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To cite this article: Hassan Z. Khiabani, Jørgen G. Bramness, Anders Bjørneboe & Jørg Mortland (2006) Relationship Between THC Concentration in Blood and Impairment in Apprehended Drivers, Traffic Injury Prevention, 7:2, 111-116, DOI: 10.1080/15389580600550172

To link to this article: http://dx.doi.org/10.1080/15389580600550172

Published online: 25 Jan 2007.

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Relationship Between THC Concentration in Blood and Impairment in Apprehended Drivers

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Objective. The most important psychoactive ingredient in cannabis, Δ(9)-tetrahydrocannabinol (THC) is one of the most frequently detected substances in blood samples from suspected impaired drivers in Norway. There is growing concern over possible links between the use of cannabis and increased risk of motor-vehicle crashes. Experimental studies have provided useful information on the role of THC and dose-effect relations with respect to psychomotor performance. The main purpose of the present study was to investigate whether a physician’s judgment on impairment in a real-life setting among suspected drugged drivers, was related to blood THC concentration.

Methods. In Norway a police physician performs a clinical test for impairment (CTI) shortly after apprehension. The Norwegian Institute of Public Health analyze blood samples from all drivers suspected of driving under the influence of non-alcoholic drugs. In the present study 589 samples from approximately 30,000 cases of suspected drug impaired driving from the period 1997–99, contained THC as the only drug. In 456 of these cases a conclusion of the CTI was available.

Results. 230 (54%) drivers were considered not impaired and 226 (46%) impaired. Impaired drivers had higher blood THC concentration than the drivers who were judged as not impaired (median; 2.5 ng/mL (range; 0.3–45.3 ng/mL) vs 1.9 ng/mL (range; 0.32–24.8 ng/mL), (p < 0.05). Furthermore, drivers with blood THC concentrations above 3 ng/mL had an increased risk for being judged impaired compared to drivers with lower concentration ranges.

Conclusion. The relationship between the concentration of THC in blood and risk of being assessed impaired found in this cross-sectional study of suspected drugged drivers, supports findings from previous experimental studies of concentration related effects of THC on psychomotor performance and driving skills.

Keywords Cannabis; Psychomotor Impairment; Drugged Driving; THC Concentration

The use of cannabis has increased considerably during the past decade in the Western world (Christophersen et al., 1990; Gmel 2002; Hall et al., 2001) and many countries are investigating the therapeutic potential of cannabis. Although the cannabis plant contains over 400 chemical compounds, it is accepted that delta (9)-tetrahydrocannabinol (THC) is primarily responsible for the psychoactive properties of the plant.

Experimental studies have repeatedly demonstrated the THC effects on cognitive functions and psychomotor skills; i.e., THC impairs learning and the acquisition of information, short-term or working memory, divided and sustained attention, reaction time, tracking, and motor control (Chait and Pierri, 1992; Kurzthaler et al., 1999; Leirer et al., 1989). In general, good correlation between THC concentration and various impairing effects have been demonstrated, and these effects of THC on cognitive and psychomotor functions can be related to driving performance (Berghaus et al., 1998a; Berghaus et al., 1998b; Robbe, 1994). Therefore, based on the concentration-effect relationship for psychomotor performance effects of the THC, it could be suggested to introduce “legal concentration limits” for blood THC concentration as it has been implemented for alcohol in many countries.

Experimental research has, however, some disadvantages. Due to ethical considerations it is not possible to administer high enough cannabis doses to obtain the THC concentrations often found in real-life settings. The studies will most often be single dose experiments. The subjects included in experimental research are less often experienced users, excluding possible tolerance as a part of the studies. It could thus be argued that findings from such experimental studies would have limited relevance for real-life impairment of cannabis in experienced users, and that concentration-effect relationship for THC not would be clear in a population with mixed cannabis experience.

