OAD : Opioid Analgesic Dependence

Tom Meeus
Clinical Liaison INDIVIOR
OAD : Opioid Analgesic Dependence

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1. Terminology

Tolerance¹

• The need for higher doses of an opioid analgesic over time to achieve the same effect.

Physical dependence¹

• Development of a withdrawal syndrome after abrupt cessation of the opioid, rapid dose reductions, decreasing plasma drug levels or administration of an antagonist.

Opioid analgesic dependence (‘addiction’)¹

• A chronic, relapsing medical condition that may include tolerance and physical dependence, but also includes a range of additional psychological and behavioural features.
1. Definition – opioid dependence (including OAD)

At least three of the following should have been present at any time in the past year:\(^1\)

- A strong desire or sense of compulsion to take opioids
- Difficulties in controlling opioid use
- A physiological withdrawal state
- Tolerance
- Progressive neglect of alternative pleasures or interests because of opioid use
- Persisting with opioid use despite clear evidence of overtly harmful consequences

( *WHO ICD-10 Classification of Mental and Behavioral Disorders; F11.2*)
2. Opioid Analgesic Dependence (OAD) prevalence: worldwide

A meta-analysis of 67 studies found 11.5% of people taking opioids for chronic pain displayed aberrant drug-related behaviours (such as frequent unsanctioned dose escalation).\(^1\)

Approximately **1.9 million people** in the **US** suffered from OAD in 2013, compared to 517,000 suffering from heroin dependence.\(^2\)

OAD is not confined to prescription analgesics; in an **Australian** survey of people using over-the-counter **codeine**, **17%** of respondents met the criteria for dependence.\(^3\)
2. The situation in the US
2. US: overdose deaths

Fig. (2). Overdose deaths in the U.S. involving opioids, cocaine and heroin (including opium). Percentage change 2006-2010 was +21%, -25%, -44%, and +45% for opioid, cocaine+heroin, cocaine and heroin, respectively. Adapted from [60].
2. OAD prevalence: Europe

An estimated **455,000 people** in Europe have OAD.¹

In 2012, 17 EU countries reported that over 10% of opioid-dependent patients entering treatment were using opioids other than heroin.²

In the **UK**, one survey found that among people who reported taking *Tramadol*:³

- 19% had taken more than they were prescribed
- 10% experienced difficulty in discontinuing their use
  - This includes both recreational users and patients in receipt of a prescription
- 34% of respondents obtained the drug from a friend rather than their doctor
2. The Netherlands
3. Consequences of OAD: mortality

In 2010, prescription opioid analgesics were responsible for nearly 17,000 deaths in the USA.¹

- This was twice as many deaths as in 2002.

In Australia, 1,745 deaths between 2007 and 2009 were associated with opioids other than heroin.²

In 2006, the number of deaths in the USA involving opioid analgesics was more than five times the number of deaths involving heroin.³

In the UK, opioids other than heroin, morphine or methadone were implicated in 757 deaths in 2013.⁴
### 3. Consequences of OAD: medical

OAD is associated with a number of comorbidities:

<table>
<thead>
<tr>
<th><strong>Hyperalgesia</strong>&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance use disorders such as OAD appear to worsen an individual’s perception of pain.</td>
</tr>
<tr>
<td>Long-term use of opioid analgesics can also lead to increased pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Psychiatric problems</strong>&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression and anxiety are common among patients with OAD.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Sleep disturbances</strong>&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>These are often experienced by OAD patients, and may exacerbate the patient’s perception of pain.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Gastrointestinal issues</strong>&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>As well as the opioids themselves, paracetamol or ibuprofen in combination analgesics (eg co-codamol) can cause gastrointestinal and liver problems.</td>
</tr>
</tbody>
</table>
Untreated opioid analgesic dependence (OAD) is associated with reduced quality of life as a result of increased sensitivity to pain, sleep disturbances, depression and anxiety.¹

Consequences of prolonged, unmanaged OAD may include unemployment, harm to family and friends, medical complications and death.²

Such consequences place a considerable burden on individual patients, society and the healthcare system.³

As with other chronic medical conditions, patients with OAD can benefit from interventions that include medication-assisted treatment (MAT or OST) and psychosocial support.⁴,⁵
4. Patients you may encounter

OAD patients with ongoing pain: patients with chronic pain who have developed addiction

OAD patients with resolved pain: pain patients who have developed addiction but the pain is no longer present

Pain patients with poorly managed pain: pain patients who display similar characteristics to people with OAD

Recreational users: people who seek prescriptions purely for diversion or misuse purposes

Often overlap occurs
4. Synergy of pain and addiction: impact on the patient
4. OAD: impact on the patients quality of life
### Who is a prescription opioid misuser?

