzodiazepines and alcohol are well documented (28). In these drivers, alcohol was detected in 54% of diazepam-positive cases, 43% of nordiazepam-positive cases, and 50% of midazolam-positive cases.

Other Drugs

In addition to benzodiazepines, a number of other drugs possessing CNS-depressant properties were also detected (Table 2). Many of these medications are prescribed with accompanying warnings regarding the dangers of operating a motor vehicle following their use, particularly when combined with alcohol. The most commonly detected drug in this category was diphenhydramine. While an effective antihistamine, the sedative properties of diphenhydramine are also well suited for its use as a sleeping agent. Gengo et al. (30) have shown that following a normal 50 mg dose, plasma concentrations associated with the onset of drowsiness range from 0.058 to 0.074 mg/L. The mean diphenhydramine concentration in this study was 0.09 mg/L (median 0.08 mg/L; range <0.01–0.19 mg/L; $n = 10$).

Poly-drug use in this population was common, and often included the combination of illicit and prescription drugs. For those cases where alcohol was negative ($n = 220$), 9.5% of cases were found positive for two or more impairing drugs. One driver had an oxycodone level of 0.33 mg/L, a trazodone level of 1.20 mg/L, a hydroxyzine level of 0.23 mg/L, and was also positive for cannabinoids. A review of the literature indicates that when taken for severe pain, a high dose (0.28 mg/kg) of oxycodone can result in a peak plasma level of up to 0.04 mg/L (31). By this standard, the whole-blood concentration in this individual would be considered comparatively high, especially after converting to its corresponding plasma concentration. Other considerations such as tolerance, postmortem redistribution, the victim's survival period following the accident and in vitro degradation must also be taken into account when interpreting these levels.

Conclusions

Revisiting the rates of drug use in fatally injured drivers has allowed us to assess the effects of changes in drug use patterns over 9 years. The principle drugs found are the illicit drugs marijuana, cocaine and methamphetamine, between them accounting for 72% of all cases. Some changes in the incidence of therapeutic drugs reflect innovations in drug therapy, but are dwarfed by the illicit drug cases. Combining both recreational and therapeutic drugs with alcohol is also a significant and worrying trend. This is especially so, since in DUI enforcement, a positive alcohol test usually means that no further investigation into a subject's drug use takes place. Most likely this means that our current assessments of impairing drug use by drivers are gross underestimates. We strongly recommend that drug screening be applied more universally in serious traffic crimes cases so that combined drug and

alcohol use can be identified, and the appropriate sanctions or treatment applied.

Measuring concentrations of drugs and their metabolites in blood is demonstrated here to have both value and limitations. Inferring the specific degree of intoxication based on the mere presence of a drug in a person's system is fraught with difficulties, due to postmortem changes, acute and chronic tolerance to drug effects, the time interval between the collision and death or autopsy, and patterns of combined drug and alcohol use which have not been specifically studied. The concentrations of drugs found in the blood of these drivers, gives us some insight into the likely significance of these positive results. Methamphetamine concentrations for example are similar to those reported in recreational users dying from other causes, and in other drivers arrested for impaired driving, who displayed objective symptoms of impairment, and subsequently tested positive for the drug. Cocaine and metabolite concentrations are consistent with those achieved from recreational use. THC concentrations indicate in many cases recent use of the drug, which overlaps with the established period for peak effects. Concentrations of many of the therapeutic drugs are also in the range associated with therapeutic effect, but within which there are known side effects which affect cognitive and psychomotor skills. For example, diphenhydramine, an antihistamine with known sedative effects was present in 10 cases, and at a mean concentration equivalent to peak levels achieved following the 50–100 mg dose recommended for sleep induction. We recommend blood as the specimen of choice in serious traffic investigation cases.

Having identified that drug use by fatally injured drivers is a significant risk factor for accident causation, and a contributor to the human toll on North American highways we should consider what the findings of this study offer in addressing those behaviors. Although sedating medications were represented in a small percentage of the cases in this population, better education and monitoring by physicians and pharmacists, and stronger advice to patients about not mixing medications with alcohol with these drugs, alone and in combination, could save lives. Better and more specific warnings about the probability of drug effects would better equip drivers to make decisions. The International Council on Alcohol Drugs and Traffic Safety (ICADTS) has developed graduated guides relating medication, dose, and duration of effect to intensity of impairment (32).

As the drugs implicated with greatest frequency are illicit recreational drugs, efforts to limit recreational drug use will have a positive effect on highway safety. The current trend towards the decriminalization of marijuana, and increased access to marijuana for medical purposes carries with it the often overlooked baggage of increased risk of driver impairment. Laws making it an offense to drive after consuming illicit drugs—the so-called zero tolerance laws—would send a strong message about the risks and dangers associated with driving after recreational drug use, and add some deterrence. Enhanced sentencing for vehicular homicide and assault committed after using illicit drugs would further promote behavioral change. Finally, meaningful sanctions including jail time, paired with court-supervised drug treatment, and drug testing before relicensing would serve the dual purposes of deterrence and rehabilitation of offenders, thus lessening risks for recidivism.

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