

## Transdermal Buprenorphine as a Short-Term Opioid Substitution Therapy Option: A Case Series

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### Abstract:

**Introduction:** Globally an estimated 40.5 million people struggle with opioid use disorder. Opioid substitution therapy [OST] with methadone or buprenorphine is the mainstay long-term management. Adverse effect such as sedation, constipation and sexual dysfunction lead to discontinuation of maintenance medications. Transdermal patch of buprenorphine obviates the need for daily dosing and may act as a short-term OST bridge while transitioning to other modalities.

**Methodology:** A case series of three opioid dependent patients successfully treated with OST approach is presented. We have discussed patient characteristics that may predict success with this novel OST strategy.

**Results:** First case was unable to attend daily clinic due to work schedule, started with transdermal buprenorphine 10mcg/hour weekly patch, had successfully transitioned to oral naltrexone at 4-week follow-up and at 6 months remained engaged in treatment. Second was a case of opioid dependence with bipolar disorder, with history of frequent missed doses. Started with transdermal buprenorphine 20mcg/hr, at 3 months was abstinent from opioids and could be switched to sublingual buprenorphine-naloxone as maintenance therapy. Last case was of heroin dependence without any treatment due to social stigma, started with transdermal buprenorphine 10mcg/hr, which was well tolerated and later switched to buprenorphine-naloxone maintenance therapy.

**Conclusion:** Transdermal buprenorphine helps to individualize care based on patient's unique need and circumstances and may act as a bridging therapy for opioid dependent patients, who are remaining out of care.

**Keywords:** Opioid Substitution Therapy, Buprenorphine, Transdermal Patch.

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### Introduction

Opioid dependence is a chronic, relapsing disorder with serious individual and societal consequences. Globally, an estimated 40.5 million people struggle with opioid use disorders.[1] In India, opioids are the most common illicit drugs of abuse, with an estimated 2.1% of the population reporting opioid use.[2] Opioid substitution therapy (OST) with methadone or buprenorphine is the mainstay of long-term management, supported by an extensive evidence base.[3] OST medications relieve withdrawal and cravings, block the effects of illicit opioids, reduce infectious disease risk behaviors, and improve psychosocial functioning.[4]

However, many barriers limit access to and utilization of OST in India. Methadone is classified as a Schedule A narcotic drug, greatly restricting its availability.[5] Buprenorphine, though more accessible, is still unavailable in many areas, particularly rural regions with limited healthcare infrastructure.[6] Stigma and discrimination against individu-

als with substance use disorders also prevent many from seeking treatment, even when available.[7] When treatment is accessed, patients often struggle with the requirement for daily supervised dosing, due to travel burdens, time constraints, and the need to balance treatment with family and work responsibilities.[8] Adverse effects such as sedation, constipation, and sexual dysfunction lead some to discontinue maintenance medication.[9] Suboptimal treatment retention remains a challenge, with some studies showing one-year retention rates below 50%.[10]

Expanding the menu of OST options may help address these challenges and improve long-term clinical outcomes. Optimal treatment requires an individualized approach that considers each patient's unique needs, preferences, and life circumstances.[11] Having a range of medication formulations with different routes of administration, dosing schedules, and side effect profiles would enable

greater treatment matching to promote adherence and retention.[12] Additional OST choices may also attract people who have previously been reluctant to engage in treatment due to dissatisfaction with standard options.

Transdermal buprenorphine is an extended-release formulation that may help meet some of these OST needs. It is delivered through a matrix patch applied weekly, which provides consistent drug levels and obviates the need for daily dosing.[13] This eliminates the burden of frequent clinic visits and may improve adherence, particularly among patients with transportation difficulties or family and work constraints.[14] Transdermal delivery also avoids first-pass liver metabolism, which increases bioavailability compared to oral dosing.[15] This route has less abuse potential than other forms of administration.[16] Transdermal buprenorphine is approved in the United States and Europe for chronic pain, but has not been extensively studied for opioid dependence treatment.[17] Limited literature suggests it may have a role as a short-term OST bridge while transitioning to other modalities.[18]

We present a case series of three opioid dependent patients successfully treated with transdermal buprenorphine as a short-term OST approach. These cases highlight the unique benefits of transdermal delivery for selected patient subgroups facing barriers to standard treatment. We discuss patient characteristics that may predict success with this novel OST strategy and identify key research priorities to establish its efficacy and safety. Transdermal buprenorphine has the potential to expand access and individualization of care, ultimately improving quality of life and clinical outcomes for patients with opioid use disorders.

