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## A 10-Year Evaluation of Chronic Pain Patients Treated with Opioids

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### Summary

Over the past 15 years laws and guidelines have been widely promulgated to allow physicians to prescribe opioids for severe, chronic pain patients who have non-malignant conditions. To date little is known about the outcomes of long-term opioid pain therapy. Reported here is an evaluation of 24 patients with non-malignant conditions who have been in continual opioid treatment for at least 10 years. Data collected indicates that some chronic pain patients greatly benefit from long-term opioid therapy. Almost all (22 of 24: 91.7%) patients report that their pain has permanently decreased over time, and the great majority (20 of 24: 83.3%) believe that opioids continue to relieve their pain as well as when treatment was initiated. All patients report they can now do a variety of activities and physical functions they could not do prior to opioid therapy. The major complications of opioid therapy detected to date are hormonal abnormalities which can be easily managed with replacement therapy.

*Key Words:* Chronic Pain - Opioid Treatment

### 1. Introduction

The general public has, in recent years, demanded improved pain cure including the use of opioid drugs. A great part of this demand has been implementation of laws and promulgation of regulations and guidelines that permit physicians to prescribe opioids for severe chronic pain. The author resides and practices in the State of California, USA that has, in the past 15 years, allowed physicians to prescribe and patients to receive opioids by enacting an "Intractable Pain Act", "Pain Patient's Bill of Rights", and issuing written guidelines for opioid treatment. Consequently, enough severe, non-malignant pain patients have now been treated with opioids to begin long-term evaluation of this treatment. Reported here is an evaluation of 24 severe, chronic pain patients who have taken daily high dosages of opioid drugs for at least 10 consecutive years. These patients remain in opioid treatment as they have had positive outcomes.

Despite the energetic and forceful efforts to make opioids available for non-malignant pain treatment, there are almost no reports available on the outcome and merits of opioid therapy beyond about three years [5-7].

Information regarding the long-term outcomes of opioid treatments is needed to determine if long-term, opioid therapy produces a quality life with acceptable side-effects, and if opioid treatment may permanently reduce pain.

#### 1.1 Criteria for Admission to Opioid Treatment

24 Patients have been treated at an ambulatory clinic in Los Angeles (West Covina) County, California, USA. All were referred by physicians who had initiated a variety of pain treatments that were incompletely controlling the patient's pain. Documentation of chronic pain severe enough to treat with opioids was done by medical and pain history, review of past medical records, physical exam showing some evidence of sympathetic discharge (i.e. tachycardia, mydriasis, hypertension,) and family member validation that pain was disabling and interfering with activities of daily living. To be eligible for opioids, patients had to describe their pain as "constant" and report that it impaired some physiologic functions such as sleep, eating, concentration, memory, and endurance.

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## 1.2 Clinical Treatment Procedures

The initial choice of opioid medication was based on previous exposure or experience and the options offered by the patient's health insurance plan. Initially patients attended the clinic daily or weekly to stabilize following opioid induction and titration. After this period, follow-up visits were monthly. Long-acting opioid dosages were titrated upward over a 4 to 6 week period to reduce baseline pain and suppress sympathetic discharge signs. Short-acting opioids were added to the regimen to provide rescue medication for pain flares or breakthrough pain. All patients were taught stretching and weight-bearing exercises specific to their pathology. All patients were highly encouraged to take daily vitamins and other dietary supplements and to eat a protein-rich diet to provide an abundant supply of systemic, amino acids. Periodic opioid blood levels have been determined to verify sufficient therapy, and patients are periodically tested for serum levels of cortisol, pregnenolone, and testosterone.

## 2. Methods

In preparation for and just prior to this conference, 24 patients who have daily taken opioid medication for a minimum of 10 years were evaluated by chart review and a 19-point questionnaire completed by the patient. Specific questions were asked to provide basic knowledge related to the treatment outcomes of these individuals:

1. Has pain increased, decreased, or remained static?
2. What activities can now be done that couldn't be done before beginning opioid treatment?
3. What complications from opioids or the pain have developed during treatment?
4. Do opioids still provide pain relief or have they lost potency?
5. What exercise and dietary measures do you do?

