ASTRID SKRETTING | CATHERINE DAMMEN

From methadone to medicine-assisted rehabilitation

The Norwegian Storting decided in 1997 that medicine-assisted rehabilitation was to be a countrywide treatment offered to opiate abusers that met a given set of criteria. The then Ministry of Health and Social Affairs had prepared provisional national guidelines for those who were entitled to such a treatment so that the treatment proceeded under the auspices of the programmes sanctioned by the Ministry (Rundskriv I-25/98). In comparison with other countries, admittance criteria were and still are strict (>25 years of age, long-term opiate abuse, other treatment measures undertaken).

Initially, substitution treatment was one-sidedly tied to methadone (methadone-assisted rehabilitation). However, several doctors prescribed buprenorphine (Temgesic) and codeine to drug users outside sanctioned programmes. The Norwegian Board of Health pursued the matter legally in order to stem non-regulated prescribing, but did not succeed in its endeavour.

Buprenorphine in from the cold

Alongside the problems the authorities had with trying to assume control over doctors who carried out non-regulated prescriptions of buprenorphine to substance abusers, a discussion arose over whether Subutex was as suitable as methadone in substitution treatment. The then Minister of Social affairs travelled to Paris in the spring of 1999 to study the French experiences with Subutex. On her return, the Minister of Social affairs made it clear that she wanted to allow the use

of substitution treatment also in Norway. Subutex was approved as a medicine in medicine-assisted rehabilitation as of 1 January 2000.

Burprenorphine equated with methadone

The guidelines for substitution treatment therefore no longer became specifically tied to methadone, but to medicine as a link in medicine-assisted rehabilitation of narcotics abuse. One thereby went from the use of the term methadone-assisted rehabilitation to medicine-assisted rehabilitation. It is up to the prescribing doctor whether opiate abusers approved for medicine-assisted rehabilitation shall be treated with methadone or buprenorphine. There are therefore an increasing number of patients in ordinary medicine-assisted rehabilitation that are treated with buprenorphine (Subutex) alongside the specific trial projects which we wish to illuminate. Of the 2,431 patients that were included in the medicine-assisted rehabilitation at the outset of 2003, twenty per cent or 484 were prescribed buprenorphine.

It is, however, still a precondition for all substitution treatment, regardless of whether methadone or buprenorphine is used, that it should happen within the framework of programmes approved for such treatment. The prescription guidelines have been changed so that doctors are no longer allowed to order and chemists no longer allowed to deliver medicine for substitution treatment of heroin abusers within procedures not approved by the Ministry of Health (Rundskriv IK-15/ 2000). Against the background of increased interest in the use of Subutex in medicine-assisted rehabilitation in Norway, a review of research literature about the use of buprenorphine has been implemented (Bachs et al. 2001).

Sobuxone (buprenorhine with a naloxone core) has been introduced in individual regional centres. The medicine is exempt from approval requirements in Norway.

Special Subutex projects

■ The Subutex project in Kristiansand

During the period of 1999-2001, a study of 50 patients (38 men and 12 women) was carried out in Kristiansand. These patients alternately received high-dose Subutex for six months and high-dose methadone for six months (Espegren & Kristensen 2002). The goal was to ascertain which medicine provided the greatest benefit and patient satisfaction. After the patients were approved for medicine-assisted rehabilitation, they were randomised to either Subutex (16 mg) or methadone (flexible dose, on average 106 mg) in an open controlled study. After 26 weeks in substitution treatment with either Subutex or methadone, the initial treatment was gradually decreased and replaced with the other medication in order to complete an additional treatment period of 26 weeks.

After a completed treatment with each of the two medications, the patient could choose with which medication he or she wished to continue the substitution treatment. At the end of the project, seven of the 50 patients continued their treatment with Subutex, 41 with methadone, while one of the patients was dead and one was waiting to be admitted to a new treatment. It was concluded that both methadone and Subutex are safe medications within the framework of medicine-assisted rehabilitation

such as it is set up in Norway. It is said, however, that high-dose methadone appears to be the most well-suited medication and the most suited one for older, heavily opiate dependent patients, although Subutex is a good alternative in cases of therapeutic failure and side effects from methadone treatments.

A cost-benefit analysis of maintenance treatment was also carried out, wherein methadone was compared with Subutex over a period of a year after treatment began (Andresen & Jentoft 2002). The analysis showed that when taking as a starting point the number of persons that discontinued the treatment and the retention rate with the 50 patients receiving methadone and Subutex respectively, the societal gains were far greater with methadone than with Subutex.

The Subutex project in Oslo

Against the background of the long waiting list to gain admittance to medicine-assisted rehabilitation a time-limited trial project was initiated with Subutex but without simultaneous psychosocial follow-up care as it is set up within the framework of ordinary medicine-assisted rehabilitation. The purpose of the project was to see whether daily use of Subutex without control and with the use of other substances and no psychosocial support reduces the problems of heroin abusers on the waiting list to gain admittance to ordinary medicine-assisted rehabilitation.

