Indian experience with OST

Anju Dhawan

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
The Story of OST in India

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Buprenorphine used for detoxification and long term pharmacotherapy at NDDTC and some NGOs from early 1990s

Strength 0.2 mg and Dose 2 mg (10 tablets) used for non-IDU as well as IDU

Clinical experience - effective

Given as take-home- some reports of diversion - involvement of family to prevent diversion
Availability of Treatment options in India

Buprenorphine 0.2 mg (1990)

Buprenorphine 2mg (2000)

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Daily supervised dispensing

- Manufacture of buprenorphine 2mg in Year 2000
- Daily supervised dispensing after induction in OPD
- Dose requirements were low initially and increased over time

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Clinical experience with Buprenorphine

Effective medication
- Response very good - even patients who showed multiple relapses/had very poor social support/homeless showed improvement
- Urine screening often corroborated self-report of abstinence

Reduced burden of family
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NDDTC – Ensuring quality of services

- Records of dispensing constantly reviewed - assessment of compliance, dosing
- Formats for dispensing register developed
- Internal auditing of stocks - duplicate prescription slips
- Dispensing card format developed

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
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Use in various settings at NDDTC

Drug Dependence Treatment Centre

Community Clinic setting (1990)
- Sagarpur in West Delhi
- Trilokpuri in East Delhi
- Sundar Nagri in East Delhi

Prison setting (2008)

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Challenges

- Distance and daily dispensing
  - Request for take home when patient started working
  - Some patients even temporarily relocated themselves
- Alternate day dispensing
- Extended hours of dispensing from the ward
- Some reports of diversion – careful dispensing, use of crushed tablets

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Research
Experimental Studies (Non-funded)

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
44 opiate dependent males randomly assigned to Buprenorphine 0.6 - 1.2 mg/day or clonidine 0.3 - 0.9 mg/day for 10 days in an inpatient setting (Nigam et al, 1993)

INTRODUCTION

Opiate withdrawal symptoms are very unpleasant and often chronic use continues solely to obtain relief from these symptoms. Hence, management of the withdrawal state is the crucial first step in treatment of opiate dependence. Of the many pharmacological agents tried, methadone has possibly been used most extensively (Jaffe, 1989). However, methadone is not available in many countries including India. Other drugs used are levo-acetyl-methadol (Blaine, 1978), d-propoxyphene (Miller, Fienberg, & Posner, 1968), and clonidine (Cam et al., 1985). Agren (1980) in a review article concluded that clonidine produced marked reduction of opiate withdrawal symptoms effectively. It binds strongly to the receptor sites and blocks euphoria caused by further opiate use (Heel, Brogden, Speight, & Avery, 1979; Harcus, Ward, & Smith, 1979; Fudala, Jaffe, & Dax, 1990). Its adverse effects and withdrawal symptoms following abrupt cessation are minimal (Harcus et al., 1979). As a matter of fact Jasinski, Johnson, and Kocher (1985) felt that buprenorphine could be an ideal agent for opiate detoxification. Bickel et al. (1988) found buprenorphine as effective as methadone.

The purpose of the study was to evaluate the therapeutic efficacy of buprenorphine for opiate detoxification as against clonidine.
Studies on effect of buprenorphine

Suppression of acute effects of morphine in subjects on Buprenorphine - using experimental design (Singh et al, 1993)

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Six male post-detoxified opiate dependent subjects were evaluated for abuse liability of buprenorphine (0.6 mg), morphine (16 mg), pentazocine (30 mg) and distilled water (placebo) intramuscular injection in a single blind cross-over random order. Subjective states, drug discrimination, drug linking, sedation and euphoria were assessed at pre-injection, 30 min and 4 hrs post-injection. Buprenorphine caused significant euphoria and was identified as heroin. On all parameters, buprenorphine resembled morphine rather than pentazocine and placebo. The data suggest that abuse liability of buprenorphine is similar to morphine i.e. moderate rather than low.

