

REGULAR ARTICLES

Inpatient Initiation of Buprenorphine Maintenance vs. Detoxification: Can Retention of Opioid-Dependent Patients in Outpatient Counseling Be Improved?

Ryan M. Caldiero, MD,¹ Theodore V. Parran, Jr., MD,^{2,4,5} Christopher L. Adelman, MD,^{3,4} Betty Piche, RN⁴

¹Department of Psychiatry, University of Washington School of Medicine, Seattle, Washington

²Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio

³Department of Family Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio

⁴St. Vincent Charity Hospital and Rosary Hall, Cleveland, Ohio

⁵Cleveland VA Medical Center, Cleveland, Ohio

Buprenorphine-naloxone is an office-based opioid agonist released in 2003 in the United States for the maintenance of heroin- and other opioid-dependent patients. Concern has been raised that the medication will distract or otherwise inhibit patients from participating in a holistic recovery program or abstinence-based counseling. Using a retrospective chart review, the first thirty opioid-dependent patients induced on buprenorphine maintenance therapy in an inpatient detoxification unit were compared to thirty age- and gender-matched patients who underwent detoxification (with a tramadol taper) and referral to intensive outpatient treatment. The clinical outcomes were a comparison of completion rates for an intensive outpatient program (IOP) and retention in treatment after twelve weeks of aftercare therapy. Patients induced on buprenorphine maintenance over three days had similar relief of withdrawal symptoms to patients detoxified from opioids over five days with tramadol. Patients maintained on buprenorphine had a markedly increased initiation of IOP and remained in outpatient treatment longer than patients who were detoxified (8.5 wks vs. 0.4 wks, $p < 0.001$). This study indicates that induction and maintenance on buprenorphine may be more effective than detoxification for engaging and retaining patients in abstinence-based comprehensive outpatient addiction treatment. (Am J Addict 2006;15:1–7)

In October of 2002, the FDA approved the use of buprenorphine for office-based opiate maintenance therapy (OMT) for opioid-dependent patients. The intention

of this move by the FDA, following acts by Congress making this approval possible, was to increase the accessibility of opiate agonist treatment for opioid-dependent patients.¹ This approval followed the successful use of the medication abroad^{2,3} and in clinical trials in the United States.^{4–10} Approval for the use of buprenorphine was granted with two important restrictions: physicians must have specific qualifications or take special training to prescribe it for office-based treatment of opioid dependence, and unless they qualify for a waiver as part of a methadone treatment center, physicians are only allowed to treat thirty patients at a given time with buprenorphine.¹¹

Many treatment providers had eagerly anticipated the availability of this new treatment method to reach more patients dependent on opioids.¹² The practical application of this new treatment following the approval by the FDA, however, has not been without challenges. In many parts of the country, there are very few physicians who qualify to prescribe the medication, few with actual experience using this medication clinically, and relatively few pharmacies that carry the new combination formulation designed to minimize diversion of the drug in the community.¹³ Additionally, there are continuing questions of how to properly initiate treatment in a community setting. Finally, there is great concern among traditional abstinence-based treatment providers that buprenorphine-maintained patients will be excessively resistant to referral for high-quality addiction counseling treatment. This is due to the nature of the enabling legislation that indicates that buprenorphine patients are required to be referred for counseling and agree to accept

Received August 6, 2004; revised August 26, 2004; accepted February 25, 2005.

Address correspondence to Dr. Parran, Cleveland VA Medical Center, 10900 Euclid Avenue, Cleveland, OH 44106-4922. E-mail: tvp@case.edu.

that referral—but does not require compliance with ongoing participation in counseling as a pre-requisite for ongoing prescribing.

Recommendations by experts for initiating treatment with buprenorphine suggest titrating up from a low dose with periodic monitoring in the office and additional doses as necessary throughout the first few days.¹⁴ The pharmacological profile of buprenorphine (a high affinity for, low activity at, and slow dissociation from the mu-opioid receptor) that makes it a safe agent for agonist therapy¹⁵ does not preclude opioid withdrawal during initiation at a low dose.