#### Case Series:

**Case 1:** A 32-year-old male with a 7-year history of opioid dependence presented seeking treatment. He had initiated oral naltrexone several times in the past but quickly relapsed each time due to inability to tolerate protracted withdrawal symptoms. Buprenorphine induction was planned, but he reported limited ability to attend the clinic daily for observed dosing due to his work schedule and long commute from a neighboring town without reliable public transportation. The patient was in a stable relationship and employed, but his opioid use was jeopardizing both. Transdermal buprenorphine 10 mcg/hour was applied, with weekly patch changes. The patient reported good control of withdrawal symptoms and cravings with no significant side effects. After 4 weeks, he successfully transitioned to oral naltrexone without relapse. At 6-month follow up, he remains engaged in treatment, reports

abstinence from opioids, and has been promoted at work.

**Case 2:** A 34-year-old male with an 8-year history of opioid dependence and comorbid bipolar disorder presented after a recent relapse. He had been maintained on sublingual buprenorphine-naloxone in the past but frequently missed doses due to his irregular work hours as a day laborer and difficulty remembering to take the medication amidst shifts in mood. He had initiated treatment for bipolar disorder with a psychiatrist but had been unable to achieve sustained adherence or abstinence. Transdermal buprenorphine 20 mcg/hour was initiated along with valproic acid for mood stabilization. Consolidating his dosing to a once weekly patch improved adherence and allowed him to maintain steady employment. His mood symptoms stabilized, cravings reduced, and he attained a 3-month period of abstinence from illicit opioids, the longest since he began using. After several months, he was able to transition back to sublingual buprenorphine-naloxone for maintenance. He remains in treatment and has sustained remission from both opioid dependence and bipolar disorder.

**Case 3:** An 18-year-old male with a 1-year history of heroin dependence presented after a failed attempt at self-detoxification. He was living at home with his parents and had dropped out of college due to his addiction. He reported injecting heroin daily and had recently shared needles with friends due to scarce supply. He had never been in treatment before. His family was highly concerned, but hesitant about agonist maintenance therapy due to the stigma associated with "substituting one addiction for another." The patient was unwilling to begin buprenorphine or methadone despite efforts at education. However, he quickly relapsed on heroin after a brief period of abstinence and began experiencing medical complications related to his injection drug use, including cellulitis. Transdermal buprenorphine 10 mcg/hour was started to provide withdrawal relief and craving control while the cellulitis was treated with antibiotics, and to serve as a bridge to long-term maintenance. He tolerated this well and significantly reduced illicit opioid use. His family was also encouraged by this progress.

After further education on opioid use disorders as a medical condition and the benefits of medication treatment, they agreed to initiate standard buprenorphine-naloxone maintenance. He successfully transitioned to sublingual dosing and continues to engage in treatment. At 9-month follow up, he remains abstinent, has re-enrolled in school, and has repaired his relationship with his family.

