Position paper on opioid treatment for chronic non-cancer pain

The Israel Pain Association, the Israel Association of Family Physicians, the Clinical Pharmacology Association, the Psychiatric Association, the Society for Addiction Medicine

-October 2016-

• Introduction

Chronic pain is considered a disease in and of itself that affects about 20% of the adult population. Apart from the personal suffering it causes the individual, chronic pain is also a public health issue due to its broad social implications, also poses a substantial financial burden on society.

For the past two decades, opioid analgesics have been used to ease chronic non-cancer pain (CNCP) as well. However, contrary to the unequivocal agreement on the role of opioids in the relief of acute pain or cancer pain, heavy concerns have been raised in recent years regarding the continued use of opioids in the treatment of CNCP. These concerns have been expressed in a series of articles, originating primarily in North America (USA and Canada). These papers show high rates of abuse, addiction and deaths in CNCP resulting from use of opioids. These articles urge physicians and health policy makers around the world to reconsider the policy of prescribing opioids to treat CNCP.

A series of response articles testifies to the fact this problem of abuse, does not exist in European countries. Although there is no conclusive explanation of the difference between the two continents, it may be that the prescription habits and the drug consumption habits differ between the USA and Europe. Indeed, the medical consumption of opioids per capita in the USA is at least 2-3 times higher than in Western European countries.

There seems to be an evident need nowadays to improve the efficacy and safety of opioid use as treatment for CNCP. The improvement must involve a balanced and
responsible prescribing of opioids: a balance must be found between the “opiophobia” approach and the “over treatment” approach. The “opiophobia” approach is now prevalent in North America and it contends that opioids need not be prescribed for all CNCP. This approach might result in lack of treatment in patients for whom opioid treatment is justified. The “over treatment” approach is characterized by excessive and unjustifiable prescriptions. This approach might increase the risk for addiction and many other side effects.

Our position is that opioids should continue to constitute an important and vital component of the pain treatment arsenal. Doctors should use them in the best and most responsible way, i.e. following a thorough diagnosis, establishment of treatment goals, review of alternative treatment options subject to the multimodal concept, assessment of risk factors of prolonged use of opioids, and a periodical re-evaluation of the achievement of the treatment goals and its safety.

The purpose of this position paper is to provide physicians in Israel with useful tools to facilitate the effective, correct and safe use of opioids in CNCP patients. Its main ideas rely on an integration of data from relevant scientific literature and expert opinions. In writing this position paper, we considered the fact that any change of policy should be made cautiously and in a manner commensurate with the Israeli reality. Therefore - there may be discrepancies between its content and the content of similar documents recently published overseas.

Finally, the purpose of this position paper is to share new insights on pain treatment and management, which is moving towards personally tailored pain relief, adjusted according to the individual patient’s pain characteristics and his expectations.

- **Definitions**

In order to form a common language between physicians, please find enclosed several definitions of terms that appear in the document. We emphasize that the concern for opioid addiction is sometimes due to the failure to differentiate between effects of physiological dependency, tolerance, pseudo addiction and addiction. Differentiating between these is crucial to the full understanding of the position paper. The definitions are as follows:
a) **Opioids**: All natural and synthetic drugs that operate by binding to opioid receptors and which are used for pain relief. These are drugs that contain codeine, morphine, hydromorphone, oxycodone, fentanyl, buprenorphine and methadone.

b) **Physiological Dependence** – A condition where the body physiologically adapts to a drug (in this case, an opioid). This means the onset of withdrawal symptoms when the opioid dosage is quickly reduced, discontinued altogether, or when an opioid antagonist is administered (naloxone).

c) **Withdrawal Syndrome** – A normal and expected effect when drugs are discontinued in a sudden manner (such as opioids, corticosteroids, benzodiazepines etc.), or when a drug antagonist is administered. Symptoms includes agitation, anxiety, sweating, dilated pupils, diarrhea, intensified pain and so on. Withdrawal syndrome following a sudden treatment discontinuation will develop in most opioid patients, but it does not suggest an addiction. Withdrawal symptoms can be prevented by gradually reducing the drug dosage over time.

