

# Nanobubbles of O<sub>2</sub> and CO<sub>2</sub> for the treatment of Peripheral Neuropathy.

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## Abstract

Peripheral Neuropathy is frequently associated with neural structures hypoxia. Nanobubbles are able diffuse deeply through tissues and reduce inflammation and cell hypoxia. A prospective study on 29 neuropathic patients using topical application of nanobubbles of O<sub>2</sub> and CO<sub>2</sub> seems to indicate that this approach can be a be very safe and effective treatment to reduce pain in neuropathic patients with a pain reduction of 50% or more in 62% of the patients. Although still preliminary, these results compare favorably to the published effectiveness of gabapentin and pregabalin.

## Literature Review

In the United States more than 40 million people are affected by Peripheral Neuropathy. Overall, 33% are labeled as Diabetic, 33% as Idiopathic and 34% with other causes including hypothyroidism, auto-immune disease and chemotherapy. There are about 20 million people in the US who are diabetic; 70-80% of them suffer from peripheral neuropathy. Some studies have shown that about 25% of the 80 million population of prediabetic patients (60% of them will become diabetic) also suffer from neuropathy. Therefore, over thirty million neuropathic people are diabetic or pre-diabetic.

There are many treatment options. Simple treatments such as vitamins, physical therapy, or topical analgesics have very limited efficacy. The most common drugs (Gabapentin, Pregabalin, etc.) used to treat the neuropathic symptoms have limited effectiveness with frequent substantial side effects. Overall most patients are dissatisfied with their treatment and many of them are actively looking for better solutions.

Although the pathophysiology of this condition is complex and not fully understood, it seems to be very frequently associated with microvasculature deficiency and local hypoxia (1). Nanobubbles of gas are bubbles 50 to 200 nm in diameter; they are very stable and can be highly concentrated in solution. These nanobubbles will very readily diffuse into soft tissues. Nanobubbles of oxygen have been shown to reduce cellular hypoxia (2) and to possess anti-inflammatory and neuroprotective properties (3). In addition, normal saline solution containing oxygen nanobubbles is effective for improving blood oxygenation. Thus, the use of oxygen fine, micro or nanobubbles containing fluids is a potentially effective novel method for improving blood oxygenation in cases involving hypoxia, ischemic diseases, infection control, and anticancer chemoradiation therapies (4).

## Statement of Purpose:

The primary aim of this feasibility study was to evaluate the safety and efficacy of using topical application of water infused with nanobubbles of Oxygen and CO<sub>2</sub> to alleviate pain in patient suffering from peripheral neuropathy.

## Methodology and Procedure

A series of 29 consecutive patients suffering from neuropathy from various etiologies were treated using a footbath with 1 gallon of water infused with Nanobubbles of Oxygen and CO<sub>2</sub> for 20-30 minutes. The first 20 patients were treated in a water bath while the system was continuously infusing nanobubbles into the bath, while the remaining patients we treated using water that was infused with Nanobubbles a few hours before treatment. As the nanobubbles are very stable in solution, no difference was expected between the 2 populations and results are combined. The system used to produce nanobubbles was manufactured by Nanobubbling (Austin, TX).

Efficacy of the treatment was evaluated by a patient reported response of their overall pain level at baseline and after each treatment to verify the hypothesis that the treatment significantly reduced the pain.