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Assessed subjective effects and psychomotor performance on psychological tests at Buprenorphine dose up to 10 mg

(Singhal et al, 2008)
Double blind randomized controlled trial of patients maintained on 2mg/4mg Buprenorphine

(De et al, 2008)
Attenuation of acute effects of Morphine with Buprenorphine

- No medication in Group 1
- 4mg/day sublingual buprenorphine in Group 2
- 8mg/day sublingual buprenorphine in Group 3

Subjects in each group received either inj morphine/ inj placebo IM in a double blind cross-over fashion

(Verma et al, 2008)
Conclusions from these studies

- Buprenorphine was superior to clonidine in alleviating both subjective and objective withdrawals
- Blocked the acute effects of morphine
- Did not have any untoward side effects
- No worsening of psychomotor performance at high doses
- Abuse liability of Buprenorphine moderate
- Did not show a difference between 2mg/4mg
- No difference in the efficacy of 4mg/8mg Buprenorphine in blocking the subjective effects of Morphine

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Studies on Effectiveness (Funded)
Early Community Based Studies

Nagaland and Delhi in 1990s

- Significant reduction in substance use, severity of addiction on Addiction Severity Index (ASI) at 6 months

Limitations

- Low dosage

(Mohan et al)

Delhi by SHARAN

- 33% of 447 IDUs on buprenorphine stopped injecting
- 35% of those injecting had reduced their frequency of injecting and sharing

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi

(Dorabjee and Samson, 1998)
Exploring other Options
Buprenorphine 0.2 mg
(1990)

Buprenorphine 2mg
(2000)

Sustained Release Morphine
(2004)

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Sustained release Morphine

- Was in use for cancer pain
- Explored due to its low cost
- Patients stabilized on it reported reduction in drug use, improvement in psychosocial functioning and minimal side effects
- Gained popularity clinically

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Due to difficulty in buprenorphine procurement for some period, 34 patients were shifted to SROM.

Assessments were made prior to the switch-over and after 4 weeks of stabilisation on SROM.

SROM is as effective as buprenorphine in controlling withdrawal, craving and quality of life on short-term follow-up.

No major side effects.
Further Steps to Increase Treatment Options

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Encouraging availability of more treatment options

Drug Controller General of India
Pharmaceutical companies

- Buprenorphine 0.2 mg (1989)
- Buprenorphine 2mg (2000)
- Buprenorphine Naloxone (2006)

Morphine lost its popularity once take home Buprenorphine Naloxone was available

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Strategies to prevent diversion

- Take home medication only to stabilized patients
- Repeated urine screening
- Involvement of family
- Admitting for short periods for observation

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
National Workshop on Office based treatment for availability of Buprenorphine-Naloxone on prescription through pharmacies (2009)

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Scale-up
Number of OST centres very few

Increased to about 50 centres through DFID funding in 2005-06

OST provided largely through NGOs and for IDU

Need for scale-up

Data and protocols from within the country
Scale-up

- Effective ness
- Safety
- Evaluation & Monitoring
- Resource material
- Capacity building

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Study on Buprenorphine

- Multi-centre effectiveness and feasibility study on Buprenorphine sponsored by UNODC (ROSA) and conducted by NDDTC, AIIMS (2005-06)

- Participating centres
  - AIIMS, New Delhi
  - SHARAN, New Delhi
  - Calcutta Samaritans, Kolkata
  - SASO, Imphal
  - Presbyterian Hospital, Aizawl

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Retention

Dhawan et al, 2010

Treatment retention

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Effectiveness

Dhawan et al, 2010

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Does buprenorphine maintenance improve the quality of life of opioid users?

A. Dhawan & A. Chopra

National Drug Dependence Treatment Centre, All India Institute of Medical Sciences, New Delhi, India

Received June 17, 2010

Background & objectives: The quality of life (QOL) of substance abusers is known to be severely impaired. Information on impact of opioid maintenance treatment on the QOL of opioid dependent subjects though available from the developed countries, is lacking from India. This study was carried out to assess the impact of buprenorphine maintenance treatment on the quality of life (QOL) of opioid dependent subjects at nine months follow up.

Methods: Based on specified inclusion criteria a total of 231 subjects were recruited from five participating centres across India. They received sublingual buprenorphine as a directly observed therapy along with brief psychosocial intervention (provided in groups of 8-10 subjects) after intake in to the study. The WHOQOL-BREF scale domain scores obtained at baseline were compared to domain scores at nine months follow up.

