IOTOD

Improving Outcomes in the Treatment of Opioid Dependence

17th annual IOTOD conference
13–14 May 2019, Frankfurt, Germany

At the forefront of treatment: challenges and innovations

Highlights report

Contents

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At the forefront of treatment: challenges and innovations

Introduction

The 17th annual 'Improving Outcomes in the Treatment of Opioid Dependence' (IOTOD) conference took place at the Steigenberger Airport Hotel in Frankfurt on 13–14 May 2019. The two-day event delivered expert presentations and discussions on a wide range of issues including novel harm reduction strategies and comorbidities, such as bloodborne viruses. The conference also dedicated a session to examining the challenges and new developments in the field of opioid dependence therapy. This session, chaired by Professor Jens Reimer, discussed abstinence-based pathways, novel long-acting buprenorphine formulations and what people who use drugs think about opioid dependence therapy.

This report summarises the key educational messages and recommendations discussed during the IOTOD 2019 session 'At the forefront of treatment: challenges and innovations'.

Educational impact

Commitments to change pledged by the audience during this session

Following IOTOD 2019, I will...
Incorporate psychosocial interventions for all opioid-dependent patients undergoing detoxification
Stay abreast of treatment advancements and their availability/appropriate use, i.e. long-acting formulations
Ensure my client is an active decision-maker in their treatment plan

Professor Jens Reimer
University Medical Center Hamburg, Germany

Refining abstinence-based pathways

Choosing the optimal detoxification process for patients can be a difficult task for clinicians. Professor Reimer provided insights into various detoxification processes, emphasising that successful abstinence requires psychosocial interventions in addition to pharmacological treatment. He explained that abstinence can be a realistic goal, but it is only suitable for certain individuals. The patient should be fully committed and informed about the process and risks. They should also be in a stable and supportive social situation and have plans in place for future support. Professor Reimer cautioned delegates that patients should not be forced to detoxify as this can lead to an increased risk of relapse.[1]

Pharmacological considerations

Buprenorphine and methadone were considered to have similar levels of efficacy for detoxification. Patients should be detoxified on the medication with which they have been stabilised during opioid substitution therapy.[1] There is substantial variation in detoxification dosing between the outpatient and inpatient setting, as well as between buprenorphine and methadone. Smaller dose reductions are used in an outpatient setting, with the overall detoxification period ranging from 12 to 30 weeks. Inpatient detoxification involves larger dose reductions and can be completed in a timescale as short as a week (depending on the patient's starting dose).[1,2] The detoxification setting choice for a patient depends entirely on the individual's medical and social requirements, as well as regional variations.[1,3] Ultra-rapid detoxification under general anaesthesia or heavy sedation should not be offered to patients due to the risk of serious adverse events.[1]

During detoxification patients can experience numerous withdrawal symptoms, such as diarrhoea, nausea, vomiting, stomach cramps, anxiety, sleeplessness, agitation, muscle pain and headaches. Professor Reimer highlighted the importance of providing additional medications to reduce the physical effects of these symptoms as needed. He pointed out that diazepam may be prescribed for anxiety, sleeplessness and agitation, but that this should only ever be prescribed in an inpatient setting due to safety concerns.[1]

The use of naltrexone, a synthetic μ-opioid receptor antagonist, as an aid to preventing relapse was also discussed. Its use was recommended only in highly motivated individuals who are deemed to be opioid-free for least 7–10 days, and who are aware of opioid overdose risks. Regular liver function monitoring was advised in these individuals as naltrexone can have hepatotoxic effects.[1]

Psychosocial interventions

A Cochrane review that examined 11 studies, comparing pharmacological treatment alone with the combination of any psychosocial intervention and pharmacological treatment, found that those who received psychosocial interventions were less likely to dropout from detoxification treatment, to miss clinic appointments or to use opioids during treatment and follow-up.[4]

When asked, 44.7% of the IOTOD audience reported that less than half of their patients

undergoing detoxification were receiving psychosocial support.

