Feasibility assessment of heroin-assisted treatment in Liège, Belgium

Etude de faisabilité du traitement assisté par heroine à Liège en Belgique

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A new heroin-assisted treatment, TADAM, has begun in Liège, Belgium. With the number of methadone patients (n=2046) in 2007, we estimated the geographical distribution of methadone treatments in the province of Liège, of heroin addicts and of potential participants for TADAM.
The methadone treatments were unequally distributed. Some urban areas showed a significant number of heroin addicts: more than 14/1000 of the population aged 15-64.
As a conclusion, the trial is appropriately targeted to those high-density addiction areas.

Keywords: Diacetylmorphine; substitution; epidemiology; methadone; buprenorphine.

Introduction

The first heroin-assisted treatment in Belgium has begun in Liège in January 2011. TADAM ("Treatment Assisted by DiAcetylMorphine") is an open-label randomised controlled trial, comparing a heroin-assisted treatment with the existing oral methadone treatments for 200 participants. The Federal Government funded two institutions to conduct the TADAM trial: our research team from the departments of Psychiatry and Criminology of the University of Liège was requested to draw up the protocol and the assessment part, while, on the basis of this protocol, the city of Liège will manage the treatment part. At the origin of TADAM was the claim of the city, sustained by methadone centres, that a new heroin-assisted treatment could help some of the numerous heroin addicts who find no solution in methadone treatment, are in poor health condition and create open drug scenes.

Since the mid-1990s, all the experience of heroin-assisted treatment has shown that it was more effective for resistant heroin addicts than oral methadone in reducing street heroin use, health problems and criminal behaviour. The first studies began in Switzerland (Perneger *et al.*, 1998; Rehm *et al.*, 2001). The others took place in the Netherlands (van den Brink *et al.*, 2003), in Spain (March *et al.*, 2006), in Germany (Haasen *et al.*, 2007), in Canada (Oviedo-Joekes *et al.*, 2009) and in the United-Kingdom (Strang *et al.*, 2010). Although those studies are different in some respects (Fischer *et al.*, 2007; Lintzeris, 2009), they all include the same patients: severely addicted heroin users, who respond insufficiently to existing treatments. All the studies compare a heroin-assisted treatment with oral methadone treatment and involve randomised controlled trials, with the exception of the study of Rehm *et al.* (2001). The largest multicentre randomised controlled trials constituted the main models of TADAM: the Dutch trial with 549 participants (van den Brink *et al.*, 2003) and the German experience with 1015 participants (Haasen *et al.*, 2007).

The scientific sources are therefore sufficient to support our TADAM experiment. However, there is no research in Liège on the opportunity for introducing the project: there are no published data on the number of treatment resistant heroin addicts who could benefit from heroin-assisted treatment. The official institutions in charge of drug epidemiology in Belgium have published no data either on the number of heroin addicts or on the number of patients in the existing methadone treatments (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2008a; Eurotox, 2007; Lamkaddem & Roelands, 2007). There is a report, available on the web site of an association of physicians (Ledoux, 2008), which gives the number of patients on methadone treatment but the Federal Government funding this study has not to date given any official acknowledgement of the method used or the results.

Nevertheless, the Pharmacy Inspector of the province of Liege gave us the listings of the methadone prescriptions delivered by the pharmacies in that area. Using those data, we were able to study the prevalence of people on methadone treatment, to calculate the prevalence rate of heroin addicts and also to try to estimate the number of potential participants for the TADAM trial.

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We were therefore able to answer the following questions in order to assess the advisability of the TADAM experiment in Liège. First, since heroin-assisted treatment is intended to be a "last resort treatment" (Fischer *et al.*, 2007; Haasen *et al.*, 2007), are the first line treatments, such as the methadone treatments, sufficiently widespread and available? Secondly, is it true that the number of heroin addicts is so significant in Liège? Finally, is the number of treatment resistant heroin addicts sufficient in Liège to enrol 200 participants over a period of 12 months?

Methods

Description of the main data

In Belgium, any physician, working in private practice or in an institution, can prescribe a substitution treatment for heroin, with methadone or buprenorphine (Law of 22 August 2002; Royal decree of 19 March 2004). Even before the issuing of those legal statements, methadone was not illegal and was widely prescribed (Jacques & Figiel, 2006; Ledoux, 2005; Pelc *et al.*, 2001; Pelc *et al.*, 2005).