d) **Tolerance** The body’s adaptation to the drug, which gradually brings about a reduction in one or more of its effects. Tolerance may develop both toward the drug’s analgesic effect and toward its side effects. For the most part, the reduction in the analgesic effect does not pose a clinical problem, since the opioid dosage can be raised as necessary or it is possible to switch to another opioid. Note that pain reappearance during treatment may also be the result of disease progression or pain aggravation, and not necessarily be due to tolerance. Tolerance does not testify to or suggest addiction.

e) **Addiction** - An addiction is a neuro-biological disease, with genetic, psychological and environmental components. An addiction can develop with or without physiological dependence during obsessive use of drugs for a purpose other than pain relief, using the drug despite its causing damage, inability to control drug intake and/or craving to use the drug not for pain relief purposes, and deterioration in daily function due to obsessive preoccupation with trying to obtain the drug and consuming it. Taking care to prescribe opioids according to the rules guaranteeing correct use of opioids, minimizes the possibility of developing an addiction.
f) **Pseudo Addiction** - Patients who suffer from pain become focused on the need to achieve pain relief and appear to the onlooker to be addicted. A real addiction can be differentiated from a pseudo addiction by the patient's reaction to the analgesic treatment. Dosage increase not accompanied by euphoria, sedation or loss of control, but which results in an improvement in the patient's function, testifies to a pseudo addiction. Pseudo addiction is not a maladaptive behavior and will resolve when the correct pain balance is achieved.

g) **Misuse** – Using opioids not as instructed by the physician and/or not for medical needs.

- **Recommendations:**

a) **Recommendations for prescribing opioids for chronic non-cancer pain**

1. Opioids should not be included in the first line of treatment of chronic non-cancer pain.
2. Use of opioids may be considered only after prior standard of care attempts have failed or when there is a contraindication against the use of other analgesics.
3. Opioid monotherapy is not recommended. The recommendation is to combine opioid treatment with other treatments, such as physical therapy, concomitant drugs, invasive procedures, psychological support.
4. Before commencing treatment with opioids, try and reach a diagnosis of the pain syndrome that is as accurate as possible.
5. When several physicians are involved in the treatment of the pain (such as: family physician, pain physician, another specialist), one of these physicians will be appointed to manage the treatment, write the prescriptions and manage communication between all caregivers.
6. Before commencing opioid treatment, the attending physician prescribing opioids must provide a detailed explanation, make sure that the patient properly understood the explanation and reach an agreement with him on the following points:
   i. Benefit versus possible risks, and coping with side effects
   ii. The type of the drug, its dosage and its suitability for the patient.
iii. The parameters for the therapeutic trial’s success, according to which continuation or discontinuation of the treatment will be determined.


7. The patient needs to be closely monitored during the trial period (titration). Further on, larger intervals are recommended between follow-ups, providing that they do not exceed three months, as long as the drug’s dosage is stable. With any change of dosage, it is advisable to resume close monitoring until balance is regained. Patients at high risk for addiction should be monitored more frequently.

Treatment necessitates accurate documentation, monitoring of side effects, and will also include the issue of addiction and comorbidity.

b) Principles of treatment

Implementing the following principles is recommended during opioid treatment:

1. Preference for oral or transdermal administration
2. Use of long-acting drugs with a well-defined supplementation of rescue doses of short-acting opioids for the treatment of “pain attacks”. It is not advisable to combine two drugs with similar pharmacokinetic properties. For example: two short-acting opioids or two long-acting opioids.
3. Start with low dose opioids and adjust/increase the dosage depending on the response.
4. Exercise extra caution when adjusting dosage for children, the elderly and patients with liver and kidney function disorders.
5. In pregnant women, use of opioids is to be considered while weighing the benefit against the risks for the mother and the fetus. One should consider discontinuation of opioid treatment during pregnancy if possible.
6. Six to eight weeks of trial treatment are a reasonable time frame for making a decision whether to continue treatment with opioid drugs for a long period.
7. When there is a history of repeated increases in opioid dosage and unsatisfactory pain relief, this trend of dosage increase is not recommended without consultation with an analgesics medicine specialist.
8. For patients whose overall opioid dosage exceeds the equivalent of 100 mg oral morphine a day, periodic follow-up at a pain clinic is recommended.
c) Patient choice

