

The Effect of Dextrose Plorotherapy on Pain and Function of Patients with Knee Osteoarthritis

Mohammad Emami Moghaddam Tehrani, MD¹, Alireza Manafi rasi, MD², Gholamhossein Kazemian, MD³, Peyman Kazemi, MD⁴, Fatemeh Safaeinik, MD⁵, Ahmad khazanchin, MD⁶

^{1,2}Assistant Professor of the Orthopaedic Department of Imam Hussein (AS) Hospital, Shahid Beheshti University of Medical Science

³Associate Professor of the Orthopaedic Department of Imam Hussain (AS) Hospital, Shahid Beheshti University of Medical Sciences

^{4,6}Orthopaedic Resident of Imam Hussain (AS) Hospital, Shahid Beheshti University of Medical Sciences

⁵Resident of Internal Medicine

Received: November 9, 2014

Accepted: January 23, 2015

ABSTRACT

Objective: The objective of this study was to determine whether Plorotherapy, an injection-based complementary treatment for chronic musculoskeletal conditions, improves pain, stiffness, and function in adults with symptomatic knee osteoarthritis (KOA) compared to baseline status.

Design: This was a prospective, uncontrolled study with 6-month follow-up.

Setting: The study was conducted in an outpatient setting. Participants: Adults with at least 3 months of symptomatic KOA, recruited from clinical and community settings, participated in the study.

Interventions: Participants received extra-articular injections of 20% dextrose at 1, 5, and 9 weeks. Outcome measures: Primary outcome measure was the validated Western Ontario McMaster University Osteoarthritis Index (WOMAC). Secondary outcome measure was the validated Knee Pain Scale (KPS). Tertiary outcome measure was procedure-related pain severity and participant satisfaction.

Results: Thirty-six (36) participants (60 – 87 years old, 21 female) with mild to moderate KOA received Plorotherapy injection and reported progressively improved scores during the 24-week study on WOMAC and KPS measures. Participants reported overall WOMAC score improvement 4 weeks after the first injection session (7.6 – 2.4 points, 17.2%), and continued to improve through the 24-week follow-up (15.9 – 2.5 points, $p < 0.001$, 32.1%). KPS scores improved in both injected ($p < 0.001$) and uninjected knees ($p < 0.05$). Satisfaction was high and there were no adverse events. Female gender, age 46–65 years old, and body-mass index of 25 kg/m² or less were associated with greater improvement on the WOMAC instrument.

Conclusions: In adults with mild to moderate KOA, dextrose Plorotherapy may result in safe, significant, Sustained improvement of knee pain, function, and stiffness scores. Randomized multidisciplinary effectiveness trials including evaluation of potential disease modification are warranted to further assess the effects of Plorotherapy for KOA.

KEYWORDS: Osteoarthritis (OA), Dextrose Plorotherapy(DP) , pain, stiffness, function

INTRODUCTION

Degenerative joint diseases (DJD) are among the most extensive worldwide conflicts of which osteoarthritis (OA) is the most common. The disease commonly involves hip, knee, spine and the fingers. OA is the fourth leading cause of disabling, and involves 3% of the disabling causes (1). Knee is the most common joint affected by OA and plays an important role in weight-bearing exercise (2). According to the researches, the outbreak of KOA is at ages more than 15 is equal to 7.9% (3). The disease affects 13-30 percent of people over 65 years and is one of the most common causes of disability in adults (4,5,6). In Iran the prevalence of knee osteoarthritis in the elderly over 15 years, have been reported to be about 15.34% which the high (7). Due to disturbances that this disease causes in the functioning of the individual, it can cause deleterious economical effects, too (4). Rising life expectancy and increased problems such as obesity, has caused the number of patients with knee OA increase and consequently the need for knee joint replacement surgery has increased significantly.

Treatment of knee osteoarthritis includes the reduction of pain and the correction is of knee deformity. KOA surgery is the definitive treatment of knee arthroplasty (TKA) is very costly and has a high risk and due to the limitations and difficulties and dangers of life the longevity of prostheses for surgical revision, we are now trying to

postpone TKA as much as possible. For this reason, several nonsurgical treatment involve the use of pain-reducing drugs (NSAIDs), glucosamine, hyaluronic acid injection, physiotherapy, occupational therapy, orthotics and Plorotherapy with dextrose were presented and desired results of the milder degrees of treatment with these method have been reported (7.8.9.10.11.12).