The purpose of this retrospective, case-controlled, chart review study was to compare the quality of symptomatic treatment of withdrawal between patients receiving inpatient induction of buprenorphine maintenance and those receiving detoxification treatment. We also sought to determine to if there was a difference in initiation and retention in outpatient treatment between patients being treated with buprenorphine versus those who were detoxified.

METHODS

Rosary Hall, St. Vincent Charity Hospital

St. Vincent Charity Hospital (SVCH) is an inner-city, 490-bed community hospital in Cleveland, Ohio. Rosary Hall (RH) is a twelve step-based inpatient detoxification and outpatient treatment center at SVCH with a seventeen-bed detoxification unit that treated 895 patients for acute opiate withdrawal in 2002. Rosary Hall is the second oldest hospital-based addiction treatment program in Ohio and has the largest detoxification service in the state.

The physicians who initially started buprenorphine therapy in the area did not have the space or staff to monitor patients for symptoms of withdrawal and provide medication in their outpatient facility, and the pharmacy was only able to stock the combination product. The thirty-patient-per-practice maximum mandated by enabling legislation made the expansion of staff and facilities (in order to provide the capacity for outpatient induction) impractical. The solution was to utilize existing inpatient detoxification facilities to initiate the induction of buprenorphine/naloxone therapy for the initial three days of treatment.

Chart Review

A proposal was made to the SVCH Institutional Review Board to review a sample of charts of patients treated for opioid withdrawal and dependence in 2003. After approval for the study, chart review was performed by a co-author (R.C., a fourth-year medical student).

Inpatient and outpatient charts for each subject were gathered using the hospital discharge diagnosis computer

database. Outpatient records were not available for patients receiving buprenorphine who were not being treated at RH (N=6). Data extracted consisted of demographics, substance use history, and diagnoses, including current use, psychiatric and medical history, withdrawal symptoms during inpatient treatment as measured by the Clinical Institutes of Narcotic Assessment (CINA) scores, and attendance in outpatient treatment, as well as reasons for discharge from outpatient treatment. Substance use and history were determined by recording the largest quantity, frequency, and durations reported in the chart from the intake, assessment, and detoxification process.

Subjects

Subjects were sixty opioid-dependent patients, ranging in age from 22 to 54 years, who had completed inpatient opioid detoxification treatment between April and September 2003. Thirty of the subjects selected were the first thirty patients to receive inpatient induction of buprenorphine maintenance therapy. The other thirty subjects were age- and gender-matched subjects who received inpatient opioid detoxification followed by drug-free outpatient counseling. All sixty patients had successfully completed inpatient treatment and agreed with discharge planning made by the treating team. Discharge plans for the group receiving the induction of buprenorphine maintenance consisted of follow-up at RH for intensive outpatient treatment and medical management of buprenorphine maintenance (n=24), or follow-up with referring physicians in the community who were qualified and licensed to prescribe buprenorphine maintenance therapy (n=6). Discharge plans for the entire group receiving detoxification treatment consisted of follow-up at RH for intensive outpatient treatment and medical management.

Treatment Protocols

Buprenorphine maintenance induction was done via a three-day protocol using suboxone (buprenorphine/naloxone) sublingual medication. Over this period, vital signs and CINA scores were assessed every two hours until CINA scores were less than 6 for a period of four consecutive hours, at which point CINA and vital signs were assessed every four hours. Buprenorphine was dosed in a graduating fashion according to CINA score such that on the first day, 2 mg buprenorphine was given every two hours as needed for CINA scores greater than or equal to 6, not exceeding 8 mg in the first 24 hours. On the second day, an equivalent of the total dose of buprenorphine given in the first 24 hours was then given in the first morning dose, with an additional 2 mg buprenorphine given every two hours as needed for CINA scores greater than or equal to 6, not exceeding an additional 8 mg in the second 24 hours (ie, a total of 16 mg may be

