Journal of Substance Abuse Treatment 69 (2016) 72–75

Contents lists available at ScienceDirect

Journal of Substance Abuse Treatment

Loss of treatment benefit when heroin-assisted treatment is stopped after 12 months

Isabelle Demaret, M.P.H. [a,b,*], Etienne Quertemont, Ph.D. [c], Géraldine Litran, M.A. [a,b], Cécile Magoga, M.A. [a,b], Clémence Deblire, M.A. [a,b], Nathalie Dubois, Ph.D. [d], Corinne Charlier, Ph.D. [d], André Lemaitre, Ph.D. [a], Marc Ansseau, M.D., Ph.D. [b]

[a] Institut des Sciences Humaines et Sociales, Université de Liège B31, Boulevard du Rectorat 7, B-4000, Liège, Belgium
[b] Service de Psychiatrie, CHU, Domaine Universitaire du Sart-Tilman B35, B-4000, Liège, Belgium
[c] Service de Psychologie, Cognition et Comportement, Université de Liège B32, Boulevard du Rectorat 5, B-4000, Liège, Belgium
[d] Service de Toxicologie, CHU, Domaine Universitaire du Sart-Tilman, B35, B-4000, Liège, Belgium

ARTICLE INFO

Article history:
Received 11 November 2015
Received in revised form 13 May 2016
Accepted 6 June 2016
Available online xxxx

Keywords:
Heroin-assisted treatment
Diacetylmorphine
Treatment duration
Substitution treatment

ABSTRACT

Purpose: In 2013, during a recent heroin-assisted treatment trial, participants in heroin-assisted treatment (HAT) decreased significantly more their street heroin use than participants in oral methadone treatment. After the trial, HAT was discontinued. To examine whether the treatment benefits were sustained three months after the trial, the use of street heroin by the participants was analyzed in a follow-up study.
Results: At the follow-up assessment, street heroin use increased in the experimental group. The two groups no longer showed a significant difference ($p = 0.55$) in the level of street heroin use.
Conclusion: A predetermined and forced end of HAT was followed by a significant increase in the level of street level use.

1. Introduction

To help heroin-dependent individuals, Belgium - alongside 89% of European countries - offers oral methadone treatment (OMT) (World Health Organization, 2010). However, a proportion of heroin-dependent persons continue to pursue their street heroin use while in OMT. For these individuals, a model of heroin-assisted treatment (HAT) was developed in Switzerland in the nineties (Khan, Khazaal, Thorens, Zullino, & Uchtenhagen, 2014; Perneger, Giner, del Rio, & Mino, 1998; Rehm et al., 2001). In HAT, patients receive medically prescribed diacetylmorphine (DAM) under the supervision of nurses, in an outpatient setting (Demaret, Lemaître, & Ansseau, 2012; Ferri, Davoli, & Perucci, 2011). HAT has showed greater efficacy than OMT (Ferri et al., 2011). After the trials, a prolonged HAT was associated with sustained improvement (Blanken, Hendriks, Van Ree, & Van Den Brink, 2010; Guttinger, Gschwend, Schulte, Rehm, & Uchtenhagen, 2003; Oviedo-Joekes, March, Romero, & Perea-Milla, 2010; Verthein et al., 2008).

In Belgium, HAT was accepted and funded by the federal government but only for a period of 12 months and as a clinical trial because prescribing DAM for heroin dependence was (and still is) illegal. This clinical trial has been conducted in Liège, a city where heroin dependence has been particularly problematic. In the urban area of Liège, OMT is widely available and people can freely choose their physician or their treatment centre. In 2007, 3000 people in this area were heroin-dependent, compared to a population of 500,000 inhabitants (Demaret, Herné, Lemaître, & Ansseau, 2011).

During the randomized controlled trial, street heroin use decreased significantly more in the experimental group with HAT compared to the control group with OMT (Demaret et al., 2015). The modalities of our trial were comparable to the other trials and we included the same target group of persons with heroin dependence and regular street heroin use in spite of a current or previous drug treatment (Ferri et al., 2011; Haasen et al., 2007; March, Oviedo-Joekes, Perea-Milla, Carrasco, & PEPSA Team, 2006; Oviedo-Joekes et al., 2008; Perneger et al., 1998; Strang et al., 2010; van den Brink et al., 2003).

The main difference in our trial was the duration of HAT (limited to 12 months), which was not based upon scientific reasons. The only other trial with a predetermined end of HAT was the Canadian one. A follow-up study of this trial showed that street heroin use rose after the end of HAT, particularly for the group of participants who did not transition voluntarily from DAM to oral methadone (Oviedo-Joekes

Abbreviations: HAT, heroin-assisted treatment; OMT, oral methadone treatment; DAM, diacetylmorphine; TADAM, Treatment Assisted by DAM.

* Corresponding author at: Institute for Human and Social Sciences (Université de Liège), Boulevard du Rectorat 7 (B31), B-4000, Liège, Belgium. Tel.: +32 4 366 31 58; fax: +32 4 366 98 08.
E-mail address: isabelle.demaret@ulg.ac.be (I. Demaret).

http://dx.doi.org/10.1016/j.jsat.2016.06.005
0740-5472/

et al., 2014). In the Dutch trial, HAT was also discontinued after 12 months, but only during 2 months. This also had a negative impact: 82% of the participants who were completers and responders deteriorated substantially at the end of this discontinuation. After this interruption however, HAT could be pursued with no predefined end point for the participants who deteriorated after the discontinuation (van den Brink et al., 2003).

In this paper, we report the results of a follow-up study and evaluated whether the decrease of street heroin use was sustained three months after the Belgian trial.