Charts were reviewed for details including opioid dosage, serum levels, and medical complications or consequences.

### 2.1 Characteristics of Patients

This group of patients consists of 16 females and 8 males. Ages range from 30 to 79 years. Major causes of their pain are post trauma neuropathies and arthropathies, spine degeneration, and abdominal adhesions or neuropathies. (Table 1) The opioids taken are quite varied, but all patients take the long-acting opioid, methadone, or a long-acting morphine, oxycodone, or fentanyl formulation and one or more short-acting opioids for breakthrough pain or emergency pain flares (Table 2). All take a variety of ancillary medications such as muscle relaxants, sleep aids, hormone replacements, and dietary supplements. The majority (22; 96.7%) report they do regular stretching exercises. Most eat a breakfast (18; 75%) and have a protein-rich diet. (20; 83.3%) all take one or more vitamins

or other dietary supplements (Table 3).

Table 1. Causes of chronic pain requiring opioids (N=24)

Cause	N (%)
Post-trauma with arthropathies and neuropathies	7 (29.2)
Spine degeneration	6 (25.0)
Abdominal Adhesions or Neuropathies	5 (20.8)
Headache	2 (8.3)
Fibromyalgia	3 (12.5)
Hip Necrosis	1 (4.2)

Table 2. Opioid currently used (N=24)

N° of opioids currently used	N (%)
1	2 (8.3)
2	14 (58.3)
3	8 (33.3)
Opioids currently used	
Hydrocodone	6 (25.0)
Morphine	8 (33.3)
Hydromorphone	4 (16.7)
Oxycodone	9 (37.5)
Fentanyl	10 (41.6)
Methadone	7 (29.2)
Meperidine	1 (4.2)
Propoxyphene	1 (4.2)
Levorphanol	1 (4.2)

## 3. Results and Outcomes

Twenty Two (22; 96.7%) of 24 patients believe their pain has decreased over time and 22 of 24 (83.3%) believe their opioids still provide the same relief as when they started treatment. The remaining 4 patients report their opioids don't "hold and provide pain relief as well as before". (Table 4) Patients were asked if they are now able to do a variety of activities and physical functions which they could not do prior to initiating opioid therapy. All patients reported one or more activities or functions that they can now do. For example, a majority reported they can get out of bed everyday, shop or visit friends, take a trip in a car, or take walks. Significant, but less that a majority, reported that before opioid treatment they

Table 3. Characteristics of chronic pain patients taking daily opioids for 10 or more years (N=24)

Age	Range 30–79
Males	8 (33.3%)
Females	16 (66.7%)
Length of Time In Opioid Treatment	10–35 Range (yrs)
N° Who Report Their Pain Has Decreased	22 (91.7%)
N° Who Report That Opioids “Still Hold and Provide Pain Relief”	20 (83.3%)
N° Who Report Opioid “Doesn’t Hold and Provide Pain Relief as Well as Before”	4 (16.7%)
N° Who Take a Dietary Supplement	
Vitamins/Minerals	21 (87.5%)
Antioxidants/Amino Acids	9 (37.5%)
Fish Oils	6 (35.0%)
N° Who Eat a Breakfast	18 (75.0%)
N° Who Report Daily Significant Protein Intake	20 (83.3%)
Consecutive Hours of Sleep	1 to 4
N° Who do Stretching Exercises and Walk	22 (91.7%)

couldn’t dress without assistance, drive a care, attend church, have normal sexual relations, garden, or care for a pet. (Table 4)

A number of new or emerging medical conditions were identified in this group over the 10-year period. (Table 5) All these conditions directly or indirectly involve the endocrine and cardiovascular systems. All but one male developed hypotestosteronemia. One male developed severe anemia requiring blood transfusions that resolved with testosterone replacement. Five (20.8%) females developed low serum pregnenolone or cortisol levels requiring replacement. Several patients developed osteoporosis (5, 20.8%) or loss of dentition (10, 41.7%). Weight gain, diabetes, and hypertension were common. Neurologic complications of seizures, myoclonus, tremors, hyperalgesia, or dementia have been observed. No hepatitis, renal, or gastrointestinal complications with the exception of minor constipation have been detected. One patient has developed symptomatic coronary arteriosclerosis.