Professor Reimer advised that psychosocial issues should be discussed with the patient before they initiate detoxification. Attending opioid substitution therapy can provide patients with a structure to their day and loss of this structure may be difficult for some. It was recommended to make plans with the patient for how they will adjust to this change and address situations likely to trigger relapse. In addition, patients should also be provided with drug-free support, such as counselling and goal setting, and overdose training as they may be at high risk for overdose due to lowered opioid tolerance.[1,3,4]

Professor Reimer concluded by re-emphasising that detoxification is only suitable for certain individuals and a combination of pharmacological and psychosocial interventions are key to achieving successful abstinence.

Conference feedback revealed that 80% of delegates appreciated this content and found it helpful

References

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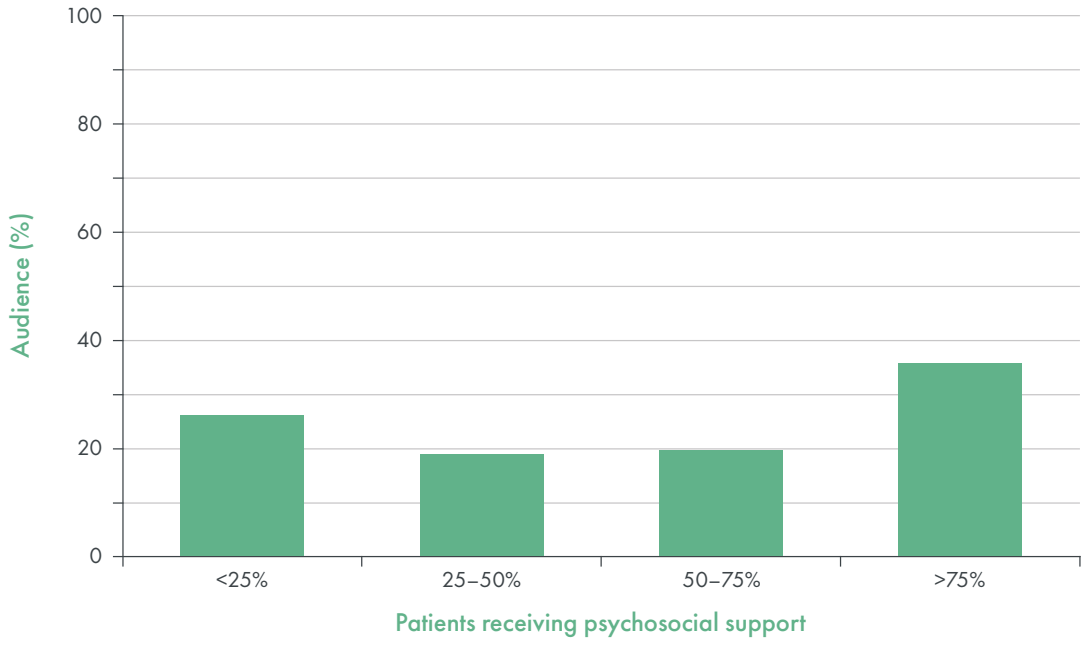
What percentage of your patients undergoing opioid detoxification also receive psychosocial support?



Professor Nicholas Lintzeris
Director - Community Based Treatment Interventions, Drug & Alcohol Services South Australia

Long-acting formulations: a paradigm shift in treatment?