THC is among the drugs most frequently detected in blood samples from suspected drugged drivers (Christophersen et al., 1990; Waller et al., 1997). In Norway a police physician performs a clinical test for impairment (CTI), in conjunction with
the collection of blood samples, shortly after apprehension of
drivers suspected of driving under the influence of non-alcoholic
drugs (Bramness et al., 2002). We wanted to address the ques-
tion raised above as to whether a concentration effect relation-
ship would be found for THC in a population using cannabis in
a potentially illegal setting (DUI) by comparing the physician’s
conclusion to the concentration of THC in blood at the CTI.

METHODS

Materials
The Division of Forensic Toxicology and Drug Abuse (DFTDA)
at the Norwegian Institute of Public Health analyzed blood sam-
pies from all drivers suspected of drugged driving in Norway.
All the present data were taken from an existing database at the
DFTDA and were handled anonymously by the researchers. This
database contained results from all cases of suspected driving
under the influence of alcohol and non-alcohol drugs, counting
approximately 30,000 cases in the period 1997–1999. The
database was searched for positive THC-blood cases. There were
589 samples that contained only cannabis with no other drugs
or alcohol above limits of detection. Of these cases, 133 cases
were excluded because the examining physician did not present
a conclusion after having performed CTI. We had no informa-
tion on reasons for not performing CTI. The remaining 456 cases
constituted the material of this study.

Analytical Methods
All blood samples received at DFTDA were routinely screened
for alcohols and common drugs of abuse (amphetamine, benz-
diazepines, cannabis, cocaine, and opiates) by immunolog-
ical methods (Christophersen et al., 1990). The immunologi-
ical method used was Enzyme Multiplied Immunoassay Test
(EMIT II Plus) produced by Dade Behring Diagnostica (Syva,
USA) analyses of extracts of haemolysed full blood that has
proved to be rapid and simple screening method for cannabinoids
(Gjerde et al., 1990; Gjerde, 1991; Peel & Perrigo, 1981). The
THC concentration was subsequently determined by a modifica-
tion of a GC-MS-method described previously (Christophersen,
1986; Gustafson et al., 2003). To achieve adequate sensitivity,
lengthy and labor-intensive liquid-extraction procedures were
used with hexane and without pH adjustment. After evaporation
of the organic phase, THC was trimethyl silylated (TMS) with
bistrimethylsilyl-trifluoroacetamide (BSTFA): acetonitrile (2:1)
making the THC/TMS derivative. Gas chromatography/mass
spectrometry (GC/MS) in SIM mode was eventually used for the
analyses (Christophersen, 1986; Gustafson et al., 2003). As a
forensic laboratory an administrative cut-off value is set clearly
above the lowest limit of quantification (LLOQ). The LLOQ
was calculated by the mean of noise adding 10 standard devia-
tion to this mean. The cut-off value for the GC/MS analysis in
whole blood for THC was 1 ng/ml. The interday coefficient of
variation at 1 ng/ml was 10%. The cut-off value for the immuno-
logical screening analyses in whole blood for cannabinoids was
10 ng/ml.

Clinical Test for Impairment (CTI)
In all the cases of suspected drugged driving, a police physician
performed CTI shortly after the apprehension of the drivers.
Norwegian drivers suspected of driving under the influence of
alcohol or non-alcoholic drugs are not at liberty to refuse blood
sampling. Due to practicalities (gaining permission, finding a
physician) the time between apprehension and completing the
CTI with collection of blood samples was about two hours. Only
in some police districts there are specially assigned doctor physi-
cians on call. Since each Norwegian physician will perform only
a few CTIs each in their life-time, and the fact that we have only
examined between one and two percent of the total number of
cases, it makes unlikely that one physician has performed more
than one CTI in the present material.