Pharmacists must register daily every time they dispense a drug considered as a narcotic, for instance methadone and buprenorphine (Law of 25 March 1964). This registration is controlled by a Federal Agency, via the Pharmacy Inspectors. The Pharmacy Inspector of the province of Liège gave us these anonymous data for the months of December 2001, 2004 and 2007.

Those data contained the name of each patient, physician and pharmacist, the location of the pharmacy and the name of the substitution product. The personal data were coded. To avoid duplication, we counted only once each unique code of a patient for each year. In 2001, there were 99% unique codes (2105 unique codes out of 2125 records), there were 92% in 2004 (2477 out of 2690) and 97% in 2007 (2046 out of 2101). The missing data were estimated as representing less than 1% a year: in 2007, five pharmacies out of the 604 in the province of Liège did not give their data to the Pharmacy Inspector; in 2004 and 2001, less than three pharmacies did not give their data.

The patients following an ambulatory methadone treatment in an institution must also go to a pharmacy to receive their methadone. So these patients were included in our data, except for some patients from the START-MASS centre, a low threshold centre in the commune of Liège. This centre is the only one in the province that orders methadone in bulk from a pharmacy and delivers it daily to its patients. The centre gave us an anonymous listing for the month of December 2007 (n = 94). Our data were therefore complete for the ambulatory delivery of methadone in December 2007 in the province of Liège.

In order to calculate the number of persons on substitution treatment, we also counted the patients who received only buprenorphine in December 2004 (n = 79) and in December 2007 (n = 127). Subutex®, a medication with enough buprenorphine for a substitution treatment (2 or 8 mg per tablet) had only been on the Belgian market since 2003.

Calculation

Availability and spread of the methadone treatments

We calculated the number of patients for each physician and each pharmacy. The location of the pharmacies helped us to draw up the geographical distribution of the methadone treatment. We used a map of the National Institute of Geography within the limits of the communes of the province of Liège (Institut Géographique National, 2001); we redrew the map and completed it with our data.

We estimated the methadone treatment distribution for each commune, for the judicial district and the agglomeration of Liège. In Belgium, a commune is the smallest political territorial division with an elected board. A province, which includes many communes, has also an elected board but has a very limited authority. The judicial district of Liège is an administrative division including 32 communes (Police locale belge, 2008) of the 84 in the province. Nevertheless these administrative divisions did not reflect the urbanisation surrounding Liège, so we also used the geographical definition of the agglomeration of Liège, covering 13 communes (Mérenne-Schoumaker, 2003).

Number of heroin addicts

In order to estimate the number of heroin addicts, we used two multipliers of the number of persons in substitution treatment. This method is one of those used to estimate the population of dependent drug users (Kraus *et al.*, 2003; Law *et al.*, 2006). Our multipliers were taken from a study of Nordt and Stohler (2006), who estimated that more than 50% of heroin addicts had been on substitution treatment in the canton of Zurich since 1994 and 64% would be on substitution treatment in 2010. We used those percentages for the following reasons: the Nordt and Stohler calculation was based on data as recent as ours, but it was more detailed (Nordt & Stohler, 2006, 2008); methadone treatment was widespread in the canton of Zurich; the treatment could be initiated by a physician in a private practice or in an institution (as in Belgium) and those data also came from a mandatory registration of the substitution treatment. We estimated therefore that the number of patients on substitution treatment would be between 50% and 64% of the heroin addicts in the province of Liège.

In order to estimate the proportion of heroin addicts in the population, we used data (by commune and by age) for the Belgian population in 2007 (Direction Générale Statistique et Information économique, 2007, 2008). In order to compare our results with those of the EMCDDA, we referred to the population aged 15 to 64.

Number of persons likely to be eligible to enter the TADAM trial

In order to estimate the number of potential participants for the TADAM trial, we took inclusion criteria of the protocol. To

be eligible a patient must fulfil these criteria: a treatment-resistant heroin dependency (as indicated by heroin dependency for at least 5 years, a daily or almost daily use of illicit heroin, a previous experience of methadone treatment); at least 20 years old; legal resident in the judicial district of Liège for at least 12 months; willing to attend the treatment site at least twice a day and accepting not to drive during the treatment.

