THE NORTHERN HOSPITAL

OPIATE WITHDRAWAL

"Vue d'Avignon et du Pont d'Avignon", oil on canvas, 1809-1836 Isidore Dagnan Musée Calvet, Avignon.

"...Beneath my head are crushed the others
who practiced simony before me,
now flattened into fissures in the rock.

"In turn, I too shall be thrust lower down
as soon as he arrives whom I mistook you for
when I called out my hasty question.

"But the time I have already roasted my feet,
standing here upside down, is already longer
Than he'll be planted with his feet on fire.

For after him shall come a lawless shepherd
from the west, one even fouler in his deeds,
fit to be the cover over him and me.

A new Jason shall he be, the one of whom
we read in Maccabees, and even as the king indulged
Jason, so the king of France shall deal with him".

Dante Alighieri, The Inferno, 19:73-87 (1306 - 1317)

Dante had no hesitation in putting Popes into Hell! For the simoniacs, that is the clerics (including Popes) who bestowed spiritual and or political favours for payment, or who bribed their way to high ecclesiastical office, he reserved a particularly horrific place, the third ditch of Malebolge in the Eighth and penultimate Circle of Hell. Here the shades of the souls of the eternally damned are cast upside down into long narrow holes that descend deep into the solid rock of the dark and barren landscape of this place. Only their legs extrude from the rock and over their feet dance tongues of fire that scorch the soles of their feet. The flames burn more fiercely over one hole in particular, the hole reserved for the simoniac Popes, who are placed end to end ever deeper into the ground. As a new simoniac arrives, he takes the place of the one last in the hole with his legs sticking out, and drives all the others deeper down. Dante indeed placed many of the Popes of his day into this region of Hell. Sensationally he directly or indirectly names four of them, and indeed by so doing damned them, if not to actual Hell, then at least to an eternal literary damnation of their memory! He held an especial personal hatred for one of them, Boniface VIII, but of all the simoniacs in the Eighth Circle, it was the Frenchman Clement V (1305 - 1314), whom Dante distinguished as the worst simoniac in the history of the Papacy, (at least up until his time, it is intriguing to ponder what he would have made of many future popes, such as the Spanish Borgia!). In fact Clement was still alive at the time of Dante's journey through the underworld, but we are informed of his fate, via the words of another Pope already in Hell, Nicholas III, who knew the future, "..For after him shall come a lawless shepherd from the west, (...read France) one even fouler in his deeds".

The Papal Conclave of 1304 was particularly protracted. A new Pope would not be elected for eleven months! This was a time of intense three way political rivalry between the Papacy, the French King and the German Holy Roman Emperor. The papacy was locked in deadly conflict with the Monarchies of Europe, not over matters of spiritual hegemony, but in matters of temporal power, where it claimed precedence even over kings. In 1304, a particularly vicious and power crazed king, Philip IV, reigned in France. He used extreme stand-over tactics to influence the outcome of the Papal Conclave of 1304. After the anti-French reign of Boniface VIII, he was determined - at any cost - to have a Frenchman elected to the Papacy. He so intimidated and bribed the cardinals that eventually he got his way, and a Frenchman, who was not even a cardinal, and who was not even in Rome for the Conclave, was elected to the Papacy; the Archbishop of Bordeaux, Bertrand de Got, who took the name of Clement V. Clement took simony to a whole new level, and turned it into an art form! He owed his position to the king and he returned the favour in spades. Clement would be the quintessential puppet of the French Monarchy. Philip finally had his man, and would use him to the

fullest advantage in order to destroy his political enemies. Clement would enrich himself and his immediate family and relatives to such an extent that when he died, the Papal treasury was utterly empty! Philip could not have had a greater stooge than Clement.