Plorotherapy (Plorotherapy) was first described by Hackett in 1950, and after that various clinical studies were conducted on animals and humans (13:14). In Plorotherapy dextrose, the increase of extracellular glucose increased multiple polypeptide growth factors in different human cells (15.16). The contact of human cells with the hypertonic environment in a few seconds to a few minutes led to increased levels of growth factors of the DNA (17.18). Hypertonic dextrose solution with the above two mechanisms leads to the increase in the amount of growth factors and has the capability of improving critical joints such as chondrocyte cells (the production of chondrocytes), Osteocytes (the production of the bone cells), and fibroblasts (production of tendon cells, ligament and other soft tissues). In few studies it has been indicated that Plorotherapy with different concentrations of dextrose can have favorable results in the treatment of knee OA. (19.20). However, although some studies have confirmed the positive effects of this method but its therapeutic effects and the quality of its results regarding the extent and durability is debatable. Considering the need to find nonsurgical, safe, simple and cheap treatments to reduce pain and improving the patients' function with severe knee OA, and the absence of information about the efficacy and safety of plorotherapy with dextrose, in this study, we try to deal the effect of this therapy in these patients.

MATERIALS AND METHODS

In this clinical trial, 36 patients with knee OA, grades I and II based on Kellgrene-Lawrence criteria who have referred to Imam Hussain (AS) Hospital in 1392, were firstly treated with 10cc of 20% dextrose plorotherapy and were also taken the treatment for two times within a month. The average age of the patients was 60 years, 21% of the patients were female and 36% of the patients had a BMI in the range of Obesity. Both knees were treated in 22 patients and in 14 patients only one knee was treated. For all the patients the questionnaires of WOMAC and KPS was completed, therefore the total number of patients who were examined in terms of WOMAC were equal to 36 and the total number of the patients who were examined in terms of KPS was 58.

Patients with KOA, grades III-IV based on Kellgrene-Lawrence criteria with a knee injection experience, had a background of using anti-inflammatory and analgesics drugs in the last three months. Posttraumatic Osteoarthritis or septic problems in the lower extremities and the existence of joint diseases in the knee, including rheumatoid arthritis and gout, history of fractures of the knee intraarticular joint, any injection of general contraindications including thrombocytopenia, coagulopathy, infection of the skin at the injection site, immune disorders or severe joint effusion were excluded from the study.

The data as Mean \pm SD and the qualitative data were presented as number and percentage. To compare the data before and after the treatment, the Paired t-test or Wilcoxon test was used. STATA 11 statistical software was used in this study. The significance level was considered as $p < 0.05$.

Table 1- description of the demographic characteristics of the patients

Variable	The number of the patients	The frequency of the patients
Sex	36	100%
Female	21	58%
Male	15	42%
Body mass index (BMI)		
Less than 25	8	22%
25 to 30	15	42%
More than 30	13	36%
History of diabetes		
Has	2	6%
Does not have	34	94%
X-ray Kellgren-Lawrence OA severity score (0-4) of treated knees		
mild OA	13	36%
moderate OA	23	64%

Table 2. Evaluation of mean and standard deviation of the variables in patients under study

variable	Mean	SD
The age of the patients	60	8.7
score KPS	2.6	0.9
Womac total Score	55.9	3.1
pain	57.9	17.5
Stiffness	51.7	23
Function	58.1	17

Table 3. Evaluation of the changes in WOMAC Score in patients during follow-up after treatment

variable	Total Score base	Changing the Score of the 5th week (SD)	Changing the Score of the 9th week (SD)	Changing the Score of the 12th week (SD)	Changing the Score of the 24th week (SD)	Significance of the difference (Pvalue)
WOMAC total score in the test	57.1 (2.8)	+7.8 (2.3)	+11.6 (2.3)	+14.9 (2.5)	+15.9 (2.5)	0.01
Percent of improvement of the scores in WOMAC test	-----	17.2 %	26.3 %	36.1 %	31.5 %	0.01
Pain of the patients on the basis of the WOMAC test	57.9 (3.0)	+7.1 (2.6)	+8.8 (2.6)	+9.1 (2.4)	+10.2 (2.1)	0.01
Improvement of the patients' pain score	---	12%	15%	16%	18%	0.02
Stiffness based on the WOMAC test	51.7 (3.5)	+5.6 (3.4)	+10.4 (3.4)	+15.6 (3.5)	+11.8 (3.4)	0.001
Improvement of the patients' stiffness score		11.6%	21.5%	32.3%	24.4%	0.001
Patients function on the basis of WOMAC test	58.1 (2.9)	+9.3 (2.3)	+13.6 (2.3)	+16.9 (2.4)	+15.4 (2.4)	0.001
Function improvement score of the patients	22.2%	32.5%	40.3%	36.8%	40.8%	0.001