Those criteria are similar to those of our Dutch (van den Brink *et al.*, 2003) and German models (Haasen *et al.*, 2007). We estimated that the proportion of our target group (treatment resistant heroin addicts) out of the total population of heroin addicts was the same as in the Netherlands in 2003 (van den Brink *et al.*, 2003): between 20% and 32% of the total number of heroin addicts.

Results

Availability and spread of the methadone treatments

In December 2007, we counted 438 unique codes for physicians who had prescribed methadone in the province of Liège. Only three physicians had more than 40 patients (respectively 42, 77 and 92 patients) and 391 (89%) had up to 10 patients.

The number of pharmacies dispensing methadone in the province of Liège was 387 in December 2007; 346 pharmacies (89%) had fewer than 11 patients and only one pharmacy had more than 40 patients (n=61).

In 2007, the pharmacies delivering methadone were particularly numerous in the agglomeration and the commune of Liège (Table I) but, in nearly 30% of the communes of the province and in 12% of the communes of the judicial district, there was no methadone dispensing (Figure 1).

Number of heroin addicts

Substitution treatments increased by 21% between 2001 and 2004 and then decreased by 15% until 2007. In December 2007, including the 94 patients of the START-MASS centre, there were 2267 persons in ambulatory substitution treatment in the province of Liège. Many patients in 2007 were found to have already been in treatment three or six years previously (Table II). Some of the people who were in treatment in 2007 and in 2001 were not found in 2004 (n=139).

The patients on substitution treatment were not distributed equally in the province; they were more numerous in some communes (Figure 1). Three towns were particularly involved: Huy (9/1000), Liège (8/1000) and Seraing (6/1000).

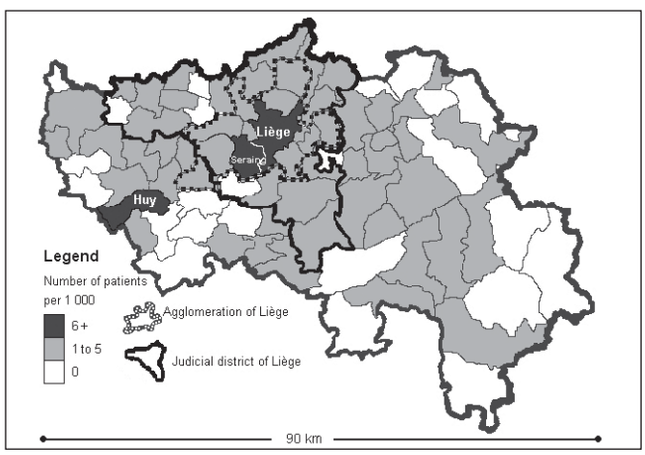

Figure I
Patients on substitution treatment per 1000 inhabitants (15-64 years) in the communes of the province of Liège.

Table I

Distribution of the pharmacies who delivered methadone in December 2007 in the province of Liège, with the number of communes and the population per territorial division

Territorial divisions of Liège	Communes per division	Population aged between 15 and 64		Pharmacies with methadone dispensing		Communes without methadone dispensing
	N	N	%	N	%	N
Province	84	681 662	100 %	387	100 %	24
Judicial district	32	411 297	60 %	276	71 %	4
Agglomeration	13	311 237	46 %	232	60 %	0
Commune	1	123 839	18 %	116	30 %	0

Table II

Number of patients on methadone treatment in 2007 who had already been in treatment in 2001 or in 2004

	Patients in 2007	Patients in 2007 already in treatment in		
Territorial divisions of Liège		2004	2001	2004 and/or 2001
Province	2 046	1 350	980	1 489
Judicial district	1 637	1 112	811	1 216
Agglomeration	1 503	1 503	731	1 108
Commune	890	576	414	635
% on all patients 2007	100 %	66 %	48 %	73 %

Number of persons likely to be eligible to enter the TADAM trial

With a proportion of 20% to 32% of all the heroin addicts (Table III), we obtained between 571 and 1170 treatment resistant heroin addicts in the judicial district of Liège.