From the outset Philip made it clear where the seat of spiritual power would now lie. Clement's coronation took place, not in Rome, but in Lyons. In fact Clement never set foot in Rome at all. He set himself and the Papal court up in a Dominican monastery in the obscure French village of Avignon. There apart from three years, the papacy would remain for the next sixty eight years, under seven successive French Popes; a period known as the "Avignon Captivity", or the "Babylonian" captivity. The first task Philip had for Clement was for him to annul all Boniface's anti-French decrees and to rehabilitate his name in the eyes of Europe. Clement enthusiastically obliged, and then went a step further to please Philip - he published a Papal Bull praising the king for the fervor in his hostility he had shown towards Boniface! But more craven still, Clement then acquiesced in helping Philip destroy France's most powerful organization next the Monarchy itself - the Knights Templar. The Knights were an immensely powerful group whose wealth exceeded even royalty. They had originally been set up as a warrior cast of monks that had supported the First Crusade. Philip was determined to crush them He conspired with Clement to bring farcical charges against them in order to destroy them with an eye to seizing their lands and wealth. On the 13th of October 1307, he had hundreds of the Templar leaders arrested to be put on trial for unspeakable "crimes". By means of sickening torture, he gained "confessions" from them and presented these to Clement. Supposedly they secretly worshipped an idol "Baphomet" and sodomized each other during secret and blasphemous initiation ceremonies!...an interesting insight into the medieval mind that these proceedings and accusations could be taken seriously in the popular mind! Clement in response called a Church council in Vienne where he dissolved the order of the Knights Templar and confiscated all of its vast lands and wealth. He then established the new order of the Knights Hospitaller, in their place who did not inherit anything of the Templar riches, which he cheerfully handed over to Philip.

During his reign, as Italian cardinals died, Clement replaced them with French cardinals. When he died in 1314, French cardinals dominated the makeup of the papal council, making up over ninety percent of its numbers. Clements's sins did not simply stop at simony, he had not the least qualms about nepotism either. Five of the new cardinals he created were members of his own family, and in his will he left all of his vast accumulated wealth to his nephews. To the papacy itself, he bequeathed a bankrupt treasury. When Clement was made Pope in 1304, he knew which side of his bread had been buttered on. If he wanted to remain Pope, which he most certainly did, he had to be beholden to the French king, a "no-brainer" for Clement really, he knew he would most certainly be damned if he didn't! What he didn't realize at that happy time however, was that he would also be dammed if he did! Dante Alighieri immortalized his memory for eternity by placing him in the Eighth Circle of Hell !

Those who are heavily beholden to opioids, will soon, like Clement V, find themselves in a very difficult situation. Should they continue to abuse these agents they will surely come to grief, but should they abruptly cease them, they will suffer the torments of opioid withdrawal. They must make a hellish decision for which, they will be dammed if they do, and damned if they don't!

OPIATE WITHDRAWAL

Introduction

Although very unpleasant opioid withdrawal is *not* a potentially life threatening condition, in *contrast* to the withdrawal syndromes associated with alcohol or the sedative-hypnotics.

Opiate withdrawal syndrome can develop when:

- There is an abrupt cessation of opioid in an opioid dependent person.
- There is an abrupt reduction in dosage in an opioid dependent person.
- An opioid dependent person is administered an opioid antagonist or partial agonist.

Pathophysiology

Opioids exert their analgesic effects by agonist activity at mu receptors within the CNS.

Mu receptors mediate their effects via membrane bound G-proteins which in turn lead to a reduction in the levels of intra-cellular c-AMP

Prolonged opioid use leads to cellular adaptation and "down regulation" of these responses. When opioids are ceased a clinical withdrawal syndrome develops.

Clinical Features

Time Course of Symptoms:

In general terms:

Opioid	Onset	Peak	Resolves
Heroin	6 hours	36-48 hours	7 days
Methadone	48-72 hours	48 hours	Up to 2 weeks.

In individual cases however the exact timing of onset of symptoms will vary according to three main factors:

- The elimination kinetics of the specific opioid that is being taken

- The usual dose that is being taken.
- The degree of dependence the individual has for it.

Note also that patients may present with withdrawal symptoms of more than one type of drug.

Typical Symptoms:

These may include:

1. CNS:
    - Intense psychological craving.
    - Dysphoria
    - Anxiety/ restlessness
    - Insomnia
2. GIT upset:
    - Anorexia, nausea, vomiting
    - Diarrhoea
    - Abdominal cramping.
3. Myalgias and arthralgias
4. Autonomic upset:
    - Hypertension and tachycardia, (more severe cases)
    - Lacrimation.
    - Diaphoresis
    - Salivation
    - Rhinorrhea
    - Piloerection
    - Mydriasis
    - Flushing

Note that more serious symptoms such as altered mental state, seizures, delirium and hyperthermia are not typical features of uncomplicated opiate withdrawal and if present, alternative diagnoses and / or secondary complications need to be considered.