The CTI in Norway consist of three elements: 1) A short in-
terview in which the suspected driver is asked about drinking
habits and drug history, as well as recent use; 2) Twenty-seven
observations and tests (including seven tests of alertness, cog-
nitive function and vestibular function, four observations of the
eyes, two observations on cardiac action, two observations per-
taining signs of intravenous drug abuse, four tests of motor activ-
ity/coordination, and eight observations concerning appearance)
(Bramness et al., 2002); and 3) An evaluation of other possible
reasons for impaired driving (disease, etc). The physician then
concludes whether the suspected driver is “not impaired” or “im-
paired.” The conclusion of the CTI is based on the physician’s
overall impression of the apprehended driver and not on a sum-
score of the individual tests included in the CTI. The conclusion
was the only variable of CTI included in the present study. Blood
sampling was performed in conjunction with CTI. Blood sam-
ples were collected in 5 ml Vacutainer containing sodium and
heparin as anticoagulants. The CTI report and the blood samples
were sent together to DFTDA by express mail. This procedure
has been controlled in separate studies as a part of the running
quality control of our procedures. Thus it has been demonstrated
that no change of THC-concentrations occurs for periods up to
one week in whole blood samples stored in the containers which
are provided by DFTDA to collect blood.

Data Analysis
Data analyses were performed using Statistical Package for So-
cial Sciences (SPSS) version 12.0.1. Differences between two
groups were examined using either Pearson’s χ²-test for cate-
gorical data, a Student’s t-test for continuous variables with a
normal distribution, or a Mann-Whitney test for variables with-
out a normal distribution. A binary logistic regression model
was applied to determine odds ratios (ORs) and their 95-percent
confidence intervals (CI). Levels of significance for all analysis
were set to P < 0.05 and P < 0.01.

RESULTS

Background Variables
Some of the background characteristics of the present material
are given in Table I. Women were more often apprehended by the
police due to crashes. Further analyses concerning crashes were not performed, because the crash data were considered incomplete. Female drivers had more often signs of i.v. drug abuse. The interrelations between all the other background variables were studied in detail. Drivers of non-private cars were older than the drivers of private cars (mean [SD]) 32 years (±7.7 years) versus 26 years (±6.7 years) (p < 0.05, Student’s t-test). Drivers apprehended after a car crash less often had signs of i.v. abuse (p < 0.05, Student’s t-test). Older drivers more often volunteered information on regular use of cannabis (p < 0.01, Student’s t-test). Older drivers more often had signs of i.v. abuse (p < 0.001, Student’s t-test). Lastly, the different signs of i.v. abuse correlated with one another.

**Blood THC Concentration**

The median blood THC concentration was 2.2 ng/mL with a range from 0.3 to 45.3 ng/mL. Male drivers had higher blood THC concentration than female (2.2 ng/mL [0.3–45.3] vs. 1.3 ng/mL [0.3–18.9], p < 0.05, Mann-Whitney test). Those with needle marks had lower blood THC concentration than those without (median 1.6 ng/mL [0.3–19.8] vs. 2.5 ng/mL [0.3–45.0], p < 0.01, Mann-Whitney test).

**Impairment**

Of the 456 apprehended drivers 230 (54 percent) were judged as impaired by the police physician. Drivers apprehended after reported crashes were less often impaired than drivers apprehended for other reasons (p < 0.01, χ²-test). Drivers who had signs of i.v. abuse were more often judged as impaired (p < 0.01, χ²-test).

These relationships between background variables and impairment were tested in multivariate analysis to check if these relationships could be explained by differences in THC concentrations in the different groups, even if these differences did not emerge in the bivariate analysis between drug concentration and background variables. The bivariate relationships (between impairment, crash, and signs of i.v. abuse) withstood adjustment for blood THC concentration.

**Regular Versus Occasional Use**

Those drivers who claimed to be regular users of cannabis were less often judged as impaired (32% vs 55%, p < 0.01, χ²-test), but there was no difference in THC concentration between regular users and non-regular users. In a multiple regression model the impact of regular use withstood adjustment for THC concentration (OR regular user = 1, OR occasional users = 1.8 95% CI [1.2–2.7], p < 0.01).

**Drug Concentration and Impairment**

The drivers who were judged as impaired had higher blood THC concentration than the drivers who were judged as not impaired (median: 2.5 ng/mL [0.3–45.3 ng/mL] vs 1.9 ng/mL [0.32–24.8 ng/mL], (p < 0.05, Mann-Whitney test). We grouped THC concentrations in six concentration intervals. The percentage of drivers judged impaired increased from 38 percent in the lowest concentration group to 57 percent in the highest (Figure 1). In a binary logistic regression model (Table II) the odds ratio (OR) for being judged impaired increased with increased drug concentrations from 2.9 ng/mL. This relationship did not withstand adjustment for regular use, but was strengthened by adjustment for signs of i.v. abuse. A fourth step involving adjustment for both regular use, signs of i.v. abuse, and gender gave a rising OR for being determined impaired from blood THC concentrations above 2.9 ng/mL.