given in the second 24 hours). The same process was followed on the third day, such that an equivalent of the total dose of buprenorphine given in the second 24 hours was then given in the first morning dose, and additional doses were given not to exceed 8 mg in the second 24 hours (ie, a total of 24 mg may be given in the third 24 hours). In addition to buprenorphine given as detailed above, additional medications were given as needed for withdrawal symptoms resulting in a CINA greater than 6 that were not covered by the buprenorphine induction. These “adjunctive” medications included tramadol, clonidine, trazodone, ibuprofen, acetaminophen, and hydroxyzine.¹⁶⁻¹⁸

Patients receiving opiate detoxification treatment were detoxified via a protocol previously described using a tramadol taper to treat withdrawal symptoms over a five-day hospital stay.¹⁶⁻¹⁸ This was the detoxification procedure utilized at the time by the RH program, comparing favorably with previously utilized injectable buprenorphine strategies and superiorly to clonidine protocols.¹⁶⁻¹⁸ All patients in both groups agreed at discharge from the hospital to begin intensive outpatient treatment. All patients were referred to Intensive Outpatient treatment (IOP), which consisted of four three-hour sessions per week, including “task oriented” twelve step-based group therapy, plus one hour of individual therapy per week for five weeks. Patients who successfully completed IOP then began aftercare, which consisted of once weekly group therapy and one hour of individual therapy every other week for a period of twelve weeks.

Statistical Analysis

Demographic data, drug use history, and medical and psychiatric history were analyzed using the Student's *t*-test for continuous measures and the chi-square test for categorical variables. Withdrawal symptoms as measured by CINA score during inpatient treatment were compared using the Student's *t*-test. Treatment outcome results were compared using the chi-square test for each outcome condition at the end of the study period. Outpatient treatment duration of the 54 patients treated at RH was compared using the Student's *t*-test comparing completion of IOP. Tests were considered statistically significant at two-sided *p* values less than or equal to 0.05.

RESULTS

Table 1 shows the demographic and substance use history of the subjects in both groups. More subjects being treated with buprenorphine were employed (50% vs. 17%, $p < 0.001$) and had more years of education (13.3 vs. 12.1, $p = 0.02$) than the group receiving detoxification. More subjects who were detoxified from opioids also had a diagnosis of polysubstance abuse (33% vs. 6%, $p = 0.002$) or any other substance use disorder (73% vs.

53%, $p = 0.01$) than patients treated with buprenorphine. No other significant differences were found among the demographic or substance abuse variables of the two groups.

Table 2 shows the CINA scores during inpatient admission reflecting the severity of withdrawal and responsiveness to treatment. There were no significant differences between subjects receiving buprenorphine or detoxification for CINA on admission, the maximum CINA score over the course of the hospital admission, the CINA at discharge, or the change in CINA scores during admission.

Table 3 shows the status of all subjects at the end of the twelve-week study period as well as the reason for discharge among those who were discharged. More subjects receiving buprenorphine were continuing treatment (40% vs. 0%, $p < 0.001$) or had been returned to the care of an outside treatment provider (20% vs. 0%, $p < 0.01$) compared to those who had been detoxified. At the end of the study period, more subjects in the detoxification group had been discharged from treatment (100% vs. 40%, $p < 0.001$) as compared to those receiving buprenorphine. Among subjects who were discharged, those in the detoxification group were more likely to have never shown up for outpatient treatment (80% vs. 24%, $p < 0.001$) or were referred for residential treatment following multiple relapses (3% vs. 0%, $p < 0.001$) than those in the buprenorphine group.

Table 4 shows a comparison of treatment outcomes of only those subjects who were intended to be treated in the Rosary Hall IOP, 24 in the buprenorphine group and thirty in the detoxification group. Those in the buprenorphine group were treated on average for significantly longer time than those in the detoxification group (8.5 wks vs. 0.4 wks, $p < 0.001$). Half of those in the buprenorphine group completed the intensive outpatient treatment, while none of those in the detoxification group did.