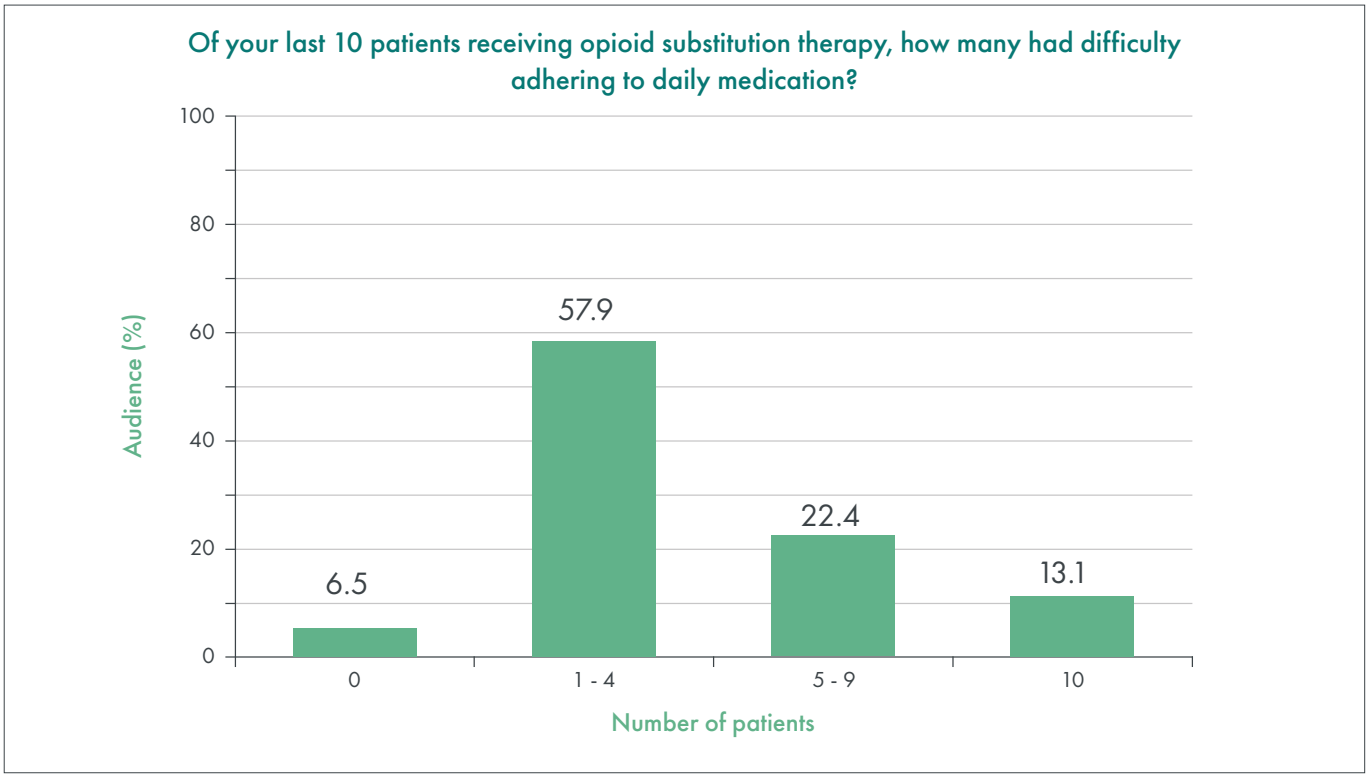
The arrival of long-acting buprenorphine (BPN) formulations is perhaps the most exciting and significant treatment advancement seen within the field of opioid substitution therapy (OST) in recent decades. Professor Lintzeris discussed the role of long-acting BPN and reviewed practical recommendations for its use. The benefits of long-acting BPN use were highlighted, including the prevention of BPN misuse and diversion, the reduction in costs and clinic resources, the improvement in patient adherence and the convenience for patient and service providers.[1]

The adherence benefit is significant for many treatment providers as voting results revealed that 93.5% of the audience faced treatment adherence issues in at least one of their last 10 patients receiving OST. Despite many advantages, it is important to consider that long-acting BPN may not suitable for all patients and several unknowns and challenges still exist.

There are currently two long-acting BPN products entering the market internationally: CAM2038 and RBP-6000. These products are currently not available everywhere, and approval and indication vary depending on location.

CAM2038

CAM2038 allows for weekly (8, 16, 24 or 32 mg)[2]



or monthly (64, 96 or 128 mg)[3] dosing through use of FluidCrystal® technology. Following subcutaneous injection, the liquid solution absorbs water and transforms into a controlled-release liquid crystal gel matrix. BPN is slowly released over time until depot biodegradation leads to complete resolution. This allows for slow dissipation of BPN plasma concentration compared with the peak and trough plasma concentrations seen with daily sublingual buprenorphine (SL BPN).[4,5] The process of CAM2038 initiation was explained, including the role of the dose conversion table in choosing a CAM2038 starting dose based on the daily SL BPN dose.[2,3]