Results: At nine months follow up, among the 64.1 per cent retained in buprenorphine maintenance, there was a significant (P<0.001) decline in opioid use from 24.9 ± 10.1 days at baseline to 1.7 ± 4.7 days at nine months follow up and improvements in score of the four WHOQOL-BREF domains (Physical, Psychological, Social relationships and Environment).

Interpretation & conclusions: The results showed the beneficial effects of buprenorphine maintenance treatment in improving the QOL of opioid-dependent subjects at nine month follow up. These results provide evidence of the potential of buprenorphine maintenance as a harm reduction strategy for the opioid dependent population.
Quality of Life

Dhawan et al, 2010

Rating of Quality of Life

Very poor  Poor  Neither poor  Good  Very good

Baseline 9mth FU

Very poor  Poor  Neither poor  Good  Very good

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
OST in Manipur and Nagaland showed that

- Retention rates on OST was about 73% at 3 months and 63% at 6 months.
- Significant improvements were observed in relation to sharing of needles, unsafe sex, detention incidents, and quality of life measures.

(Armstrong et al, 2010)
OST intervention in Manipur and Nagaland covered 1200 IDUs and was found to be acceptable to the clients, their families, the general community, religious leaders as well as militant groups

(Kumar, 2009)
Safety

Post Marketing Surveillance

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
• Of the 5551 observations from 10 centres, common symptoms were weakness (48.9%), euphoria (44.5%), muscle aches (39.5%), relief from pain (37.5%) – related to acute effects/withdrawal

• Systolic hypertension recorded (5%)

• Raised levels of AST in 12 and of ALT in 9 subjects

• Adverse events (12) – seizures, epistaxis, panic attacks, constipation, dyspnoea. No mortality was reported.

• Significant relation between duration of use and time since last dose and subjective symptoms reported

Most effects related to intoxication or withdrawals
POST MARKETING SURVEILLANCE OF SUBLINGUAL BUPRENORPHINE NALOXONE COMBINATION TABLETS

RAJAT RAY, MEERA VASWANI, KOUSHIK SINHA DEB, HEM SETHI, ANITA CHOPRA, NAND KISHORE AND RAKESH COYAL

- Data from 1132 observations; muscle aches (44%), sleepiness (44%), relief from pain (41.3%)
- Lab investigations normal except for abnormal LFT (52%)
- Eight adverse events reported- seizure, angioedema, pedal oedema, papular rash, blisters on feet and significant weight loss. No dangerous events/mortality reported.
National Workshop for development of training course curriculum for doctors, nurses, counsellors (2008) at AIIMS as MOH- WHO Collaborative Programme

Training courses on OST for a mixed group of professionals (2009)
- NDDTC
- RIMS, Imphal

Refined - GO-NGO collaborative project

Presented at the national CME "OST: Policy and Practice" by 11th-19th April 2015 at AIIMS, New Delhi
Resource Material

- Clinical Practice Guidelines
- Standard Operating Procedures
- Training of Trainers Manual
- Quality Assurance Protocols

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Treatment guidelines

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Monitoring and Evaluation

- Increase in centres to 51 by DFID (2005-06)
- NACO to take up the centres
- Evaluation of OST (2007)

- Interviews with staff, patients and family
- On-Site observation
- Examination of Records

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Minimum Essential Requirements

- Availability of a trained doctor and nurse/pharmacist
- Availability of clear guidelines for suitability for OST
- Clinical Assessment at baseline and follow-up - adequacy of dose and side effects
- Dispensing only as Directly Observed Therapy
- Record keeping
- Safekeeping of buprenorphine
- Preparedness to prevent diversion

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Buprenorphine treatment in India: Milestones

2007

- NGO OST sites evaluated (NDDTC and UNODC)
- NACO took over NGO OST sites

2008-09

- NACO developed practice guidelines, SOPs with NDDTC assistance
- Accreditation of OST sites by NABH

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
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- NACO took over NGO OST sites in 2007
- NACO developed practice guidelines, SOPs with NDDTC assistance
- Accreditation of OST sites by NABH in 2008-09
- NACO initiates OST through government centres (in addition to NGO centres) in 2010