**Table 1: Key features of transdermal buprenorphine compared to other Sublingual BMT**

Feature	Transdermal Buprenorphine	Sublingual Buprenorphine/Naloxone
Dosing Schedule	Once weekly	Daily or every other day
Route of Administration	Transdermal patch	Sublingual tablet or film
Pharmacokinetic Properties	Avoids first-pass metabolism Slower onset of action Lower peak plasma concentrations Steady-state drug delivery Longer time to reach steady state	Undergoes first-pass metabolism Faster onset of action Higher peak plasma concentrations Fluctuating drug levels Shorter time to reach steady state
Abuse Potential	Lower	Moderate
Side effects	Nausea, Constipation, Headache, Application site reactions	Nausea, Constipation, Headache, Sweating, Insomnia
Logistics	Weekly visits for patch changes No need for daily supervised dosing	Requires daily or alternate day dosing May require supervised dosing, especially early in treatment
Overdose Risk	Lower due to slower absorption and lower peak drug levels	Moderate due to ceiling effect on respiratory depression
Diversion Potential	Moderate due to ease of patch removal and potential for sale or trade	Lower due to combination with naloxone and sublingual route

### Discussion

These cases demonstrate the potential utility of transdermal buprenorphine as a short-term OST strategy for selected opioid dependent patients facing barriers to standard treatment. In each case, patients had previously been unable to enter into or adhere to first-line OST due to logistical, psychological, or social challenges. The unique pharmacologic properties of transdermal buprenorphine were leveraged to address their specific impediments and support their recovery goals.

For the patient in Case 1, the weekly dosing schedule of transdermal buprenorphine eliminated the need for daily clinic attendance, which had previously led to treatment drop-out. For the patient in Case 2, the steady drug delivery of transdermal dosing provided the stability needed to allow him to engage in psychiatric care and maintain employment. It served as a bridge to transition him back to sublingual buprenorphine/naloxone, which he had been unable to adhere to consistently on his own.

For the patient in Case 3, transdermal buprenorphine served as an initial option that was acceptable to both him and his family and provided rapid withdrawal relief. This opened the door to long-term agonist maintenance that had previously been resisted.

These cases illustrate how the pharmacokinetic differences of transdermal buprenorphine may offer significant advantages for some patient subgroups. Buprenorphine itself has a strong evidence base for treating opioid dependence, with established efficacy for reducing illicit opioid use, promoting treatment retention, and improving health outcomes.[3]

However, the most commonly prescribed formulation (sublingual buprenorphine/naloxone) has some drawbacks that can limit its acceptability

and utility. It requires daily or near-daily dosing, which can be a major barrier for patients with transportation difficulties, competing family or work responsibilities, or simply the burden of keeping and taking a medication multiple times per day.[8]

Transdermal buprenorphine largely eliminates this adherence challenge by allowing for once-weekly dosing. Patients can apply the patch and not have to worry about taking additional doses for a full week, which may fit better into busy lives and reduce the risk of missed doses leading to withdrawal or relapse.

The steady-state drug delivery also prevents the peaks and troughs of medication effect that can occur with sublingual dosing, potentially reducing side effects and craving.[12] For patients who have attained stability and want a more convenient maintenance option, transdermal buprenorphine may promote long-term retention by making treatment less burdensome.

The unique pharmacokinetics of transdermal buprenorphine may also provide safety advantages in some clinical scenarios. Buprenorphine has a ceiling effect on respiratory depression, making it less risky for overdose than full opioid agonists like methadone.[13] However, the risk is not zero, and fatal overdoses have occurred, especially when combined with other sedatives.[19]

The slower absorption and lower peak drug concentrations achieved with transdermal delivery may further reduce this risk, making it an attractive option for patients with a history of overdose or medical conditions that increase vulnerability.

The lack of first-pass hepatic metabolism also makes transdermal buprenorphine a better choice for patients with liver disease or at risk for hepato-

toxicity from acetaminophen combinations.[20] Transdermal buprenorphine may have particular benefits for patients with comorbid psychiatric illness who struggle with medication adherence, as illustrated in Case 2. People with opioid dependence have high rates of depression, anxiety, bipolar disorder, personality disorders, and other mental health conditions. These can both contribute to the development of addiction and make recovery more challenging.[21] Depressed or anxious patients may find it harder to keep regular appointments and stick to a daily medication schedule. Those with thought disorders or cognitive impairments may simply forget to take their medication amidst psychiatric instability. Having a once-weekly patch eliminates the need to remember daily doses and provides steadier drug delivery that may reduce the risk of missed doses leading to a destabilizing relapse. For patients whose mental health issues have made it difficult to succeed with sublingual buprenorphine/naloxone maintenance, transdermal delivery offers a potential alternative.

