

A 10 AND 20 YEAR  
FOLLOW-UP OF SEVERE,  
CHRONIC PAIN PATIENTS  
TREATED WITH DAILY  
OPIOIDS

by

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Partially presented at

EUROPAD CONFERENCE 2008  
Sofia, Republic of Bulgaria

## **ABSTRACT**

Over the past 20 years laws and guidelines have been promulgated throughout the USA to allow physicians to prescribe opioids for chronic pain patients who have non-malignant conditions. To date, however, little is known about the outcomes of long-term opioid pain therapy. Reported here is an evaluation of 30 patients with non-malignant conditions who have been in continual opioid treatment for at least 10 years. Ten (10) of these patients have been in continuous opioid treatment for over 20 years. Data collected indicates that some chronic pain patients greatly benefit from long-term opioid therapy. Almost all patients report that their pain has permanently decreased over time, and the majority believe that opioids continue to relieve their pain now as well as when their treatment was initiated. All patients report they can now do a variety of activities and physical functions that they could not do prior to opioid therapy.

## Introduction

The general public has, in recent years, demanded improved pain care 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.

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.<sup>1-4</sup> Information regarding the long-term outcomes of opioid treatment is needed to determine if long-term, opioid therapy produces a quality life with acceptable risks, and if opioid treatment may lead to permanent reduction in pain.

In the 1970's and early 80's the author participated in a pilot effort to begin treating chronic non-malignant pain with opioids as well as identify those persons who were abusers of prescription, opioid drugs.<sup>5-8</sup> Both situations correctly appeared to be public health and clinical needs which have progressively emerged and been addressed until this time. Initially, a small cohort of non-malignant pain patients in Los Angeles County were admitted to out-patient, opioid therapy.<sup>2,8</sup> Some of the initial cohort are still alive and in treatment. Thirty (30) chronic, non-malignant pain patients treated with opioids for at least 10 years are reported here. Ten (10) of these patients have been treated for over 20 years, and they are individually listed in a Table to provide physicians and other interested parties information on some of the few long-term patients who are available for study. This follow-up shows that long-term, daily opioid therapy can be associated with positive clinical outcomes.

## Criteria For Admission To Opioid Treatment

Patients have been treated at an ambulatory clinic in Los Angeles (West Covina) County, California, USA. All were referred by physicians who had declared the patient to be intractable and had initiated a variety of pain treatments that were incompletely controlling the patient's pain. Documentation of chronic pain severe enough to require daily, around-the-clock dosing 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.

## 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 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. 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 urine and blood tests have been done to verify compliance and help eliminate any non-prescribed, abusable drugs.

## Methods

In June and July of 2008, the 30 patients reported here 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.

## Characteristics Of Patients

This group of patients consists of 18 females and 12 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 One) The opioids taken are quite varied, but almost all patients take a long-acting opioid formulation of morphine, oxycodone, fentanyl, or methadone. Most use one or more short-acting opioids for breakthrough pain or emergency pain flares. (Table Two) All take a variety of ancillary medications such as muscle relaxants, sleep aids, hormone replacements, and dietary supplements. The majority (27; 96.7%) report they do regular stretching exercises. Most eat a

breakfast (20; 66.7%) and have a protein-rich diet. (25; 83.3%). All take one or more vitamins or other dietary supplements. (Table Three)

### Results and Outcomes

Twenty Two (27; 96.7%) of 30 patients believe their pain has decreased over time and 25 of 30 (83.3%) believe their opioids still provide the same relief as when they started treatment. The remaining (5; 16.7%) patients report their opioids don't "hold and provide pain relief as well as before". (Table Three) 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, and reported one or more activities or functions that they can now do with opioid therapy. 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 than a majority, reported that before opioid treatment they couldn't dress without assistance, drive a car, attend church, have normal sexual relations, garden, or care for a pet. (Table Four) Table Five shows the 10 patients who have been followed for at least 20 years.

A number of new or emerging medical conditions were identified in this group over the extended time period of treatment. (Table 6) Most of these conditions appear to directly or indirectly involve the endocrine and/or cardiovascular systems. All but one male developed hypotestosteronemia. One male developed severe anemia requiring blood transfusions that resolved with testosterone replacement. Five (16.7%) females developed low serum pregnenolone or cortisol levels requiring replacement. Some patients developed osteoporosis (6, 20.8%) or loss of dentition (13, 41.7%). Weight gain, diabetes, and hypertension were common. Neurologic complications of seizures, myoclonus, tremors, hyperalgesia, or dementia have not been observed. No hepatitis, renal, or gastrointestinal

complications with the exception of minor constipation has been detected. One patient has developed symptomatic coronary arteriosclerosis.