Table 4. Evaluation of the KPS changes in treated and untreated knee over 24 weeks

	Untreated knee of 14 patients		Treated knee of 58 patients	
	Pain Frequency	Pain severity	Pain Frequency	Pain severity
Score base	1.64 (0.2)	1.19 (0.2)	2.6 (0.13)	2.09 (0.13)
Changes in relation to the basic situation				
Fifth week	-0.23 (0.23)	0.08 (0.25)	-0.38 (0.12)	-0.39 (0.12)
Ninth week	-0.78 (0.23)	-0.54 (0.25)	-0.85 (0.12)	-0.78 (0.13)
Twelfth week	-0.74 (0.25)	-0.66 (0.26)	-0.85 (0.12)	-0.78 (0.13)
Twenty-fourth week	-0.94 (0.24)	-0.67 (0.25)	-0.78 (0.12)	-0.70 (0.13)

DISCUSSION AND CONCLUSION

Based on our findings, the conditions of the patients under the treatment with Plorotherapy over the 24 weeks of follow-up, indicates 32 percent of improvement (based on WMAC and KPS (Table 3)). Such a finding is better and higher than that of mentioned in previous studies (12% (32) to 25% (33)).

In studies conducted by Reevas et al. and Rabago et al. the extent of improvement has been reported to be high. So that Reevas et al. have reported up to 44% improvement in the amount of pain and up to 63% improvement in the rate of inflation of the patients and also 14 degrees of improvement in the amount of patients' Flexion, where these findings confirm our results, however, patients have reported higher improvement. Differences in the methodology of conducting the study by Reevas et al. with that of our study and Rabago and also the difference in the skillfulness of the injector have been studied for 12 month along with the attention to this issue in the studies conducted by Reevas et al. and Rabago et al., but in this study, the patients were only studied for 6 months, and this can be a major

cause of better results in these studies. Overall, Plorotherapy with other materials which often has an inflammatory condition toward glucose, have also been confirmed, the results of the studies that examined the effect of injecting chondroitin sulfate (23), glucosamine (24) and NSAID (25, 26), have also reported similar results.

The patients have also stated a significant improvement in their non-treated knees. These findings are probably due to the removal of Compensatory effect from the unaffected knee. Patients with KOA knee also face limited hip movements so that more pressure is applied to the intact knee (34, 35) and consequently by the treatment of the knee with KOA the burden to the intact knee also declines, therefore, they feel less pain in the intact knee. (34, 36) In general, it can be said that based on the findings of this study, we can introduce plorotherapy as a standard therapy which leads to the improved quality of patients' survival. This improvement in women, people with proper weight and are also in middle ages, is more significant.

Plorotherapy is a developing modality which is gradually acquiring more popularity in sports medicine and family. (73) However, its mechanism of action is not well known, there are hypotheses that the injection of dextrose leads to the activation of repair mechanisms of intra-articular and extra-articular in the joints. (38) Animal studies indicate an increase in inflammatory markers (39) and a significant expansion of the Cross-sectional area in medial collateral ligaments. (40) The findings also suggest the existence of a positive neural effect. (41)

The source of pain in KOA is usually multi-factorial. Plorotherapy also affects several Nociceptors. Including the impact on Avascular Articular Cartilages and effect on the tissues which are rich regarding Innervation and contain intra-articular and extra-articular tissues like periosteum, Periarticular ligaments, Periarticular muscles, synovial and joint capsule (44, 43, 42).

Plorotherapy is a safe method for a meaningful, stable improvement to improve pain and function and the stiffness of patients with KOA. Plorotherapy by an experienced professional can be considered as an effective way to improve the condition of patients with moderate to severe KOA.