2. Methods

2.1. Design

TADAM (Treatment Assisted by DAM) was an open label, randomized controlled trial; it began in January 2011 and ended in January 2013. The Ethics Committee of the University of Liège approved this trial (number 2009/189) on March 16, 2010, including a follow-up after 3 months. After the end of the trial (i.e. at 12 months from treatment start) HAT was stopped in the experimental group and the most appropriate treatment at the time of the transition was offered to each participant. The detailed method and inclusion criteria were as described previously (Demaret et al., 2015).

2.2. Assessments

Every three months from baseline to 15 months, street heroin use and cocaine use were measured by the number of days of use during the previous month, using the European Addiction Severity Index (Kokkevi & Hartgers, 1995). During each assessment, participants also provided a urine sample. In urinalysis (ultra-high-pressure liquid chromatography coupled with mass spectrometry), street heroin use was indicated by the detection of meconin, a metabolite of an opium constituent (noscapine) that is not found in DAM. The presence of benzoylecgonine, a metabolite of cocaine in the sample, revealed cocaine use. In case of discrepancy between self-reported and toxicological data, we replaced the self-reported value by a value based on prior use. At each assessment, physical health was measured by the Maudlsey Addiction Profile – Health Symptoms Scale (MAP-HSS) (Marsden et al., 1998); mental health by the total score of the Symptom Check-List (SCL–90–R) (Gosselin & Bergeron, 1993; Pellet, 1997); criminal involvement was characterized by self-reported facts committed or experienced as a victim, during the previous month (Ansseau et al., 2005).

At each assessment, participants who were not (or were no longer) in the HAT centre received a compensation (between 15 and 60 euro depending on the presence of medical examination, blood and urine sample). The research team remained independent from the treatment staff.

2.3. Statistical analysis

Mixed-design analyses of variance (ANOVA), with the experimental group (two levels) as a between-subject factor and time post-inclusion (six levels: baseline, 3, 6, 9, 12 and 15 months post-inclusion) as a within-subject factor, were used for the analyses of continuous data (for self-reported value). The ANOVAs were followed by Newman–Keuls post-hoc comparisons to assess between-group differences. To analyze the level of meconin, Friedman tests for non-parametric repeated measures comparisons were carried out on both groups separately. Non-parametric Spearman correlations were used to examine the association between urinalysis and self-reported values on street heroin use at each assessment. Statistical analyses were performed with STATISTICA 10. Statistical significance was set at $p < 0.05$. Only participants seen at each assessment were included in these analyses.

3. Results

3.1. Participants' characteristics and follow up

Participants' characteristics were described previously (Demaret et al., 2015). Among the 74 participants included in the trial, 13 were excluded from this analysis: in the experimental group, 1 refused to be interviewed, 1 had died and 3 could not be reached at an intermediate assessment; in the control group, 5 refused to be interviewed and 3 could not be reached at an intermediate assessment. 61 (82%) participants were interviewed at each assessment: 31 in the experimental group and 30 in the control group. Of these 61 participants, 2 (one in each group) could not provide a urine sample (they were interviewed in prison) and 2 (both in the experimental group) reported no street heroin use but gave a positive urine sample. The retention rate in substitution treatment was higher for the participants in the experimental group, but the difference was not significant: 30 (97%) versus 26 (87%). The 5 other participants were neither in a substitution treatment, nor abstinent.

3.2. Evolution of the efficacy indicators

Table 1 shows the evolution of efficacy indicators from baseline to 15 months for the 61 patients. Compared to baseline, the decrease of street heroin use at the 15-month assessment was significantly higher in the experimental group than in the control group ($p < 0.001$). MAP-HSS scores also indicated a significantly higher improvement in the experimental group ($p < 0.05$). The other efficacy indicators revealed no significant difference between both groups.

3.3. Other analyses of street heroin use

Newman–Keuls post-hoc tests showed significant differences of street heroin use between the two groups at each assessment (Fig. 1), except at baseline and at the 15-month assessment ($p = 0.55$). Newman–Keuls post-hoc-tests also showed a significant increase of street heroin use in the experimental group between the 12 and 15-month assessments ($p = 0.0052$). Mean levels of meconin (Fig. 2) improved significantly in the experimental group ($\chi^2(5) = 35.01$; $p < 0.00001$) but not in the control group ($\chi^2(5) = 5.59$; $p = 0.35$). Non-parametric Spearman correlations between self-reported values and meconin levels were significant except at baseline (data not shown).

4. Discussion

During the trial, participants in the experimental group showed a decrease of street heroin use significantly more important than in the control group, as in five other trials (Haasen et al., 2007; March et al., 2006; Oviedo-Joekes et al., 2009; Perneger et al., 1998; Strang et al.,

Table 1
Evolution of the efficacy indicators.

Efficacy indicators	Group (n = 61)	T0	T03	T06	T09	T12	T15	P[a]
Street heroin use[b]	DAM	25	6	5	4	8	14	p = 0.00094
	METH	28	18	17	18	16	17	
Cocaine use[b]	DAM	3	2	3	2	1	2	p = 0.83
	METH	5	5	3	4	2	3	
Criminal involvement[b]	DAM	9	2	3	2	1	2	p = 0.35
	METH	8	4	4	5	6	5	
MAP-HSS - total score	DAM	18	13	15	13	16	13	p = 0.0195
	METH	19	17	17	17	17	18	
SCL-90-R - total score	DAM	109	75	70	70	71	71	p = 0.056
	METH	110	98	92	95	86	94	

[a] p for mixed-design analyses of variance (ANOVA).
[b] Self-reported data (number of days in past month) complemented with toxicological analysis or registered criminal proceedings.