**DISCUSSION**

In the present study we found a positive relationship between the concentration of THC in blood and risk of being judged
impaired by a police physician after suspected drugged driving. Although this relationship is not so obvious as in the case it is for alcohol or benzodiazepines (Bramness et al., 2002), it was significant. We found that the OR for being judged as impaired was increased in the groups with elevated blood THC concentration. This increased OR withstood adjustment for background variables as gender, needle marks, and regularity of use. THC has previously been shown in a series of experimental laboratory studies to impair psychomotor function in a concentration related fashion (Berghaus et al., 1998a). These have generally demonstrated that THC in doses up to 300 µg/kg causes a dose dependent reduction in performance. The highest THC dose resulted in impairing comparable to the impairing effects of an alcohol dose producing a BAC ≥ 0.05 g/dl (Berghaus et al., 1998a; Berghaus et al., 1998b; Ramaekers et al., 2000; Robbe & Smiley, 1994).

In the present study the median concentration of THC in the impaired drivers was 2.5 ng/ml, significantly higher than those not judged as impaired. Previous studies demonstrated that recent exposure and possible measurable impairment have been linked to plasma THC concentrations in excess of 2–3 ng/ml (Huestis et al., 1992; Mason & McBay 1984), or 3–5 ng/ml (Tzambazis & Stough, 2002). The THC concentration in hemolyzed whole blood is approximately one-half the concentration of the plasma THC concentration and these concentrations would thus correspond to 1.0–1.5 and 1.5–2.5 ng/ml in whole blood (Mason & McBay 1984). Gjerde and Kinn suggested that 1.6 ng/ml THC in whole blood may indicate possible impairment (Gjerde & Kinn, 1991). Krüger and Berghaus, however, estimated from experimental studies the impairment accompanying plasma THC concentrations of 11 ng/ml or 6 ng/ml to be roughly equivalent to the impairment accompanying a blood alcohol concentration of 0.073 g/dl (Krüger & Berghaus, 1995).

Drivers who claimed to be using cannabis on a regular basis were less often judged as impaired despite no difference in THC concentration between regular users and non-regular users. This may support other studies that report that experienced users develop some degree of tolerance to the acute effects of THC (Howlett et al., 2004). Blood THC concentration is dependent on mode of intake, as well as dose. The meta-analysis by Berghaus et al. indicates that the performance impairment after cannabis intake was highest during the first hour after smoking and between 1–2 hours after oral intake and declined after 3–4 hours (Berghaus et al., 1998a; Berghaus et al., 1998b; Kurzthaler et al., 1999). Experimental studies limit themselves to assessing the acute effects of THC on performance, not addressing the question of tolerance in the experienced user (Sexton et al., 2000; Smiley et al., 1981). In the present study, only 30 percent of the drivers volunteered information on current cannabis intake, indicating that the information given by drivers on other issues like drug experience were also unreliable. As a result, we cannot fully investigate if cannabis users adapt to the acute effects of the drug as a result of tolerance. The effects of THC in novel users versus experienced users are currently not known in sufficient detail, but the present study may suggest some degree of tolerance.

