

In conclusion, plasma level monitoring of the enantiomers of MTD is recommended when MTD treatment has to be adapted in patients. The knowledge of the enzymatic mechanisms which are implicated in the stereoselective biotransformation of MTD helps to select appropriate comedications in MTD-treated patients, if needed.

#### ULTRA-RAPID OPIATE DETOXIFICATION: A CLINICAL INVESTIGATION

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Although largely discussed in public media, there are few scientific reports about the ultra rapid detoxification procedure during which the opiate addict is given a benzodiazepine-induced general anaesthetic while an opiate antagonist is administered. These scarce reports are generally enthusiastic about this method whereas many experienced clinicians are rather reluctant to develop upon it. Clearly more clinical studies are needed.

We report an open study with twenty patients treated using a procedure of direct transition to naltrexone (50 mg) twenty to thirty minutes after the oral administration of midazolam (90 to 120 mg), clonidine (0.300 mg), ondansetron (8 to 16 mg) and an anti-diarrhoea medication. Seventeen patients were on methadone maintenance (among them 4 regularly using heroin) and three patients were heroin dependent. The indications were detoxifications before admission in a therapeutic community (n = 4), a long lasting stay abroad (n = 4) or transition to a naltrexone out-patient treatment (n = 12). The procedure appears to be safe: no serious problems occurred. Patients were able to sleep most if not all of the first 5–8 hours, although they could not be considered anaesthetized. Clonidine and other comedications were prescribed for the rest of the first day and the next few days, but most of the patients were able to leave the hospital 36 hours after their admission. The procedure however was not well tolerated: almost all the patients had diarrhoea and/or vomiting. A six month follow-up has shown a high rate of relapse (80%) as usual after any detoxification and a rather high variability among the patients self-evaluated satisfaction.

After these first twenty patients, we modified the method and introduced a transition to a mixed agonist-antagonist (buprenorphine) one week before transition to naltrexone, resulting in a better clinical tolerance to the detoxification, particularly for vomiting and diarrhoea. The future of the method probably relies on this two step transition: full agonist/mixed agonist-antagonist/full antagonist. This method could than find a place among the different detoxification methods although the indications will probably remain limited.

#### BUPRENORPHINE IN THE TREATMENT OF OPIATE ADDICTION

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Buprenorphine is a semi-synthetic opioid with agonist/antagonist properties. Since 1980, its pharmacological properties have led some to suggest that it could be used in the treatment of heroin addicts (Mello and Mendelson, *Science*. 1980; 207: 657–659).

In 1985, we published the first study of maintenance treatment of opiate-dependent subjects with buprenorphine (*Drug Alcohol Depend* 1985; 16: 257–262). Of 34 patients followed over a period of 2–17 months, 5 (15%) finished treatment after a progressive decrease in the dose of buprenorphine (starting around 2 mg/day). Their treatment lasted 2 months in one case and 7–8 months in the 4 others. Urine samples collected 3–12 months later were free of opiates; 26 (76%) patients were still in treatment; 3 (9%) patients abandoned treatment after 4–8 months.

More than 90% of the patients who undertook the treatment with buprenorphine for more than 2 weeks followed it. However, almost 50% of the addicts to which treatment was proposed abandoned it after less than 2 weeks. This high percentage of dropouts at the beginning might be due to the fact that the initial dosage of buprenorphine was too low for those patients.

In fact, recent studies have shown that 2 mg of buprenorphine were inferior to 35 mg of methadone in reducing illicit opioid use (Kosten and al., *J. Nerv. Ment. Dis.* 1993; 181: 358–364) and that 8 mg/day of buprenorphine were as effective as 60 mg/day of methadone (Johnson et al., *JAMA* 1992; 267: 2750–2755). As 50 mg of methadone is now widely accepted as the lowest effective dose, it appears that buprenorphine effective dose should be higher than 2 mg/day.

Under this condition, buprenorphine may be an interesting alternative to methadone treatment, especially since regulations make the availability of methadone treatment inferior to the demand in many countries. One advantage of buprenorphine treatment may be that the possibility of lethal overdose is remote owing to the opiate antagonist properties of buprenorphine (Cowan and Lewis, *Buprenorphine*, Wiley-Liss, 1995: 247).

#### MORTALITY IN THE METHADONE-MAINTENANCE-PROGRAM/NORDRHEIN WESTFALIA, GERMANY

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In a retrospective analysis all cases of death among patients of the Methadone-Maintenance-Program in Nordrhein Westfalia are reviewed and evaluated. Patients who died after exclusion from substitution are analysed with special attentiveness.

In a 6 years observation period, 27 patients out of the total number of 244 died by different reasons. The cumulated death risk related to the real number of a defined cohort was about 15% after 6 years. Half of them died by drug related reasons.

It is shown, that patients excluded from substitution by different reasons show a highly increased risk of drug related mortality in the near future.

So the cumulated probability after a 6 years observation period to stay alive (it means not to die by drug related causes) for patients remaining in substitution (n = 184) is about 98%, whereas in the excluded population (n = 60) the correspondent value is only about 77%.

This finding indicates a protective effect of this methadone-program on the drug related mortality. Aspects of psychiatric comorbidity and possible consequences for treatment settings are discussed.

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## S18. Ethnic diversity and mental health in Europe

*Chairmen: J van Os, D Brugha*

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#### PROVIDING MENTAL HEALTH CARE FOR IMMIGRANTS

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International migration is increasingly affecting industrialised coun-