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
OST in Government sector

Strengths of Government health care sector

- Large number of Government health care institutions (psychiatry department in medical colleges & MOH funded DACs)
- Availability of referral services - STI, ICTC, ART, DOTS
- Ensuring sustainability

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Proposed model

- Linkage between the government health care facility (providing OST) and the nearest NGO facility (providing IDU TI services)

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Location of OST sites in Punjab

Amritsar: Medical College (Psychiatry)

Taran-Taran: Civil Hospital

Batala: Civil Hospital

Jalandhar: Civil Hospital

Ludhiana: Civil Hospital

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
GO-NGO Project

Central level: NACO
Overall ownership (as part of NACP III)

DFID TAST
(Overall coordination)

NDDTC AIIMS
(Technical Support, Training and Quality Assurance)

State Level

Implementing agencies: Government Hospitals and NGO TIs
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- Training of Trainers Manual
- Quality Assurance Protocols

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Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Scale-up of OST

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Capacity Building for Scale-up

- Initial training coordinated by NACO

- Subsequent trainings by NACO through the National Technical Training Centres (NTTC) and Regional Technical Training Centres (RTTC) and funded by Global Fund Round 9

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Data from service providers of 42 OST centres and 192 clients

- Most centres follow NACO norms and guidelines
- Low doses of buprenorphine (mean dose 6 mg / day) but most satisfied with their dosages although 40% clients reported craving or withdrawal
- 70% clients stopped injecting
- 40% clients missed their dose in last one month and about half among them reported using opioids in the last one month

(Rao, Ambekar and Agrawal, 2012)
### OST under NACP: *Current Status*

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Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
• With support from UNODC (ROSA)

• Location in Government De-addiction Centres

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
MMT initiative in India – Processes

DCGI Approval: June 2009

HMSC clearance: May 2011

Feasibility assessment: June 2011

Licenses for storage and transport: Nov 2011 – May 2012

Procurement of methadone: January 2012

Initiation of Methadone: Feb 2012 – August 2012
• Majority of on MMT are IDUs
  • Predominant injecting of heroin in two centres and pharmaceuticals in three centres

• Methadone: used as liquid of 5mg/ml strength dispensed through a manual dispenser

• Dose requirements 40 mg

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
METHADONE MAINTENANCE TREATMENT IN INDIA
A FEASIBILITY AND EFFECTIVENESS REPORT

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi

(Dhawan et al, 2014)
Effectiveness Findings

- Methadone treatment was effective in:
  - Reducing drug use as confirmed by urine screening
  - Reducing injecting risk behaviour
  - Reducing severity of addiction in multiple domains
  - Improving quality of life in multiple domains
  - Improved psychosocial status

- Had minimal side effects
- No major adverse events

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Feasibility Findings

- Feasible to be implemented in India
- Usual processes and procedures for OST
- Additional requirement of a license
- Clients and family members find methadone acceptable
- Diversion can be prevented following the usual protocols for safekeeping

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
2712 observations were collected from 3 centres

The ten most common subjective effects reported:
- generalised weakness (57%);
- relief from pain (24.9%);
- muscle aches;
- sleeplessness;
- yawning;
- headache;
- dry mouth;
- constipation;
- sleepiness;
- craving

Adverse effects such as seizures and sexual problems reported in < 1% of the observations

(Ambekar et al, 2015)
To sum up...

- Initial years of the journey with Buprenorphine, Buprenorphine-Naloxone and now Methadone

- Buprenorphine started with a few centres in the country largely through external funding and now scaling up being done by NACO through Global Fund Round 9

Presented at the national CME "OST: Policy and Practice" on 18th-19th April 2015 at AIIMS, New Delhi
Challenges at national level

- Almost no services for non-IDU
- Inadequate coverage
- Services in the private sector
- Use of plain Buprenorphine only for scale up

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Future

- NACP IV targets - OST centers to be established in all districts with more than 250 IDUs and coverage of more than 20% IDU

- Will probably include Buprenorphine and Methadone
Future

- DDAP, MOH approved establishment of Drug Treatment Clinics (DTC) in government medical colleges/district hospitals in a phased manner
- OST for both IDU and non-IDU
- Buprenorphine and Methadone
- Support for medicines and staff to be provided by DDAP, MOH

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THANK YOU