#### 4. Discussion

While several reports of opioid-treatment of non-ma-

Table 4. Activities and functions patients report they can now do with opioid treatment (N=24)

Activity / Function	N (%)
Get Out of Bed Everyday	17 (70.8)
Dress Without Assistance	8 (33.3)
Eat a Regular Diet	9 (37.5)
Drive a Car	5 (20.8)
Attend Church	9 (37.5)
Shop or Visit Friends / Relatives	17 (70.8)
Have Normal Sexual Relations	7 (29.2)
Play Games	4 (16.7)
Work Puzzles	4 (16.7)
Read Newspapers, Books, Magazines	9 (37.5)
Take a Trip in a Car	13 (54.2)
Hold a Regular Job	5 (20.8)
Garden	9 (37.5)
Care for a Pet	10 (41.7)
Participate in a Hobby / Collection	8 (33.3)
Take Walks	16 (66.7)

Table 5. New medical conditions during opioid treatment (N=24)

Condition	No. %
Tachycardia	8 (33.3)
Hypertension	5 (20.8)
Diabetes	3 (12.5)
Hyperlipidemia	4 (16.7)
Loss of over 50% of teeth and/or 10 or more fillings	10 (41.7)
Osteoporosis	5 (20.8)
Hormone abnormalities	12 (50.0)
Coronary heart disease	1 (4.2)
Anemia Requiring Transfusion	1 (4.2)
Weight Gain	12 (50.0)

lignant conditions relate positive results, this report is the only one to evaluate patients with non-malignant conditions who have been treated with opioids for 10 or more years [1, 5-7]. The longest follow-up we can identify is about three years. [5]. A most cogent outcome is that the majority of patients reported that their pain had decreased and their opioid drugs were still effective in relieving their pain. Patients reported a variety of activities and physical functions that were possible with opioid treatment.

In addition to humane, relief of suffering, the ability of patients to be able to have a quality life will continue to drive a public demand for opioid treatment.

Some patients developed medical conditions during opioid therapy. Just how many are pain induced, opioid produced, or simply inherent to the patient is not clear. Opioid therapy is known to lower serum testosterone in males, and this occurrence was found in most male patients [4]. Severe pain is known to over-stimulate the pituitary-adrenal-axis and raise serum cortisol and catecholamine levels that may be related to the development of obesity, diabetes, tooth decay, osteoporosis, hyperlipidemia, tachycardia, and hypertension [3]. No neurologic complications including dementia, hyperalgesia, tremor, or seizures have been detected [2]. It may be that these conditions would be more prevalent and serious in this group if they had not been treated with opioids. It is also very possible that opioids prevented early deaths in this group. Much additional study is needed to determine cause and effect of medical conditions in opioid-maintained patients.

On-going evaluation of long-term pain patients will have to be done without the benefit of comparisons with randomized, placebo controls. It is now considered unethical and even illegal in some states such as California to withhold opioid treatment if a patient requests it.

## 5. Conclusions

The majority of long-term, opioid treated patients report that their pain has decreased suggesting that opioids may allow or even promote some neurologic healing. It may be that opioid therapy prevents a number of medical complications of pain and prevents early death that may emanate from over-stimulation of the pituitary-adrenal-axis and possibly by excess electrical stimulation produced by damaged nerves. No neurologic complications such as dementia or hyperalgesia have been observed. Even though the number of patients evaluated here is relatively small, the great improvement in their quality of life and physical functioning is so positive and the complications of the therapy so easily managed that long-term opioid therapy should continue to be provided and evaluated.

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## Conflict of Interest

The author has no relevant conflict of interest to report in relation to the present study.

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