Figure 1 illustrates the survival in treatment of the subset of subjects who were “intended to be treated” in IOP among the group receiving buprenorphine ($N=24$) and the detoxification group ($N=30$). On the very first day of outpatient treatment following discharge, there were 24 subjects among the detoxification and two subjects among the buprenorphine group who were “no-show” for the first day of IOP. At the end of the first week, an additional three subjects from the detoxification group and two subjects from the buprenorphine group had dropped out of IOP. At the end of week 2, one subject from the detoxification group was referred for residential treatment following multiple episodes of opioid use during IOP. After week 3, one subject from the detoxification group dropped out, and after the following week, the last subject from the detoxification group dropped out after a relapse. Fourteen buprenorphine/naloxone-maintained subjects received treatment through

TABLE 1. Demographic characteristics of sixty opioid-dependent patients who received either inpatient induction of buprenorphine maintenance or inpatient opioid detoxification

Item	Buprenorphine (N = 30)		Detoxification (N = 30)		<i>p</i>
	N (%)		N (%)		
Gender (male)	23 (77)		23 (77)		1.00
Race (white)	22 (73)		17 (57)		0.12
Marital status					
Single, never married	9 (30)		13 (43)		0.14
1st marriage	6 (20)		4 (13)		0.28
Remarried	7 (23)		4 (13)		0.11
Separated	1 (3)		4 (13)		0.11
Divorced	6 (20)		4 (13)		0.28
Widowed	1 (3)		1 (3)		1.00
Employment	15 (50)		5 (17)		<0.001
Opioid use, type					
Heroin	28 (93)		28 (93)		1.00
Prescribed	10 (33)		8 (27)		0.41
Both	8 (27)		6 (20)		0.36
Substance use disorders					
Cocaine abuse/dependence	9 (30)		10 (33)		0.70
Cannabis abuse/dependence	8 (27)		8 (27)		1.00
Alcohol abuse/dependence	7 (23)		11 (37)		0.13
Polysubstance abuse	2 (6)		10 (33)		0.002
Any other SUD	16 (53)		22 (73)		0.01
Prior methadone treatment	7 (23)		4 (13)		0.11
History of sobriety >1 yr	13 (43)		16 (53)		0.27
Co-morbid psychiatric illness	12 (40)		10 (33)		0.44
Current legal problems	19 (63)		17 (57)		0.46
	Mean	SD	Mean	SD	
Age	41.2	8.8	41.4	9.0	0.93
Education, yrs.	13.3	3.5	12.1	3.4	0.02
Opioid use, yrs.	14.9	11.1	15.7	11.6	0.79
Heroin use, bags/day	9.1	7.7	11.0	7.4	0.27
Substance use treatment					
Prior detoxifications	2.3	2.1	2.3	2.6	0.94
Prior treatments	3.4	2.5	2.7	2.9	0.27

all twelve weeks of IOP and aftercare. At the end of week twelve, two subjects in the buprenorphine group were discharged due to non-compliance with treatment.

DISCUSSION

These data indicate that inpatient induction of buprenorphine therapy is an effective and well-tolerated method for initiating acute stabilization and addiction treatment. CINA scores at admission and discharge and the maximum difference over the hospital stay were similar between the group of patients receiving a three-day inpatient induction of buprenorphine maintenance and the group being detoxified from opiates with a tramadol detoxification protocol.¹⁹

In the outpatient setting, buprenorphine proved to be effective at retaining opioid-dependent patients in an intensive outpatient counseling program, as half of those who were treated with buprenorphine completed IOP and were still receiving aftercare treatment after twelve weeks. These data are comparable to that found by other investigators over a similar treatment period.²⁰ Most significant was the difference in length of outpatient treatment retention between patients receiving buprenorphine and those who had been detoxified. A large majority of the patients who completed detoxification did not show up for even one day of IOP, and none of the six patients in the detoxification group who started IOP completed more than four weeks of counseling. This dramatic difference in IOP treatment initiation and retention shows that

