

Postmortem redistribution of cannabinoids: first results of a study performed in a pig model

B. BRUNET^{1,2}, F. FAVREAU^{1,3}, T. HAUET^{1,3}, W. HEBRARD⁴,
Y. PAPET², G. MAUCO^{1,3}, P. MURA²

¹ INSERM E-0324, Poitiers, France,

² Centre hospitalier universitaire Laboratoire de toxicologie et pharmacocinétique, Poitiers, France,

³ Centre hospitalier universitaire Laboratoire de Biochimie, Poitiers, France,

⁴ INRA, GEPA Laboratoire de chirurgie expérimentale, Surgères, France

AIMS: Cannabis acute toxicity is regarded to be low. However due to its widely usage throughout the world, cannabis may be involved in numerous deaths related to forensic cases. Little is known about cannabinoids concentrations in postmortem tissues. To elucidate this problem, we have developed a large animal model using the Large White pig.

METHODS: Ten Large White male pigs (9-12 weeks old) weighting 33 to 44 kg received THC by intravenous injections (200 µg/kg). Pigs were sacrificed by KCl injection two hours after THC administration. Two pigs were autopsied immediately after death. Others were stored in dorsal recumbency at ambient temperature for 6, 15, 24, or 48 hours. Cannabinoids concentrations were determined in peripheral antemortem and postmortem blood, postmortem left and right cardiac blood, vitreous humor, and bile.

In addition various tissues were sampled: lung (left and right, apex and bases), liver (left and right lobes), cardiac muscle, spleen, kidney, fat, skeletal muscle and brain. Tissues were homogenized with a Potter-Elvehjem homogenizer in phosphate buffer at pH 7.4. Homogenates or biological fluids were extracted with heptan/ethyl-acetate after addition of deuterated standards. Analysis by gas chromatography/mass spectrometry was performed after derivatization with BSTFA/TMCS.

RESULTS: Mean THC blood values were: 4.1 ng/mL for antemortem blood, and 2.9; 10.0; 14.6 ng/mL respectively for peripheral, right and left cardiac postmortem blood. Evolution of THC concentrations in the different postmortem bloods at any time was measured in term of ratios between postmortem and antemortem blood concentrations. The results are expressed as mean ± standard error of the mean (s.e.m).

	Mean ± s.e.m
<i>Postmortem left cardiac blood/Antemortem blood concentration ratio</i>	4.06 ± 1.59 (n = 8)
<i>Postmortem right cardiac blood/Antemortem blood concentration ratio</i>	2.44 ± 0.71 (n = 8)
<i>Postmortem peripheral blood /Antemortem blood concentration ratio</i>	0.56 ± 0.17 (n = 7)

In the different tissues postmortem toxicokinetics of THC showed a relative stability with time in lungs (ranging from 735 ng/g to 135 ng/g), liver (7 ng/g to <5 ng/g), kidneys (58 ng/g to 19 ng/g), fat (50 ng/g to 11 ng/g) or brain (25 ng/g to 14 ng/g). On the contrary a significant postmortem fall was observed for THC concentrations in skeletal (14 ng/g to <5 ng/g) and cardiac (17 ng/g to <5 ng/g) muscles or in the spleen (15 ng/g to <5 ng/g). In bile THC concentrations were low at any time, and only trace amounts were detected in vitreous humor. 11-OH-THC was detected only in liver and THC-COOH only in bile.

CONCLUSION: THC, an alkaline and lipophilic compound with a large distribution volume, is particularly susceptible of being involved in postmortem redistribution. Mechanisms such as diffusion and putrefactive breakdown of the drug can compete and complicate the interpretation of the results. This preliminary study in a pig model shows that peripheral blood concentrations of THC are significantly lower than left or right cardiac blood THC concentrations ($p < 0.05$ Kruskal-Wallis).

In the different organs, brain is the tissue where THC concentrations are found to be the most stable, probably because brain is not really affected by postmortem redistribution. Including the fact that if THC is detected in brain it shows evidence for impairment, brain should be taken as the most suitable sample in autopsy for identifying cannabis consumption.

KEYWORDS: *Cannabinoids, Post-mortem redistribution, Animal model, Pig*

Corresponding author: brunet.bertrand@neuf.fr