Induction Phase of Buprenorphine (Suboxone) Treatment is Clinically Unnecessary and Can Be Safely Eliminated in Practice

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Abstract

Buprenorphine is a partial opioid agonist that has revolutionized the treatment of narcotic addiction. Clinicians, however, have been slow to incorporate buprenorphine treatment in their practice. This is partly because DEA requires special training and unique identification number to prescribe it. However, many doctors even after obtaining the special number do not prescribe buprenorphine because they find the induction phase too complex, time consuming, and impractical. The guidelines require that in the first day, hourly or bihourly assessment of the patient, preferably with a rating scale, should be done to make sure the patient is in sufficient withdrawal before giving the first dose of Subutex (buprenorphine without naloxone) and to repeat the procedure in the next few days to titrate the optimum dose before switching to buprenorphine plus naloxone.

In our office we have successfully eliminated the induction phase. We will present data on 42 narcotic addicts who were treated without induction phase, receiving buprenorphine plus naloxone (Film or Tab Suboxone; average dose 12 mg/day) for the entire first week, at their first visit, after a 45-minute evaluation. In only 2 patients there was precipitation of withdrawal symptoms with this approach, but not severe enough to require active intervention. The treatment success as measured by abstinence at 3 months was 59.5%. Contrary to prevailing clinical wisdom, the feared adverse effects from taking buprenorphine while the patient is not in full withdrawal are highly overestimated. Demystifying buprenorphine therapy and making it simpler will greatly improve treatment of narcotic addiction.
**Suboxone (buprenorphine) Induction protocol per prevailing clinical wisdom and drug company’s information package insert and it's drawbacks:**

1. The recommendation is that the patient must come to the office after at least 12-24 hours of abstinence. With long acting opioid, Methadone, after 48 hours of abstinence

**Drawback:** Many patients will not show up for appointment after making one, relapsing before even beginning the treatment.

2. After the patient arrives the physician is required to do hourly assessment of the withdrawal symptoms, preferably with a rating scale COWS (Clinical Opiate Withdrawal Scale), till the patient is in sufficient withdrawal as defined by the rating scale, to give the first dose of 4 mg. buprenorphine without naloxone. The protocol requires for the patient at that point to be given a prescription to get two or three bupronorphine (Subutex) tablets from the pharmacy to start the induction.

**Drawbacks:** Making the patient wait in the waiting room or in one of the office cubicles is time consuming for the physician and patient. Psychiatrists generally do not have the luxury of multiple exam rooms. Addicts, who are often disheveled, exhibit motor restlessness and other signs of withdrawal, and can be socially inappropriate with other patients, and can scare them and be disruptive to the waiting area ambiance.

The rating scale being one-dimensional instead of improving assessment may detract from making correct judgment as to the patient’s state of withdrawal. Paying attention to the subjective report and the signs such as sweating, yawning, rhinorrhea, lacrimation are better gauge than the numbers generated via the rating scale. Also the therapeutic alliance between the physician and the patient, and the overall feel for the patient’s true clinical status, are much better if one assesses him or her qualitatively with evenly hovering attention than by seeing him through the eyes of rating scales.

Sending the patient with a prescription to a pharmacy to get a few buprenorphine tablets is highly impractical. Since DEA does not allow the doctor to hold patient’s medication overnight, and the protocol advises to give him prescriptions just enough for a day, going to the pharmacy ritual is expected to be repeated daily till the correct dosage for stabilization is ascertained.

The biggest drawback of this complicated and time consuming ritual, supposedly to avoid giving buprenorphine too much and too early and thus “precipitating iatrogenic withdrawal”, is that it dramatically escalates the cost of treatment. For spending so much time the doctor feels entitled to charge patients anywhere from 200 to 400 dollars for their first visit and much higher fees than what he normally charges his other patients for the subsequent visits. Addicts who barely have money to buy the buprenorphine, let alone pay that kind of medical fees, do not build a very positive transference towards doctors who want to charge hundreds of dollars for putting them through hoops of long and worthless medical protocols. Suboxone doctor has become a pejorative term, conjuring image of doctors who charge exorbitant monies rather than those who bring people out of addiction.
**Suboxone (buprenorphine) Induction protocol per prevailing clinical wisdom and drug company’s information package insert and its drawbacks (2):**

3. After making the patient come daily anywhere from 2 to 5 days, when supposedly the correct stabilization dose is found through the close monitoring, the switch is done from buprenorphine without naloxone (Subutex) to buprenorphine with naloxone (Suboxone, Zubsolv). The rationale behind it is that buprenorphine with naloxone is more likely to precipitate withdrawal than buprenorphine by itself.

**Drawback:** Theoretically this rationale is not justified. Naloxone when given sublingually does not get absorbed. Also it has no effect upon the sublingual absorption of buprenorphine when the two are given together. The blood level of buprenorphine is the same when it is given with or without naloxone. Naloxone is added to buprenorphine to prevent it from being abused through intramuscular and intravenous routes. For when buprenorphine is given by itself through parenteral routes it acts primarily as an opiate agonist, but when injected with Naloxone, the combination is more of an opiate antagonist and precipitates withdrawal.

So starting on buprenorphine and then switching from buprenorphine to buprenorphine plus naloxone at the end of Induction phase is of no great clinical significance. It adds unnecessary complexity to the treatment, justifying higher billing of patients without any clinical benefits. Once again this is more a financial than medical play.