Discussion

Availability and spread of the methadone treatments

With 276 pharmacies distributed between 28 of the 32 communes, methadone treatment was widespread in 2007 in the judicial district of Liège, the area involved in the TADAM trial. In addition, the important rate (89%) of physicians and pharmacies with fewer than 11 patients could indicate that most of the physicians and pharmacists are not overloaded with methadone treatments. However, the substitution treatment might demand a high level of involvement so the saturation point of the professionals could be quickly reached, even with a few patients.

Each of the 24 communes of the province that did not dispense any methadone had fewer than 7000 inhabitants aged between 15 and 64 years. The absence of methadone administration in those communes could represent the absence of heroin addicts, the preference of the patients for pharmacies in urban zones (perhaps in order to remain anonymous) or a lack of a physician and/or pharmacy willing to receive those patients. The last two reasons could explain why there are a lot of patients in the urban area. Huy, for instance, is surrounded by communes without any pharmacy dispensing methadone.

Even though the availability of the substitution treatments is not equal within the province, it is sufficiently widespread in the area of the judicial district of Liège to justify a second line treatment such as TADAM.

Number of heroin addicts

Nearly three-quarters of the patients registered in 2007 had already been on methadone treatment in 2004 or in 2001. There is therefore a high percentage of patients for which heroin addiction is a chronic disease requiring long term treatment, if not a brain disease as Leshner (1997) said.

The European average of problematic heroin users is estimated at between 4/1000 and 5/1000 inhabitants aged 15 to 64 (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2008b). The maximum number observed in a country of the European Union is 6/1000. With a rate of between 5 and 7/1000, the prevalence of heroin addiction is especially important in the province of Liège. Our results also showed that a regional average can hide great disparities, since we found rates from 0/1000 up to 14 or 17/1000 in the communes of Liège.

With rates from 13 to 17/1000, the problem of heroin addiction is especially significant in the commune of Liège. Since we deduced our results from the localisation of the pharmacies dispensing methadone, we did not know the residence of the patients. The gathering of services in the agglomerations could attract patients from the surrounding areas. This effect could be reinforced, as there seems to be less availability of methadone treatments outside of the agglomerations. In addition, there is a greater choice of institutions treating addiction in Liège (n=28) and in Huy (n=8), each of the other communes having fewer than four specialised institutions (Maison du social, 2008).

Our results are subject to some limitations. Using our multipliers, we estimated the number of heroin addicts, but we could not estimate the number of persons who use heroin and who will never enter into a treatment programme. In addition, our data do not include all the patients from one year but only those who went to a pharmacy for the dispensing of their substitution product in the province of Liège in December of 2001, 2004 or 2007. There may be patients who did not appear in our data because they were on holiday, in residential treatment, in prison or because they used their prescription in a pharmacy outside of the province or in one that did not send any data to the Pharmacy Inspector. In addition, the multiplier method based on the number of persons in treatment can only give valid results in areas where the treatment concerned is widespread and available

Table III

Number of patients on substitution treatment and number of heroin addicts per territorial division of Liège in December 2007

Territorial divisions of Liège	Patients on methadone treatment (pharmacy)		Patients on substitution treatment (pharmacy and START-MASS)		Heroin addicts			
	N	Rate[a]	N	Rate[a]	1/64%	Rate[a]	1/50%	Rate[a]
Province	2 046	3	2 267	3	3 542	5	4 534	7
Judicial district	1 637	4	1 828	4	2 856	7	3 656	9
Agglomeration	1 503	5	1 691	5	2 642	8	3 382	11
Commune	890	7	1 049	8	1 639	13	2 098	17

[a] Rate per 1000 inhabitants aged 15 to 64

(Kraus, *et al.*, 2003; Law, *et al.*, 2006). Therefore our results on the number of heroin addicts should be especially valid in the area of the judicial district and the agglomeration of Liège.

Number of persons likely to be eligible to enter the TADAM trial

The patients most likely to match the inclusion criteria for the TADAM trial are the treatment resistant heroin addicts who were found in our study to go to a pharmacy in the judicial district of Liège. The participants in the trial must be prepared to go to the heroin-assisted centre at least twice a day, without driving a car. As the area of the judicial district is widespread (32 communes), the patients most likely to accept this are those who live in the agglomeration of Liège (n=528 and 1082), as the urban areas are also better furnished with public transport.