## Level of Evidence

Level IV. Therapeutic

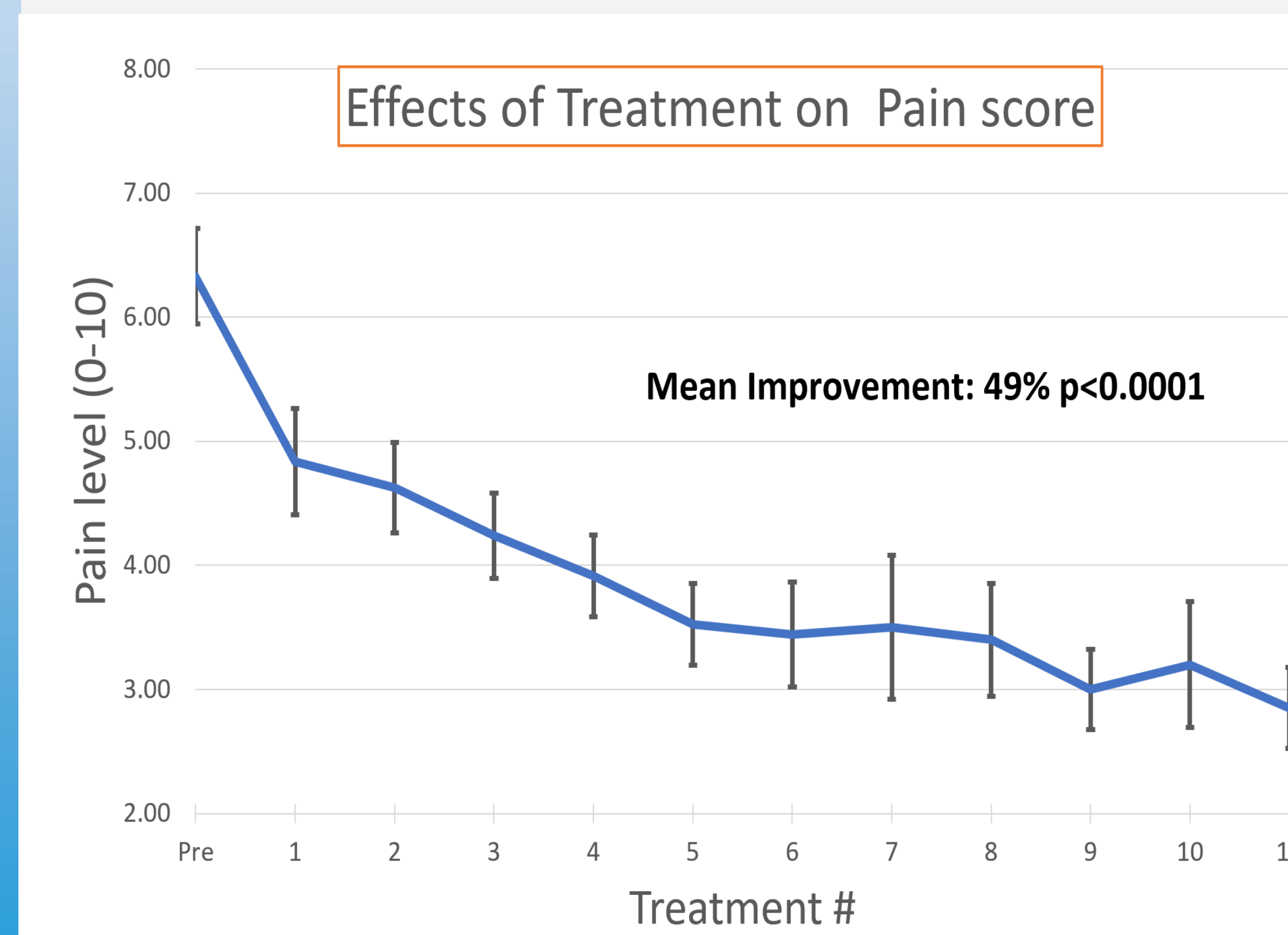
## Demographics

N=29	Mean ± standard deviation
Age	Mean: 71.9 ±10 (48 – 88)
Gender	F: 17 (59%) M: 12 (41%)
Etiology	Diabetes: 19 (66%) Unknown: 8 (28%) Chemotherapy: 1 (3%) Rheumatoid Arthritis: 1 (3%)
Time since Neuropathy onset	Mean: 6.35 ±8.45(0.5 – 35) yrs
Number of treatments	Mean: 7.8 ±3.74 (1 –11)
Time between treatments	3.75±3.86 (2-46) Days Mode: 2 Days