1. Use of opioids in dysfunctional pain syndromes such as fibromyalgia or irritable bowel syndrome is not advisable.
2. Chronic use of opioids for primary headaches is not advisable.
3. Exercise extra caution before starting opioid treatment in patients with risk factors for opioid addiction, such as:
   i. Addiction to/abuse of alcohol, drugs, tobacco and/or other medications (past or present).
   ii. Family history of addiction
   iii. Existence of a psychiatric disorder
   iv. Hostile social environment (dysfunctional family) – substantial psychosocial problems or involvement with the law
   v. History of child abuse

In patients for whom there is uncertainty regarding the risk for addiction, it is recommended to use a validated Hebrew version of one of the following questionnaires assessing such risk:
ORT = Opioid Risk Tool – before treatment onset
PDUQ = Prescription drug use questionnaire
COMM = Current opioid misuse measure- in the course of treatment


d) Rules for treatment discontinuation

In circumstances where patient behavior raises suspicion for misuse of/addiction to opioids, there is room to consider treatment discontinuation. These circumstances include:

1. Dosage escalation at patient discretion.
2. Asking for prescriptions from other sources/excessive preoccupation with getting the drug.
3. Recurring “loss” of prescriptions or drugs.
4. Constant report of absence of pain improvement and/or reduced functionality
5. Urine tests that suggest irregular use (such as use of opioids/drugs in addition to those prescribed).

Discontinuation of opioid treatment for any reason must be done gradually to prevent withdrawal syndrome.
e) Treatment of addiction

When there is suspicion for addiction, the following steps should be taken, depending on the circumstances:

1. Referral to a psychiatrist dealing with addictions therapy.
2. Referral for treatment in a designated framework for patients suffering from an addiction.
3. Change of opioid treatment – withdrawal (in designated center – such as the Ministry of Health drug rehabilitation centers), or referral to a buprenorphine or methadone center if continued treatment with opioids is necessary.
4. Under all circumstances – adherence to therapeutic continuity and continued rehabilitation and withdrawal support (psychosocial treatment of addictions in municipal day center or therapeutic community, self-help group, comorbidity centers etc.).

f) Additional general recommendations

1. It is necessary to develop a central computer registration and monitoring system that will allow for the control and supervision of opioid dispensation in pharmacies across Israel, both private and public: Prescription Drug Monitoring Programs by Electronic Health Records (EHR).
2. It is necessary to promote the education of medical students and of physicians in all professions and levels regarding the benefits and risks associated with long-term administration of opioids.

*Note: the instructions are written in masculine tense but refer equally to both genders*

*Prepared by:* Eisenberg Elon, Brill Silviu

Download the full document from www.europeanpainfederation.eu under ‘Education’ category and core curricula sub-category

Participants

Eisenberg Elon, Brill Silviu, Goor-Arieh Itay, Dolberg Orit, Midbari Ayelet, Schwartzman Pesach (The Israel Pain Association), Daliyahu Yael, Lev-Ran Shauli, Roshka Paula (the Psychiatric Association, the Israeli Society for Addiction Medicine), Simovich Vered (the Israel Association of Family Physicians), Krivoy Norberto (the Clinical Pharmacology Association)
g) Select literature


10. van Amsterdam JG, Wartenberg HH, van den Brink W. Steep increase in prescribed opioids in the Netherlands. Are we going the same way as the U.S.? Ned Tijdschr Geneeskd 2015;159:A9245