TABLE 2. Withdrawal and treatment response to buprenorphine induction and detoxification among sixty opioid-dependent inpatients

CINA score	Buprenorphine N=30		Detoxification N=30		<i>p</i>
	Mean	SD	Mean	SD	
Admission	6.6	3.0	6.4	2.9	0.81
Inpatient course maximum	8.4	2.0	7.5	2.1	0.12
Discharge day maximum	2.6	2.5	2.7	2.0	0.86
Discharge day minimum	0.9	1.9	0.6	1.1	0.52
Admission maximum – discharge minimum	6.7	3.1	6.1	2.9	0.47

TABLE 3. Status of sixty opioid-dependent patients twelve weeks after hospital discharge following buprenorphine maintenance induction or detoxification

Status	Suboxone N=30		Detoxification N=30		<i>p</i>
	N	%	N	%	
Continuing treatment	12	40	0	0	<0.001
Returned to outside treatment provider	6	20	0	0	<0.01
Left treatment	12	40	30	100	<0.001

buprenorphine maintenance therapy may be very helpful in keeping opioid-dependent patients engaged in treatment. Interestingly, the inclusion of buprenorphine-maintained patients in a very traditional, twelve step-based, abstinence-oriented IOP proved to be not disruptive to the functioning of the groups or the counselors.

If corroborated in larger and better controlled trials, these data will help to refute the assertion voiced by many in the abstinence-based treatment community that the pharmacotherapy of addictions merely distracts patients from counseling and “real” recovery, increasing treatment dropout rates as patients overly focus on the medication as an “easy” magic bullet. Far from distracting patients from IOP, our data suggest that buprenorphine maintenance can actually reinforce the need to comply with counseling. It appears that if the provision of buprenorphine maintenance is done with an initial explicit expectation of full and documented participation in a comprehensive IOP, then many buprenorphine-maintained patients will meet that expectation.

This report engaged a somewhat unique approach to buprenorphine maintenance. The patients were all induced over three days as inpatients in a traditional detoxification setting. They were then all referred to the same IOP program and were followed for the initial several week-period by the same addiction medicine

physicians who supervised the detoxification/induction and IOP periods. Subsequent to the completion of this phase, successful patients have been referred for long-term ongoing monitoring and management by other “buprenorphine-certified” physicians in the community who have less addiction treatment training. Continuing consultation by the initial addiction physicians and the detoxification/IOP treatment program are always available. This model permits buprenorphine induction without office practice disruption, monitoring by specialists in the early, less stable period, and the referral of a stable successful patient for ongoing primary care management. This use of specialized addiction services combined and followed by more primary care management may be a very efficient and effective use of resources in other geographic areas. The added incremental cost of a brief inpatient or residential level of care during induction may well be offset by the advantage of obtaining a quality comprehensive assessment, re-enforcing the necessity of IOP participation and completion, and having physician and nursing expertise constantly available during the induction period. The gains in retention and recovery program completion may well outweigh the increased costs of this induction strategy. A final advantage is that to date, virtually every certified physician in the region is now managing buprenorphine maintenance patients

TABLE 4. Treatment outcomes for 54 opioid-dependent patients after inpatient induction of buprenorphine maintenance or detoxification *Intended for IOP*

Treatment outcome	Buprenorphine N=24	Detoxification N=30	<i>p</i>
Completed IOP, n (%)	12 (50)	0 (0)	<0.001
Weeks of outpatient treatment, mean (SD)	8.5 (4.6)	0.4 (1.0)	<0.001