<table>
<thead>
<tr>
<th><strong>Onset</strong></th>
<th>Voluntary abuse and diversion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Young adults</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male &gt;</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Either precarious or well integrated</td>
</tr>
<tr>
<td><strong>Effects</strong></td>
<td>Recreational use, avoids pain (withdrawal) Improves mood, anxiety, sleep, performance</td>
</tr>
<tr>
<td><strong>Products</strong></td>
<td>Medication ± illicit drugs</td>
</tr>
<tr>
<td><strong>Acquisition</strong></td>
<td>Friends,..., physician(s), others, o-t-c</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td>OST, painkiller</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>IV inj, snorting, smoking, oral...</td>
</tr>
<tr>
<td><strong>Doses</strong></td>
<td>High</td>
</tr>
<tr>
<td><strong>Consciousness</strong></td>
<td>Denial of consequences</td>
</tr>
<tr>
<td><strong>MD awareness</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>As illicit drug users</td>
</tr>
<tr>
<td><strong>Prescription for pain</strong></td>
<td>From young adults to elderly</td>
</tr>
<tr>
<td><strong>Female &gt;</strong></td>
<td>Married, educated, higher incomes</td>
</tr>
<tr>
<td><strong>Relieves pain, then dependence, improves mood, anxiety, sleep, performance, avoids withdrawal sd</strong></td>
<td>Medication only</td>
</tr>
<tr>
<td><strong>Physician(s), over-the-counter, other Painkiller</strong></td>
<td>Oral, buccal, spray, inj, patch</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>Denial of the addiction, unknown risks</td>
</tr>
<tr>
<td><strong>Often no</strong></td>
<td>No consensus</td>
</tr>
</tbody>
</table>

Many people who misuse prescribed medication or display aberrant behaviour:
- are not detected with current monitoring
- do not seek help from addiction treatment services

A hidden population!
5. Addiction to opioids: principle of OST
6. SUBOXONE® substances

Contains a combination of buprenorphine and naloxone in a 4:1 ratio in 1 sublingual tablet.

2 dosages:

- Buprenorphine 2 mg/naloxone 0.5 mg
- Buprenorphine 8 mg/naloxone 2 mg
6. Mechanism of action Suboxone®

SUBOXONE®

Combines buprenorphine and naloxone in 1 tablet.

Recommended: correct intake via sublingual route

Buprenorphine | Naloxone
---|---
Suboxone®: only buprenorphine is active

If Suboxone® is taken under the tongue as indicated, then naloxone remains silent...it has no effect.

NOT recommended: wrong intake via IV or IN

Buprenorphine | Naloxone
---|---
Suboxone®: Naloxon is also active and acts more rapidly

Naloxon will cause withdrawal symptoms in people who have heroin or methadone (full agonists) in their body at the time of injection.
6. Respiratory depression

- **Full agonists:** heroin, morphine, methadone, codeine
- **Partial agonists:** buprenorphine
- **Antagonists:** naltrexone, naloxone
Dose–response relationships for (A) fentanyl and (B) buprenorphine in healthy volunteers (opiate naïve). The response is the peak ventilatory depression. Data are mean (SD).

**Suboxone® Induction**

<table>
<thead>
<tr>
<th>Day</th>
<th>Description</th>
<th>Initial Dose</th>
<th>Additional Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Patients with mild or moderate withdrawal</td>
<td>2 - 4 mg</td>
<td>2 - 4 mg (max 8 mg)</td>
</tr>
<tr>
<td></td>
<td>Initial dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>An additional dose may be administered depending on the individual patient’s requirement.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>Increase dose in steps of 2-8 mg depending on the individual patient’s requirement.</td>
<td>Up to 16 mg (max)</td>
<td></td>
</tr>
<tr>
<td>From day 3</td>
<td>Continue with a progressive increase in steps of 2 – 8 mg depending on the individual patient’s requirement.</td>
<td>Up to 24 mg (max)</td>
<td></td>
</tr>
</tbody>
</table>

**Precautions to be taken before induction**
Baseline liver function tests and documentation of viral hepatitis status are recommended prior to commencing therapy. Patients who are positive for viral hepatitis, on concomitant medicinal products and/or have existing liver dysfunction are at risk of accelerated liver injury. Regular monitoring of liver function is recommended.
6. **SUBOXONE®**: optimal sublingual administration

1. Make your mouth wet
2. Place tablet(s) (max 2) under the tongue
3. DO NOT SWALLOW
4. Wait 5 to 10 minutes until the tablet is completely dissolved to make sure it is effectively absorbed.
7. OAD : van gewenning tot verlies van controle

Variatie van het pharmacokinetische profiel
Zorg dat **pijnstillers** (opiaten) geen grip krijgen op uw leven!

Ik zit in zo'n negatieve spiraal, hoe kom ik hieruit?

Het gaat niet goed op mijn werk. Misschien raak ik mijn baan kwijt?

Ik slaap slecht, ben moe en kan me slecht concentreren.

Ik ben geirriteerd en maak vaak ruzie.

Heeft u het gevoel gevangen te zitten in uw pijnstillergebruik en vormen zich om u heen problemen waar u niet meer uit lijkt te komen?

PRAAT EROVER MET UW ARTS!
Bedankt voor jullie aandacht!

Vragen of opmerkingen: tom.meeus@indivior.com of 0477/900 053