Comorbidities:

Important comorbidities to consider in these patients will include:

1. Dehydration.
2. Electrolyte disturbances
3. Concomitant alcohol and/or benzodiazepine withdrawal
4. Medical illness, such as sepsis, and other complications of IV drug abuse.
5. Psychological/ psychiatric disturbances

Investigations

There are no specific or routine investigations required for patients suffering from opiate withdrawal, this will depend on the severity of symptoms and the need to rule out alternative diagnoses or secondary complications.

The following may need to be considered:

1. FBE
2. CRP
3. U&Es/ glucose
4. Blood alcohol.
5. Urine drug screens
6. Septic workups, according to clinical suspicion.

Management

Many patients can be managed as outpatients but close supervision is required.

Hospital admission may be required for:

- Severe symptoms.

- Significant medical complications such as dehydration, or electrolyte disturbances.
- Significant co-morbidity or intercurrent illness/ infection.
- Psychiatric co-morbidity.
- Significant social issues.

Symptomatic treatment:

In general terms pharmacological management of symptoms will consist of:

1. IV fluid resuscitation.
    - As clinically indicated.
2. Anti-emetic:

    For nausea and vomiting, as indicated:

    - Metoclopramide
    - Prochlorpromazine
    - Ondansatron, or similar (in more severe cases)
3. Buscopan (hyoscine) or atropine-diphenoxylate:
    - For abdominal cramps or diarrhoea
4. NSAIDS, (or paracetamol for milder symptoms)
    - For myalgias or arthralgias.
5. Benzodiazepines:
    - For dysphoria, agitation, insomnia or anxiety.
6. Clonidine [1]

    This is a centrally acting alpha $_2$ adrenergic receptor agonist that can attenuate both the physical and psychological symptoms of opioid withdrawal.

    Postural hypotension can be a problem, especially in pre-existing dehydration.

An initial test dose of **75 microgram orally** can be given followed by lying and standing blood pressures over the next one hour.

If symptomatic postural hypotension does not occur:

- 50 micrograms orally tds, can be commenced.
- This dose may be increased as tolerated up to 200-300 micrograms three times per day
- When there has been control of symptoms, the dose can then be tapered over a period of 5 days.

Opioid replacement therapy:

Note that in **severe and urgent** cases opioids (such as methadone) in sufficient amounts can abolish all symptoms of withdrawal, and this may be necessary in order to:

- **Gain acute control of severe symptoms**
- **Allow for treatment of other significant medical conditions.**

Methadone or Buprenorphine can be used, for "managed withdrawal" and for replacement "maintenance" in abstinence therapy, via:

- A rapid tapering program.
- Close specialist supervision.

These programs greatly reduce the risk of inadvertent heroin overdose and suicide in general.

Disposition:

Detoxification programs:

The efficacy of rapid detoxification programs will depend on:

- Patient selection factors.
- Close supervision by a team of experienced specialists in drug and alcohol treatment.

Detoxification programs should only be undertaken by registered and experienced specialist practitioners in this field.

Pharmacological agents used in the rapid detoxification of patients include, (individually or in combination) the following:

1. Naltrexone:

    - This is a competitive opioid receptor antagonist.
    - It may be used to help *maintain abstinence* after withdrawal from heroin or other opioids has occurred.
    - Ultra rapid detoxification involves the use of naltrexone for the rapid detoxification of opioid dependent persons that is often done under general anesthesia to avoid the severe withdrawal symptoms that may occur. It is currently considered controversial and unproven.

2. Buprenorphine:

    - This is a partial opioid receptor **agonist and as such will have the same effects as any narcotic if taken in large enough doses.**
    - Buprenorphine is generally viewed to have a lower dependence-liability than methadone

3. Clonidine:

    - As described above.

Counselling:

Patients who are cooperative and motivated, should also be referred to a specialist **Drug and Alcohol Counsellor.**

Cameo of Pope Clement V, (1264 - 1314; Pope, 1305 - 1314),
Notre Dame Cathedral, Paris

References

1. Opiate Use Disorder in: Murray L et al. Toxicology Handbook 3rd ed 2015.

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Reviewed August 2016.