Two studies were carried out during the course of the project. One of these was a randomised, double blind study lasting 12 weeks and comprising 106 patients (70 men and 36 women) where 55 patients received Subutex (16 mg) and 51 patients received a placebo (Krook et al. 2002). The results showed that those who were in the Subutex group on average remained 42 days in the project compared with 14 days in the placebo group. Sixteen of the patients in the Subutex group participated in the whole project period while none did in the placebo group. The Subutex group reported a greater reduction in the use of opioids and other intoxicants than the placebo group. The Subutex group also reported improvements in their life situation. None of the patients participating died during the trial period.

In the other study everyone received an individually adjusted dose of Subutex for almost a year before admittance to ordinary medicine-assisted rehabilitation. All those who were included in the first study received an invitation to participate. In this study, which began with 96 patients, 38 completed the project and were directly admitted to ordinary medicine-assisted rehabilitation, while the rest were admitted gradually thereafter.

It was concluded that heroin abusers waiting to gain admittance to medicine-assisted rehabilitation would reap substantial benefits from buprenorphine (Subutex) as a temporary intervention. Those who received Subutex reported minor use of narcotics and an increased subjective feeling of well-being. It is said, however, that high-dose buprenorphine treatment is not enough to keep patients in treatment over a longer period without psychosocial support.

The Subutex project in Helseregion Vest

In 1999, a local-based buprenorphine-assisted project was initiated under the guid-

ance of the methadone clinic at the Bergen Clinics Foundation in Helseregion Vest for clients on the waiting list to gain admittance to medicine-assisted rehabilitation. The goal was to extend a time-limited offer under the direction of the local health and social services for clients that met the criteria for methadone-assisted rehabilitation. Those who participated in the project would receive an offer of ordinary methadone treatment. After Subutex was placed on an equal footing with methadone during the trial period, this was changed so that patients could choose if they wanted to continue with the Subutex, switch over to methadone or complete the treatment within a year. During the course of the project 59 patients were admitted (43 men and 16 women) whereof 43 completed the project (Haga et al. 2002). Most of these received a daily dose of 16 mgs. It was reported that the project appeared to be effective with regard to reducing the waiting time for treatment. The project showed positive effects for many of the patients, although so-called side use was still an occasional problem for many. The methadone clinic at the Bergen Clinics Foundation prefer Subutex in searching for the right dosages in the first phase. After having a decentralised prescription of Subutex, this has now been reined in due to problems with leakage. Now all the patients at the methadone clinic are administered Subutex initially.

■ Subutex in abstinence-oriented treatment

Not all heroin users are suited for maintenance treatment such as it is organised in Norway. They may be too young, have too "short careers as substance abusers", or not have completed a non-medicinal treatment regime yet. In addition, not all heroin users want a maintenance treatment that in practice might last their entire lives.

The University of Oslo has a research project that comprises 75 patients (Kornør & Waal 2003). The criteria for inclusion are as follows: opioid dependence in accordance with the ICD-10 criteria, ≥ 22 years of age, a clear motivation as regards time-limited substitution treatment with freedom from opiates as the goal. Subutex is administered for nine months with three months adjusting to the right dosages and stabilising treatments, three months of treatment as a basis for problem-solving psychosocial interventions and three months of detoxicification/slow withdrawal. Forty-nine patients have completed the treatment plan, 10 have discontinued the treatment, while 13 continued the treatment with the buprenorphine and three have died. Of the 49 who completed the treatment plan, 11 have since then recontinued the buprenorphine treatment. Twenty-four of the 75 have in other words switched over to the long-term maintenance treatment. There are no conclusions available yet, as the study is still underway.

Non-regulated prescribing – abuse of buprenorphine (Subutex)

When it comes to quota prescriptions there is continued non-regulated prescribing of Temgesic (low dose buprenorphine) and Dolcontin (morphine sulphate) to narcotics abusers in Norway. The extent of this is not known, however.

So far we have scant knowledge in Norway as to the extent of buprenorphine substances in user milieus, whether it be leak-

age from patients in approved treatment regimes or Subutex/Temgesic imported illegally. However, there have been some seizures of buprenorphine; in 2002, there was a seizure of 50,000 Temgesic tablets for instance.

Dammen, Cathrine,
Advisor at the Directorate for Health and Social Affairs, PB 8054, Dep. 0031 Oslo
e-mail:cad@shdir.no
Skretting, Astrid, Researcher,
National Institute for Alcohol and Drug Research (SIRUS), PB 565 Sentrum, 0105 Oslo
e-mail:as@sirus.no

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