This result is only an indication and does not correspond to the population who will present itself to the research team in 2009 for the TADAM trial. In fact, we took into account only some of our inclusion criteria. Another inclusion criterion for the trial is that the patient's heroin addiction must have lasted for at least 5 years. If we have no information on the duration of dependency, we know at least that 48% of the patients in 2007 were in treatment 6 years previously. After applying this rate to the treatment resistant persons, there are between 253 and 518 heroin addicts, who have been dependent for at least 5 years, who are treatment resistant and who live in the agglomeration of Liège. This approach might undoubtedly lead to an underestimation as some persons may have been dependent for over 5 years without being continuously under treatment during the last years.

However, other factors may reduce the number of available participants. The decrease in the number of patients will perhaps continue until 2009. In addition, not all patients on methadone treatment are ready to follow a heroin-assisted treatment (Perneger *et al.*, 1998). Even if the patients are prepared to participate, some additional factors could still go against their participation. For example, the City of Liège has announced that a police station will be installed next to the heroin-assisted centre. Even though the commissariat is independent of the trial, his presence could alarm some potential participants, since a significant percentage of our target group may be engaged in illegal activities (Haasen *et al.*, 2007).

Finally, in this kind of project, the research team must see a great number of patients before the inclusion of the required number of participants. For instance, in the Netherlands, 1500 patients came to the first meeting and only 549 patients were included. In that study, the participants had to wait two months between the randomisation and the treatment (van den Brink *et al.*, 2003), but in the TADAM project, we will send the patients directly to treatment after the randomisation. In Germany, for 2000 persons interviewed in a first meeting, 1015 persons were included in the project (Haasen *et al.*, 2007). If we base our calculations on the German numbers, the research team of the TADAM trial will have to assess about 400 patients in order to include 200 participants.

In conclusion, the introduction of the TADAM trial is recommended in Liège owing to the significant number of heroin addicts and to the availability of the methadone treatment, but the enrolment of the 200 participants will certainly be difficult and the 12 months of inclusion as planned in the project will be necessary. In addition, as the TADAM project is aimed at patients who have already tried a methadone treatment, the collaboration of the physicians and the institutions treating those patients is an essential condition for conducting the trial.

It would be interesting to reproduce our study in other parts of Belgium and in Europe, to discover the situation in other cities and to compare this with our own results. The advantages of this kind of study are firstly, the limited number of variables (unique codes for the patients, physicians and pharmacies, the localisation of the pharmacies and the name of the substitution product) and secondly, other easily obtainable data (geographical maps of the communes and a population aged between 15 and 64 years).

Résumé

Un nouveau traitement assisté par diacetylmorphine (TADAM) a débuté à Liège en 2011. Grâce au nombre de patients en traitement par méthadonde (n=2046) en 2007, nous avons estimé la distribution géographique des patients en traitement par methadone dans la province de Liège ainsi que le nombre de personnes dépendantes de l'héroïne et le nombre de participants potentiels pour l'étude TADAM.

Des zones urbaines de la province montraient un nombre significatif de personnes dépendantes de l'héroïne : plus de 14/1000 sur la population agée de 15 à 64 ans.

En conclusion, l'expérimentation TADAM est correctement dirigée vers une zone à forte concentration de personnnes dependantes à l'héroïne.

Samenvatting

In 2011 heeft een nieuwe behandeling met diacetylmorfine (TADAM) in Luik begonnen. Uitgaande van het aantal patienten dat in 2007 met methadon behandeld werd (n=2046), hebben we een schatting gemaakt van de geografische spreiding van deze patiënten in de provincie Luik, evenals van het aantal heroïneverslaafden en het potentiële aantal deelnemers aan het TADAM onderzoek.

De verstedelijkte gebieden bleken een hoog aantal heroïneverslaafden te tellen: meer dan 14/1000 inwoners in de leeftijdscategorie van 15-64 jaar.

De conclusie is dat het TADAM-experiment terecht gericht is op een gebied met een hoge concentratie aan heroïneverslaafden.

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