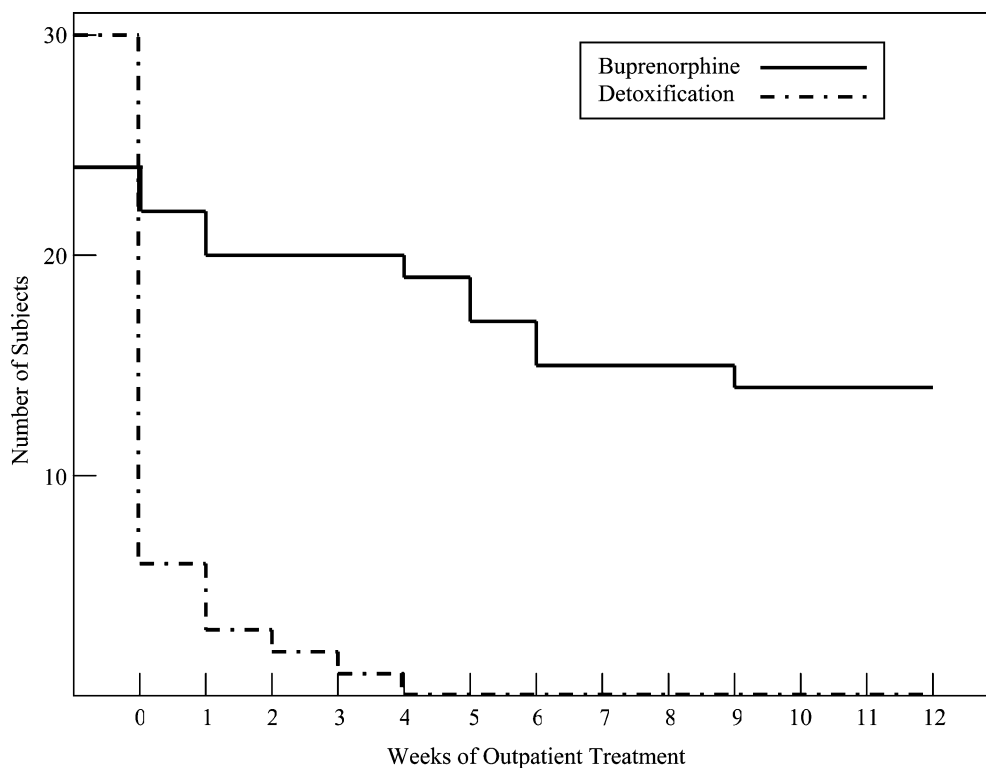


FIGURE 1. Retention in Outpatient Treatment of Patients Following Inpatient Induction of Buprenorphine Maintenance vs. Inpatient Detoxification

($n=15$), where if left to their own initiative, only three had decided to actually attempt true office-based inductions.

This study has a number of limitations. This was a retrospective, non-randomized, non-blinded chart review with a relatively small number of subjects. The control subjects were selected as age and gender matches, but there were major demographic and substance use differences between the groups. The subjects receiving buprenorphine had significantly higher rates of employment and education, which one would expect to result in better treatment retention, and more subjects in the detoxification group had a diagnosis of polysubstance abuse, which is a poor prognostic factor for treatment retention. Of note, there were no significant differences in the quantity of heroin used and years of opioid use.

Despite these limitations, the superiority of buprenorphine at retaining subjects in outpatient treatment was remarkable, and this raises questions about how limited public funds for addiction treatment should be allocated. Although there is concern among physicians about the availability of insurance coverage for this treatment,²¹ our experience was that many health insurance providers were ignorant about buprenorphine maintenance but willing to pay for a brief hospital stay in order to ensure induction on buprenorphine maintenance and referral to

IOP. The majority of private insurers, even on a case-by-case management level, ultimately provided coverage, although Medicare and Medicaid did not participate during the time of this project. County funds were available for addiction treatment to pay for the inpatient stay of some patients receiving buprenorphine but not available for the ongoing provision of buprenorphine. The large disparity in the effectiveness of these two interventions in terms of retaining patients in outpatient treatment should lead to a reexamination of how we allocate public funds for addictions treatment.^{22,23}

This study was supported in part by grant funding from the Cryle Foundation Summer Research Grant as well as CWRU School of Medicine and Veterans Health Administration Special Fellowships in Substance Abuse. No other external support was received for this study, including commercial support.

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