Two key studies were discussed. The first, a double-blind double-dummy study involving new-to-treatment patients, demonstrated that CAM2038 was non-inferior to SL BPN + naloxone.[6] The second study, an open-label observational study, involved both new-to-treatment (n=37) and existing patients who had received SL BPN (n=190). A retention rate of 82.8% at 6 months and 73.6% at 12 months was seen in the patients receiving CAM2038. The number of new-to-treatment patients achieving opioid-free urine while on CAM2038 increased over time. Additionally, the stable patients who transferred from SL BPN to CAM2038 continued to remain stable.[7] Of the patients who had experienced both treatments, 83% rated CAM2038 as 'slightly better' or 'much better' than SL BPN.[5] Professor Lintzeris pointed out that some patients preferred the SL BPN, noting the importance of acknowledging the patient's perspective and matching the treatment modality accordingly.

RBP-6000

RBP-6000, is a monthly subcutaneous injection that uses the Atrigel® delivery system, which consists of biodegradable polymers dissolved in a biocompatible solvent. Following injection, precipitation of the polymer occurs, which leads to the creation of a solid depot containing BPN. BPN is then released via diffusion from, and biodegradation of, the depot. This provides sustained BPN plasma levels over the dosing interval. It was highlighted that patients must be on SL BPN for at least 7 days before starting RBP-6000. They are then initiated on 300 mg monthly for the first two months followed by maintenance on either 100 mg or 300 mg monthly, depending on their response.[8,9]

The efficacy of RBP-6000 was assessed in a randomised, double-blind, placebo-controlled study. Patients entered this study with an open-label run-in phase of up to 2 weeks treatment with SL BPN + naloxone. Eligible patients were then randomised to receive RBP-6000 300 mg/300 mg (n=201), RBP-6000 300 mg/100 mg (n=203) or the placebo (n=100) monthly. The 300 mg/300 mg regimen group received 6 monthly doses of RBP-6000 300 mg while the 300 mg/100 mg group received 2 monthly doses of RBP-6000 300 mg followed by 4 monthly doses of 100 mg. Participants' abstinence from opioid use, defined using self-reporting and urine samples negative for illicit opioids, was higher in both RBP-6000 regimen groups versus the placebo group. Patient retention was also higher in the RBP-6000 groups compared with the placebo group with more than 60% of participants in the RBP-6000 groups completing the 6-month study versus only 34% of the placebo group.[10]

2,3,5,8,9

Drug characteristics	***CAM2038***	***RBP-6000***
Dosage regimen	Weekly or monthly	Monthly
Administration route	Subcutaneous injection	Subcutaneous injection
Delivery mechanism	FluidCrystal® technology	Atrigel® delivery system
Injection site(s)	Abdomen, arm, buttock, thigh	Abdomen
Storage	Room temperature	Cold storage (4°C)

Future challenges

Both of these long-acting formulations are designed to be administered by healthcare providers only and not dispensed to the patient under any circumstances. Potential adverse events were acknowledged, including the potential systemic effects of BPN (e.g. headache, insomnia, nausea, vomiting and constipation), as well as local injection site reactions.[2,3,8,9]

Professor Lintzeris concluded that these new products are valuable additions to the armamentarium of OST, but that there are still unknown factors and challenges remaining. For example, how can patients be transferred between long-acting BPN and methadone? What is the cost-effectiveness of long-acting BPN? Will long-acting BPN be an option for use in the prison setting? Going forward, it will be necessary to update guidelines, train healthcare professionals, organise drug handling and supply chains, ensure these treatments are not automatically prescribed to all patients, and decide how patients can be optimally informed.

Conference feedback revealed that 90% of delegates appreciated this content and found it helpful

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Dr Magdalena Harris
London School of Hygiene & Tropical Medicine, UK

People who use drugs: what do they think about pharmacotherapy?

The previous talks focused mainly on pharmacotherapy; however, numerous social and cultural factors also impact drug treatments and their effects. Dr Harris's talk provided an insight into these factors, highlighting that people who use drugs (PWUD) are not a homogenous group with a single perspective and that their OST medication choice should be a shared decision between the patient and their clinician.

