



## Pain Management with Vitamin D

Author

**Dr Dina Soliman**

American Board in Regenerative Medicine from AARM

Interventional Regenerative Orthopedic Medicine Certified from AAOM

Member of AAOM and AABRM

### Abstract

*Vitamin D receptors are ubiquitous in tissue distribution, which opens the possibility for its unforeseen biological functions. It is very important in the treatment of many conditions including heart conditions, high blood pressure and high cholesterol. It is used for diabetes, obesity, muscle weakness, multiple sclerosis, rheumatoid arthritis, chronic obstructive pulmonary disease, asthma, bronchitis, premenstrual syndrome, tooth and gum disease. It is also used for skin conditions including vitiligo, scleroderma, psoriasis, actinic keratosis, and lupus vulgaris. Vitamin D boosts the immune system, preventing autoimmune diseases and preventing cancer. Prolotherapy is an injection treatment designed to stimulate tissue healing. Dextrose is the most commonly used proliferant solution with its different concentrations. Platelet rich plasma is very powerful because it delivers growth-factors to the tissues. Adult mesenchymal stem cells is the hot topic nowadays in the non-surgical field of pain management.*

**Objectives:** *Stimulate tissue regeneration by an injection technique called Prolotherapy using different proliferant solutions such as dextrose solution with vitamin D, platelet rich plasma, or adult mesenchymal stem cells. This treatment helps the tissues to regain their strength, to decrease the neurogenic inflammation and to stop the neuropathic pain.*

**Methods:** *In this paper, 270 patients suffering from chronic pain and dysfunction of different body areas (knees, hips and low backs), were treated with: (1) Dextrose prolotherapy with an extra or intra-articular vitamin D injection. (2) Platelet rich plasma "PRP". (3) Adult mesenchymal stem cells "AMSCs". The patients were assessed regarding the improvement of pain and function.*

**Results:** *Patients treated with dextrose and vitamin D in group (1) showed very good improvement regarding their musculoskeletal pain and function.*

**Conclusions:** *Adding vitamin D to dextrose prolotherapy helped the patients to show good results close to those of the patients treated with PRP or AMSCs, regarding the pain and function of the musculoskeletal system.*

**Keywords:** *Musculoskeletal Pain, Prolotherapy, Vitamin D, Dextrose, Platelet Rich Plasma, Stem Cells.*

### Introduction

Vitamin D is a group of fat-soluble secosteroids. The most important compounds in this group are vitamin D<sub>3</sub> (also known as cholecalciferol) and

vitamin D<sub>2</sub> (ergocalciferol)<sup>[1]</sup>. Cholecalciferol and ergocalciferol can be ingested from few foods and from supplements<sup>[2,3,4]</sup>. The major natural source is the synthesis of cholecalciferol in the skin from

cholesterol through a chemical reaction that is dependent on sun exposure (specifically UV radiation)<sup>[5]</sup>.

Sufficient vitamin D levels are important not only for a healthy skeleton but also for a healthy immune system. It is not strictly a vitamin, it is considered a growth hormone in the endocrine system as its synthesis and activation occur in different locations and it plays a role in a wide range of processes in the body<sup>[6]</sup>.

Vitamin D has unforeseen biological functions as its receptors are ubiquitous in tissue distribution. It regulates genes that govern the release of growth factors which are important for normal tissue growth and regeneration. It regulates a set of replication-linked genes which are critical for rapid cellular proliferation (DNA replication-differentiation switch)<sup>[7]</sup>.

Possible mechanisms for vitamin D in pain management are the anti-inflammatory effects mediated by reduced cytokine and prostaglandin release and effects on T-cell responses<sup>[8]</sup>.

In observational studies, low vitamin D levels have been associated with increased pain and higher opioid doses. Both observational and interventional studies have shown promising effects of vitamin D supplementation on cancer pain and musculoskeletal pain<sup>[9]</sup>. A recent systematic review of published RCTs concluded that vitamin D supplementation leads to a significantly greater mean decrease in pain score compared to placebo in patients with chronic pain<sup>[10]</sup>.

Prolotherapy is an injection treatment designed to stimulate healing. Dextrose is the most commonly used proliferant solution in prolotherapy. In osmosis, concentrated solutions cause a net flow of fluid across a semi permeable membrane causing cellular dehydration and releasing the cellular fragments in the extra-cellular space.