## Results:

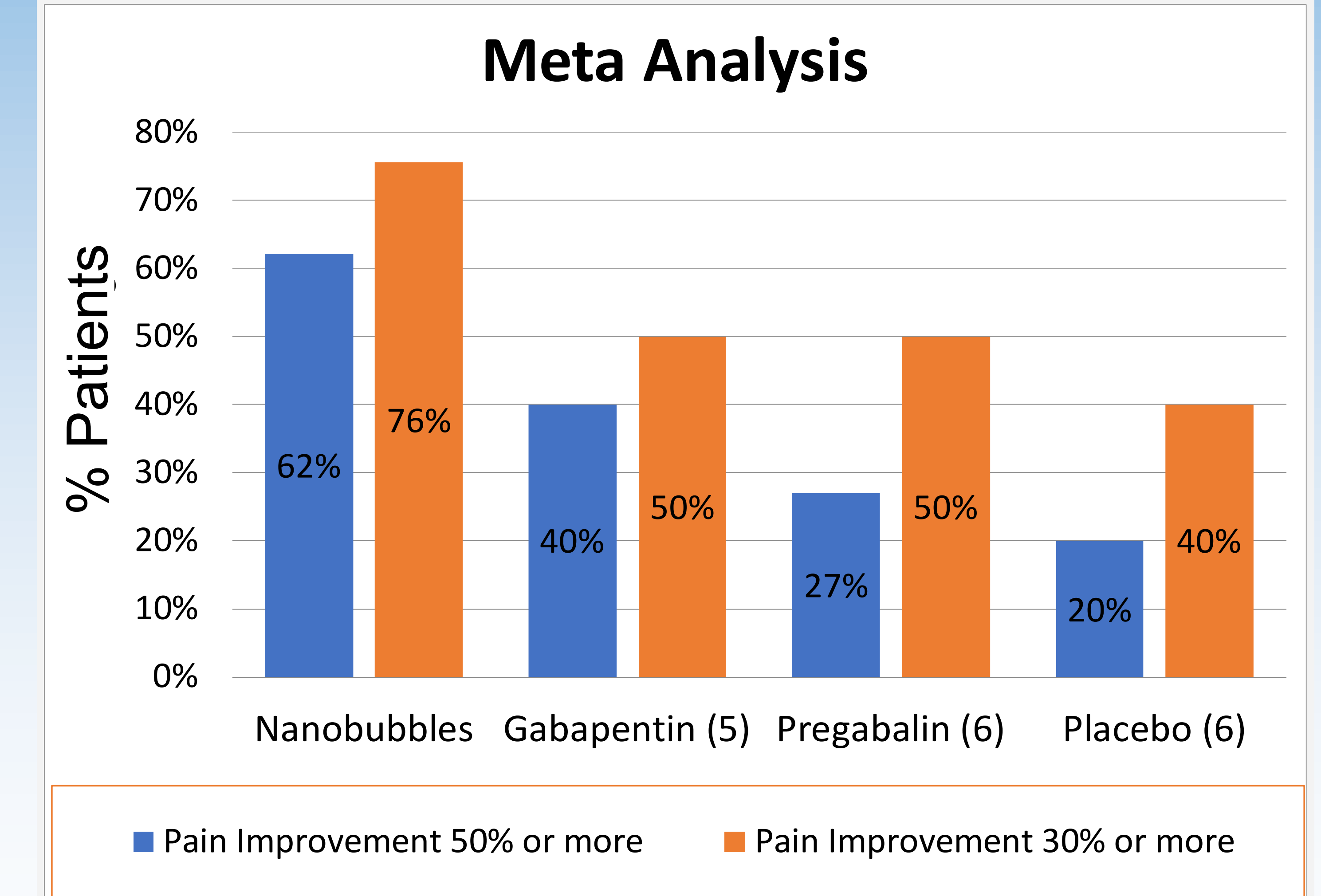
N=29	Mean ± standard deviation	Range
Complications / Side Effects	0	
Initial Pain (± standard error)	Mean: 6.33 ± 2.07	2.5 - 9
Final Pain	Mean: 3.19 ± 1.81	1 - 9
Relative Improvement	-49.59% ± 23%	p<0.0001
Patients with 50% pain reduction or more	18 (62.1%)	

Pain improved significantly (p<0.0001—Paired T-test) by the end of the treatments and only 2 patients, both diabetic, did not have any improvement. Pain level seems to decrease progressively with every treatment for the first 6 to 8 treatments. No correlation was found between the level of pain improvement and the etiology of the Neuropathy or the time since the onset



## Discussion and Conclusion:

The number of patients (18, 62.1%) who had an improvement of 50% or more compares very favorably with the results reported in literature for Gabapentin (5) or Pregabalin (6).



Several patients have also reported improvement in their sensitivity, and a few reduced intake of narcotics or Gabapentin. Restoration of sensitivity may also explain that 3 patients reported temporary increase of pain while “numbness” improved. More studies are required to better understand the effects of topical Nanobubbles on all the neuropathic symptoms. Although this data is based on a small sample size, it seems that topical application of nanobubbles of O<sub>2</sub> and CO<sub>2</sub> may be a safe and effective alternative for the treatment of peripheral Neuropathy for those patients who are dissatisfied with current pharmacological approaches.

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## Financial Disclosure:

Equipment to produce nanobubbles was provided by Nanobubbling LLC. No financial support was provided to perform this study.