The issue of ambivalence to pharmacotherapy

Dr Harris explained how PWUD can experience profound ambivalence regarding OST due to the tension between freedom and control. OST can enable freedom and a sense of stability, as well as removing the fear of arrest and need to generate money for illicit drugs. However, at the same time, an individual may feel 'controlled' by OST due to the imposition of restrictive treatment regimens and drug side effects. Dr Harris reflected that some PWUD refer to methadone as 'liquid handcuffs'. A participant in one of Dr Harris's studies commented that methadone allowed him:

'some sort of normality of life'

...but also made his life feel...

'just like one big appointment'

What influences this ambivalence?

Numerous factors may influence this ambivalence in patients. Dr Harris explained how some PWUD feel that all the power in the prescribing relationship lies with the clinician. Patients may be reluctant to contribute their own opinion about their OST, for fear it may jeopardise their prescription. A participant in one of Dr Harris's studies commented that:[1]

'...the person who writes the script, they hold the power...'

Some PWUD avoid OST entirely due to fears of social service interventions, for example, potentially losing their children. These patients may instead resort to buying methadone on the street.[2]

The environment and process by which OST is dispensed can impact PWUD, with restrictive hours and location of services creating barriers to treatment. In addition, negative interactions with staff and feelings of stigmatism can adversely affect the self-worth and self-perception of PWUD. As one of Dr Harris's study participants observed:[3]

'They would literally watch you and follow you to the door'

A particularly concerning impact of these negative interactions is that it may deter PWUD from accessing other services such as needle and syringe exchange programmes or HCV/HIV care.

The concept of supervised consumption versus take-away medication is also important. Supervised consumption may create a sense of mistrust among certain PWUD and lead to disengagement from services. Dr Harris highlighted how this distrust around supervised consumption led to one of her study participants disengaging from his HCV treatment. Many participants commented on how important self-regulation is for them to feel in control of their own medication. Inflexibility regarding OST is a serious issue for PWUD. For example, if individuals miss their dose pick-up, especially a weekly pick-up, it can lead to withdrawal and unsafe injecting practices, which can increase the risk of bloodborne viruses. Fear of inability to acquire their OST medications may also deter individuals from presenting themselves to and staying in hospital to address other health concerns.[1]

Are long-acting formulations the solution?

It was emphasised that long-acting formulations are not a quick-fix solution. Yes, they may be embraced by some PWUD but others will still feel an ambivalence regarding the tension between freedom and control. While long-acting formulations can remove the need for daily appointments and provide ease of mind against missed doses, they may also cause a sense of disempowerment due an inability to self-regulate or remove the medication.[4]

Dr Harris stressed the importance of recognising and working with this ambivalence in a clinical setting. Patients should be offered multiple treatment options using a shared decision-making process. Going forward, efforts should be increased to remove the multiple barriers caused by stigma, inflexibility and restrictive policies.

Conference feedback revealed that 91% of delegates appreciated this content and found it helpful

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Panel discussion key highlights

The panellists acknowledged that during OST dispensing, and needle and syringe exchange, multiple pharmacy staff members may be in contact with PWUD. These interactions are all potential sources of stigma generation which can determine whether PWUD engage or disengage from services. It was recommended that training should therefore target all staff members and not just pharmacists. The training of staff, however, is not always a straightforward process. Professor Lintzeris commented on how the average community pharmacy in Australia has nine different pharmacists working over a seven-day period, including locums. Consequently, it can be difficult to provide staff with adequate training and for them to form strong and stable patient relationships due to continuous staffing changes.

Concerns regarding the potential coercive use of long-acting buprenorphine were also raised. It was discussed that, especially in areas with poorly set up treatment systems and long distances to travel, long-acting BPN may be imposed as a quick-fix solution. The panellists agreed that long-acting BPN will be embraced by many PWUD. However, it is vital to understand that long-acting BPN will not suit every patient and it must only be used based on a shared decision-making process with the patient.

The commitments to change were then disclosed, bringing this enlightening discussion to an end.

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