### Discussion and Comments

While several reports of opioid-treatment of non-malignant 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.<sup>1-4</sup> The longest follow-up the author can identify is about three years.<sup>3</sup> 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. (Tables 4 and 5) In addition to humane, relief of suffering, the ability of patients to be able to have a quality life as demonstrated in these patients 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.<sup>9</sup> 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.<sup>10</sup> No neurologic complications including dementia, hyperalgesia, tremor, or seizures have been detected.<sup>11</sup> 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 that may develop in opioid-maintained patients.

On-going evaluation of long-term pain patients treated with opioids 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. Consequently, other groups of long-term patients in other parts of the country should be studied.

### Summary

The majority of long-term, opioid treated patients reported here stated that their pain had decreased over time 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 in the patients reported here. 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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## TABLE ONE

### PRIMARY CAUSE OF CHRONIC PAIN REQUIRING OPIOIDS

N = 30

<u>CAUSE</u>	<u>NO./%</u>
POST – TRAUMA WITH ARTHROPATHIES AND NEUROPATHIES	7 (29.2)
SPINE DEGENERATION	10 (33.3)
ABDOMINAL ADHESIONS OR NEUROPATHIES	5 (20.8)
HEADACHE	23 (8.3)
FIBROMYALGIA	3 (12.5)
HIP NECROSIS	2 (6.7)

**TABLE TWO**  
**OPIOID CURRENTLY USED**  
(N = 30)

<u>No. of Opioids Currently Used</u>	<u>No./ % Patients</u>
1 -	3 (10.0)
2 -	15 (50.0)
3 -	12 (40.0)
 <u>Opioids Currently Used</u>	
Hydrocodone	7 (23.3)
Morphine	10 (33.3)
Hydromorphone	5 (16.7)
Oxycodone	9 (30.0)
Fentanyl	14 (46.7)
Methadone	9 (29.2)
Meperidine	2 (6.7)
Propoxyphene	2 (6.7)
Levorphanol	2 (6.7)
Oxymorphone	2 (6.7)

### TABLE THREE

## CHARACTERISTICS OF CHRONIC PAIN PATIENTS TAKING DAILY OPIOIDS FOR 10 OR MORE YEARS

(N=30)

Age Range	30–79 years
Males	12 (40.0%)
Females	18 (60.0%)
Length of Time In Opioid Treatment	10–35 Range (yrs)
No. Who Report Their Pain Has Decreased	27 (90.0%)
No. Who Report That Opioids “Still Hold and Provide Pain Relief”	25 (83.3%)
No. Who Report Opioid “Doesn’t Hold and Provide Pain Relief as Well as Before”	5 (16.7%)
No. Who Take a Dietary Supplement	
Vitamins/Minerals	27 (90.0%)
Antioxidants/Amino Acids	14 (46.7%)
Fish Oils	8 (26.7%)
No. Who Eat a Breakfast	20 (66.7%)
No. Who Report Daily Significant Protein Intake	25 (83.3%)
Consecutive Hours of Sleep	1 to 4
No. Who do Stretching Exercises and Walk	27 (90.0%)

## TABLE FOUR

### ACTIVITIES AND FUNCTIONS PATIENTS REPORT THEY CAN NOW DO WITH OPIOID TREATMENT

N = 30

<u>Activity / Function</u>	<u>No. %</u>
Get Out of Bed Everyday	22 (73.3)
Dress Without Assistance	10 (33.3)
Eat a Regular Diet	11 (36.7)
Drive a Car	8 (26.7)
Attend Church	11 (36.7)
Shop or Visit Friends / Relatives	21 (70.0)
Have Normal Sexual Relations	10 (33.3)
Play Games	5 (16.7)
Work Puzzles	5 (16.7)
Read Newspapers, Books, Magazines	11 (36.7)
Take a Trip in a Car	16 (53.3)
Hold a Regular Job	7 (23.3)
Garden	10 (33.3)
Care for a Pet	13 (43.3)
Participate in a Hobby / Collection	10 (33.3)
Take Walks	20 (66.7)

## TABLE SIX

### NEW MEDICAL CONDITIONS DURING OPIOID TREATMENT

N = 30

<u>Condition</u>	<u>No. %</u>
HYPERTENSION	5 (16.7)
DIABETES	3 (10.0)
HYPERLIPIDEMIA	4 (13.3)
LOSS OF OVER 50% OF TEETH AND/OR 10 OR MORE FILLINGS	12 (40.0)
OSTEOPOROSIS	6 (20.0)
HORMONE ABNORMALITIES	16 (53.3)
CORONARY HEART DISEASE	1 (3.3)
ANEMIA REQUIRING TRANSFUSION	1 (3.3)
WEIGHT GAIN	18 (60.0)