There are several limitations to the present study. Previous studies have indicated that instruments like the CTI may have a low sensitivity for detection of driving performance impairment (Kuitunen, 1994). One study failed to find a relation between THC concentration and results of such a test (Reeve et al., 1983). Introducing alternative tests like looking for the presence of head jerks might improve the sensitivity of the CTI to THC induced impairment. A time lag between intake of cannabis and blood sampling could obscure the relationship between blood THC concentration and clinical outcome. Due to inverse hysteresis

### Table II

<table>
<thead>
<tr>
<th>Blood Δ^9-THC concentrations (ng/mL) and OR (95% CI)</th>
<th>0.7</th>
<th>0.8–1.6</th>
<th>1.7–2.9</th>
<th>3.0–4.8</th>
<th>4.9–10.1</th>
<th>&gt;10.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug concentration unadjusted</td>
<td>1</td>
<td>1.5 (0.8–2.7)</td>
<td>1.5 (0.8–2.7)</td>
<td>2.1 (1.1–4.0)</td>
<td>1.9 (1.1–3.6)</td>
<td>2.3 (0.9–5.6)</td>
</tr>
<tr>
<td>Drug concentration adjusted for regular use</td>
<td>1</td>
<td>1.5 (0.8–2.8)</td>
<td>1.3 (0.7–2.4)</td>
<td>1.8 (0.9–3.7)</td>
<td>1.8 (0.9–3.4)</td>
<td>2.5 (1.0–6.6)</td>
</tr>
<tr>
<td>Drug concentration adjusted for the presence of needle marks</td>
<td>1</td>
<td>1.6 (0.8–3.0)</td>
<td>1.6 (0.9–3.0)</td>
<td>2.6 (1.3–5.3)</td>
<td>2.6 (1.3–5.1)</td>
<td>2.9 (1.2–7.3)</td>
</tr>
<tr>
<td>Drug concentration adjusted for gender, needle marks and regular use</td>
<td>1</td>
<td>1.7 (0.9–3.2)</td>
<td>1.6 (0.8–3.0)</td>
<td>2.4 (1.1–5.0)</td>
<td>2.5 (1.3–5.0)</td>
<td>3.2 (1.2–8.7)</td>
</tr>
</tbody>
</table>

1 reference category.
2 $P < 0.05.$
3 $P < 0.01.$
even low blood THC concentrations may be seen as impaired. Furthermore, it is difficult to be sure of the external validity of the CTI (what would be the gold-standard to test external validity?). But the internal validity has been studied in several papers from our department (Bachs et al., 2003; Bramness et al., 2002; Bramness et al., 2004). Likewise, we do not know the reliability of the CTI. As each doctor performs only some tests during their career they have little experience in judging impairment. All these limitations could, however, have reduced any concentration effect relationship. But neither the low sensitivity of the CTI, individual variation in drug sensitivity, nor the low reliability or inter-examiner variation obscured the relationship between blood THC concentration and CTI performance. Hence, our findings must be viewed as a robust result and indicate that THC has impairing effects also in a real-life setting as described for benzodiazepines by our group (Bramness et al., 2002).

Culpability studies estimate the odds ratios for being responsible in fatal or injurious traffic accidents. Such studies have been performed for drivers with cannabis alone or in combination with alcohol in their blood samples. Many studies have used THC-acid as a measurement, and have failed to demonstrate an increased culpability risk (Drummer, 1994; Hunter et al., 1998; Movig et al., 2004; Terhune et al., 1992; Terhune & Fell, 1982). This is not surprising since THC-acid is an inactive metabolite of THC. Drummer et al. demonstrated an elevated risk for THC blood concentration between 1 and 100 ng/mL, and an even more elevated risk at blood concentrations between 5 and 100 ng/mL (Drummer, 1994; Drummer et al., 2003; 2004). A recently published population-based case-control study also indicated that habitual use of cannabis was strongly associated with car crash injury (Blows et al., 2005). The paucity of studies addressing the relationship between blood THC concentration and impairment in real-life settings makes the present results of some interest, as we replicate the findings of experimental research in a diverse population most likely having variable cannabis experience, as well as variation in dose ingested and in time between intake and testing.

In conclusion, a positive relationship between the concentration of THC in blood and the risk of being assessed as impaired, observed in this study, is compatible with the assumption of concentration dependent negative effect of cannabis upon driving performance previously indicated by experimental and accident culpability studies.

ACKNOWLEDGMENTS

The Norwegian Institute of Public Health has fully financially supported this work and there were no other external financial support. None of the authors have had a financial conflict of interest that could impose on the present work.

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