By upsetting the delicate balance of the cells, the arachidonic acid pathway is stimulated causing an influx of inflammatory cells and initiating the healing cascade. Also dextrose provides a gradient of a desirable nutrient which attracts the mobile

cells of the body's repair apparatus to the injection site<sup>[11]</sup>.

Platelet rich plasma (PRP) delivers the growth factors that stimulate the tissue progenitors. Platelet-derived growth factors are synthesized and stored in the alpha granules of platelets. Being a potent mitogen for cells of mesenchymal origin, they are released upon platelet activation to regulate cellular growth and division, stimulating the local tissue progenitor cells to facilitate the tissue maintenance, regeneration, growth and healing<sup>[11]</sup>.

Nowadays, stem cells are the hot topic in the non-surgical field of pain management. Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide - through mitosis - to produce more stem cells. Adult stem cells, are found in various tissues in the body, they are progenitor cells and act as a repair system for the body replenishing the adult tissues. Autologous adult mesenchymal stem cells are either derived from bone marrow aspirate (requiring drilling in the bone), adipose tissue (requiring liposuction), or peripheral blood pluripotent stem cells (requiring a centrifuge machine)<sup>[11]</sup>.

## Methods

Over the last three years, 270 patients (90 suffering from knee pain, 90 suffering from hip pain, and 90 suffering from low back pain), have been recruited from one of the biggest rural and poorest areas in Cairo. For the knee and hip joints, intra-articular injections were done with 5cc of proliferant solution inside the joint cavity. For the knee joints, extra-articular injections were done at one or more of the following areas: Medial collateral ligament, lateral collateral ligament, medial and lateral coronary ligaments, arcuate ligament, origin and insertion of popliteus muscle, tendon of biceps femoris as well as insertions of the pes anserina (sartorius – gracilis - semitendinosus), patellar retinaculum and patellar tendon. For the hip joints, extra-articular injections were done at one or more of the

following areas: Ilio-femoral ligament, pubo-femoral ligament, ischio-femoral ligament, inter-trochanteric anterior femoral ligament, and posterior hip capsule. For the low backs, injections were done at one or more of the following areas: Posterior sacro-iliac ligament (areas A, B, C and D of Hackett), sacro-spinous and sacro-tuberous ligaments, inter-osseous ligament, ilio-lumbar ligament, and dorso-lumbar fascia. Each 90 patients were randomly divided into 3 groups of 30 patients for 3 different treatments:

Group (1): Buffered dextrose prolotherapy (15% concentration extra-articular and 25% concentration intra-articular). One ampoule of vitamin D (600.000 iu) was added to the extra-articular D15W and / or to the intra-articular D25W.

Group (2): Platelet rich plasma (PRP) was mixed with buffered dextrose either 15% or 25% and injected either extra or intra-articular.

Group (3): Bone marrow aspirate was centrifuged and bone marrow stem cells were mixed with buffered dextrose and injected extra or intra-articular.

The injections took place once every 2 months, the patients in group (1) were injected from 1 - 4 times, and the patients in groups (2) and (3) were injected from 1 – 3 times. The assessment of the patients was done before the start of the treatment, and every month over a period of 12 months, by using VAS for pain evaluation and through the evaluation of functional improvement.

### Conclusions

1. Vitamin D has very good results in the treatment of musculoskeletal pain and function.
2. Vitamin D is a promising alternative to PRP and stem cells especially for patients suffering from:
  - a) Anaemia.
  - b) Thrombocytopaenia.
  - c) Blood diseases.
  - d) Bone diseases.

e) Bone marrow diseases.

f) Very thin patients with no adipose tissue.

3. Vitamin D can be used in the rural and poor areas where the facilities for the use of PRP and stem cells are limited. It helps in making poor people able to regain easily and quickly their pain free life.

Prolotherapy is an injection technique designed to stimulate tissue healing to regain its structure and strength in order to decrease the pain. Over the years, dextrose has been the most commonly used proliferant solution in prolotherapy. More powerful proliferants are the platelet rich plasma “PRP” and the adult mesenchymal stem cells “AMSCs” which are the hot topics nowadays. Adding vitamin D to dextrose helped the tissue to regenerate and to get repaired faster and stronger than used to do dextrose alone. Vitamin D added a strength to the dextrose prolotherapy treatment which made the results close to those of the PRP and the AMSCs, giving a promising alternative for these powerful proliferants when their use is restricted.

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