The only exception to this is when switching patients from Methadone to Suboxone. The very long half-life of Methadone makes the induction and stabilization phase of Suboxone treatment very rocky. In these patients it is a good idea to treat them for quite some time, in fact for weeks, with just buprenorphine (Subutex) alone and then switch them to Suboxone.

The switching from one buprenorphine preparation to another has another drawback. Getting small doses of Subutex filled daily and then having Suboxone prescription filled benefits the bottomline of the pharmacies and depletes from the limited resources opiate addicts have to begin with.
Method: A retrospective chart analysis was done on all patients who entered in to treatment or were in active treatment in the previous 8 months in our office based private practice. To be included in the study the patient at the time of starting treatment were not on buprenorphine and were actively abusing narcotics. 42 patients met the criteria. Incidence of adverse reactions was based upon subjective complaints of the patient as documented in the medical record. Abstinence was assessed by absence of narcotics and other illicit drugs in the urine drug screen at 3 months point from the beginning of treatment.

Results in Tabular Form

<table>
<thead>
<tr>
<th>Patients</th>
<th>No Adverse Reaction</th>
<th>Adverse Reaction</th>
<th>Abstinent at 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 42</td>
<td>40 (95%)</td>
<td>2 (5%)</td>
<td>25 (59.5% success rate)</td>
</tr>
</tbody>
</table>

Results in Histogram
**Details of the two Adverse Reactions:**

Patient 1 - Patient was started on Suboxone (Buprenorphine & Naloxone) 8 mg. tablets, one and a half tabs. a day. He was prescribed 11 tablets for seven days. He ran out of Suboxone on the 5\textsuperscript{th} day, because contrary to the instructions, he was either taking more than the prescribed amount or diverting it. On the 6\textsuperscript{th} day patient took some Oxycodone to control withdrawal symptoms. This paradoxically made him feel very sick. Patient went to an emergency room, where, after being kept for a few hours under observation he was discharged with instructions to see his psychiatrist the next day.

Patient 2 – Patient was abusing very high doses of heroin and alprazolam that he was buying on the street. He was started on Suboxone 16 mg/day and given 14 tablets for the first week. He was also given alprazolam 1 mg and quatepine 100 mg at bedtime for insomnia and anxiety. Patient found the dosages of these medications insufficient to control his cravings and anxiety, and tried to alternate the prescribed medications with heroin. This made him quite sick but not bad enough to require any special intervention. During his next visit his Suboxone dose was raised to 24 mg/day and alprazolam to 1 mg 3 times a day. Quatepine was discontinued and Temazepam 30 mg was given for sleep. He had no further adverse reactions. His medications were titrated down very slowly because of his addiction to very high doses of heroin and alprazolam for very long time.
A streamlined, Cost- and-Treatment-effective Protocol for initiating (Suboxone) buprenorphine treatment

Our clinical approach is simple. At the heart of it is our belief that the patient is a better judge of his/her state of withdrawal than the doctor with or without his rating scales. We believe that at his first visit if the patient is psychiatrically interviewed for full 45 minutes and a good therapeutic alliance is established he can be adequately trained to not take the prescribed buprenorphine before the natural withdrawal becomes unbearable. In that 45 minutes one can devote adequate time to teach the patient how premature taking of Suboxone will cause precipitated withdrawal and cause them to get very sick. In our judgment much of the protocol of induction phase of Suboxone therapy was concocted to make treatment with Suboxone look more complex than it really is and for vested financial interests.

Our approach is cheaper for the patient and his likelihood of relapsing during the induction phase is much less if he is trusted to not take buprenorphine but as instructed and is given an entire week’s supply of the medication. We instruct his to do urine drug screen in a standard laboratory or for 15 dollars at our office, on the fifth day of starting buprenorphine when the illicit drugs will be out of his system, and to return for further treatment on the seventh day. On average our patients require 11 tablets of 8 mg Suboxone for the first week. Some require as low as 4 mg, very few require 24 mg a day. If they run short they are allowed to make an emergency appointment, our seen on the same day, a urine drug screen is done in the office, and extra Suboxone is given to last them till their next scheduled appointment. Though we give data on 42 patients, we have no serious precipitated withdrawal in any of our patients in the last 10 years.

We also find no place for Subutex in induction phase other than for the treatment of Methadone addicts. Their withdrawal is generally quite rocky and erratic and somehow Subutex works better than Suboxone in stabilizing them. For rest of the patient initiating treatment with the combination of buprenorphine and naloxone works fine.

Take Home Point: Treating narcotic addicts with Suboxone (buprenorphine) is a much simpler affair than what it is made out to be. Starting patients on buprenorphine for narcotic addiction is no more complicated than starting a schizophrenic patient on antipsychotics or depressed patient on antidepressant and can be done with equal safety in an outpatient setting after a 45 minute psychiatric session.

The Induction phase of buprenorphine treatment is an artificial construct that emerged because of an overestimation of the adverse consequences of precipitated withdrawal from buprenorphine and an overestimation of doctor’s ability to assess the correct level of withdrawal than the patient’s who is actually experiencing the subjective discomfort. In actual practice the Induction phase of Suboxone treatment can be safely dispensed with without adverse consequences.