The cases presented here also highlight how transdermal buprenorphine may support treatment entry for individuals who might not otherwise engage in OST. People with opioid addiction face many barriers to entering treatment, including the stigma of being labeled an "addict," lack of information about available options, and fear of the requirements of treatment itself. The patient in Case 3 initially refused agonist therapy entirely due to these barriers. Transdermal buprenorphine offered a more acceptable on-ramp that aligned with his and his family's goals at that stage, while still providing potentially life-saving withdrawal and craving relief. This got him in the door and established an initial therapeutic alliance that eventually allowed for a transition to standard maintenance treatment.

Relatedly, transdermal buprenorphine may be a useful option for patients ambivalent about long-term maintenance who desire a gradual taper off opioids. In contrast to methadone or sublingual buprenorphine, which can be challenging to taper due to the need for daily visits and observed dosing, transdermal formulations could allow for a more seamless outpatient taper by sending patients home with lower dose patches over time. Tapering schedules could be flexible based on individual stability and comfort. While evidence is lacking for the effectiveness of short-term tapers compared to long-term maintenance, many patients express a preference for detoxification.[9] Having a range of options that meet patients where they are may improve overall treatment engagement.

Despite its many potential benefits, transdermal buprenorphine is not a panacea and important questions remain about its efficacy and safety in opioid dependence treatment. Buprenorphine is still a partial opioid agonist with abuse potential and over-

dose risk, even in transdermal form. Diversion is also a possibility, as patches could be sold or traded on the illicit market.[22] Risk may be mitigated by requiring frequent visits for patch changes, but this diminishes the adherence benefits of transdermal dosing. There may also be a subset of patients, likely those with more severe dependence and higher opioid tolerance, who do not find transdermal doses sufficient to control withdrawal and craving.[12] More research is needed to establish the appropriate patient selection criteria for transdermal buprenorphine as a short-term OST approach.

Optimal dosing and duration of treatment for opioid dependence have also not been established for transdermal buprenorphine. In the chronic pain literature, transdermal doses range from 5 mcg/hour to 40 mcg/hour and are sometimes titrated up to 80 mcg/hour.[23]

The doses used for the cases in this series ranged from 10-20 mcg/hour, which may represent a reasonable starting point, but more systematic dose-finding studies in the opioid dependence population are needed. Duration of treatment is another important consideration, as the long-term safety and efficacy of transdermal buprenorphine for opioid dependence is unknown. Whether it should be used as a true maintenance approach or only as a short-term bridge to sublingual buprenorphine/naloxone or another formulation remains to be studied.

Overall, while many questions remain, transdermal buprenorphine shows promise as a novel approach to expand the OST armamentarium and individualize care for the diverse population of people with opioid dependence. No single treatment is right for everyone, and the availability of multiple options with different routes of delivery, dosing regimens, and side effect profiles allows for better patient-treatment matching to optimize outcomes.[11] The unique properties of transdermal buprenorphine make it a useful tool for certain subgroups who face challenges succeeding with standard OST, such as those with employment constraints, transportation difficulties, comorbid mental illness, or ambivalence about agonist maintenance. By improving the acceptability and accessibility of OST, transdermal buprenorphine may help attract people into treatment, promote adherence and retention, and ultimately reduce the devastating toll of opioid addiction.

### Conclusion

As the cases presented here illustrate, transdermal buprenorphine expands the menu of options to individualize care based on patients' unique needs and circumstances. While it may not be right for everyone, it gives clinicians an additional tool to help patients who have struggled with first-line OST. The societal crisis of opioid dependence demands creative solutions and a commitment to

patient-centered care. In the right clinical scenario, transdermal buprenorphine may make the difference between a patient remaining out of care and entering into what becomes life-saving treatment. Further research and clinical experience will help refine its role in supporting recovery from this devastating disease.

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