REFERENCES

1. World Health Organization (WHO). Symmons D, Mathers C, Pflieger B. Global burden of osteoarthritis in the year 2000. [Internet] 2000 [2010 April 12]; Available from: http://www.who.int/healthinfo/statistics/bod_osteoarthritis.pdf
2. Gök H, Ergin S, Yavuzer G. Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. *Acta Orthop Scand* 2002;73(6):647-652
3. Haq SA, Davatchi F. Osteoarthritis of the knees in the COPCORD world. *Int J Rheum Dis* 2011;14(2):122-9
4. Katsuragawa Y, Fukui N, Nakamura K. Change of bone mineral density with valgus knee bracing. *Int Orthop* 1999;23(3):164-7.
5. Baker K, Goggins J, Xie H, Szumowski K, LaValley M, Hunter D. J, Felson Dt. A randomized crossover trial of a wedged insole for treatment of knee osteoarthritis. *Arthritis & Rheumatism* 2007;56(4):1198-1203
6. Poitras S, Avouac J, Rossignol M, Avouac B, Cedraschi C, Nordin M, Rousseaux C, Rozenberg S, Savarieau B, Thoumie P, Valat J. P, Vignon E, Hilliquin P. A critical appraisal of guidelines for the management of knee osteoarthritis using appraisal of Guidelines Research and Evaluation criteria. *Arthritis Research & Therapy* 2007;9:R126.
7. Buckwalter JA, Stanish WD, Rosier RN, Schenck RC Jr, Dennis DA, Coutts RD. The increasing need for nonoperative treatment of patients with osteoarthritis. *Clin Orthop Relat Res* 2001;(385):36-45
8. Leslie M. Knee osteoarthritis management therapies. *Pain Manag Nurs* 2000;1(2):51-7.
9. Divine G. J, Timothy E, Hewett T. E. Valgus bracing for degenerative knee osteoarthritis. *The physician and sportsmedicine* 2005;33(2).
10. Haim A, Rozen N, Dekel S, Helperin N, Wolf A. Control of knee coronal plane moment via modulation of center of pressure: a prospective gait analysis study. *J Biomech* 2008;41(14):3010-6.
11. Shelburne K. B, Torry M. R, Steadman J. R, Pauly M. G. Effects of foot orthosis and valgus bracing on the knee adduction moment and medial joint load during gait. *Clin biomech(Bristol.Avon)* 2008;23(6):814-21.
12. Chung S. H, Huang M. H, Chen T. W, Weng M. C, Liu C. W, Chen C. H. Effect of knee sleeve on static and dynamic balance in patients with knee osteoarthritis. *Kaohsiung J Med Sci* 2007;23(8).

13. Mazzuca S. A, Page M. C, Meldrum R. D, Brant K. D, Petty-saphon S. Pilot study of the effects of a heat-retaining knee sleeve on joint pain, stiffness, and function in patients with knee osteoarthritis. *Arthritis and Rheumatism (Arthritis Care & Research)* 2004;51(5):716-721.
14. Hackett GS. Joint stabilization through induced ligament sclerosis. *Ohio Med* 1953;49(10):877-84.
15. Di Paolo S, Gesualdo L, Ranieri E, Grandaliano G, Schena FP. High glucose concentration induces the overexpression of transforming growth factor-beta through the activation of a platelet-derived growth factor loop in human mesangial cells. *Am J pathol* 1996;149(6):2095-106.
16. Murphy M, Godson C, Cannon S, Kato S, Mackenzie HS, Martin F, et al. Suppression subtractive hybridization identifies high glucose levels as a stimulus for expression of connective tissue growth factor and other genes in human mesangial cells. *J Biol Chem* 1999;274(9):5830-4.
17. Krump E, Nikitas K, Grinstein S. Induction of tyrosine phosphorylation and Na⁺/H⁺ exchanger activation during shrinkage of human neutrophils. *J Biol Chem* 1997;272(28):17303-11
18. Okuda Y, Adrogué HJ, Nakajima T, Mizutani M, Asano M, Tachi Y, et al. Increased production of PDGF by angiotensin and high glucose in human vascular endothelium. *Life Sci* 1996;59(17):1455-61.
19. Hashemi SM, Madadi F, Razavi S, Nikooseresht M, Hassanzadeh Kiyabi F, Nasiripour S. Intra-articular hyaluronic acid injections Vs. dextrose Plorotherapy in the treatment of osteoarthritic knee pain. *Tehran University Medical Journal* 2012;69(2): 872-877.
20. Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose Plorotherapy for knee osteoarthritis with or without ACL laxity. *Altern Ther Health Med* 2008;6(2):68-74, 77-80.
21. Felson DT. Osteoarthritis of the knee. *NEJM* 2006;354:841-848
22. Rabago D, Patterson JJ, Mundt M, Kijowski R, Grettie J, Segal NA, Zgierska A. Dextrose Plorotherapy for knee osteoarthritis: a randomized controlled trial. *Ann Fam Med* 2013;11(3):229-37.
23. Bucsi L, Poor G. Efficacy and tolerability of oral chondroitin sulfate as a symptomatic slow-acting drug for osteoarthritis (SYSA D OA) in the treatment of knee osteoarthritis. *Osteoarthritis Cartilage*. 1998; 6(5): 31-36.
24. Leffler CT, Philippi AF, Leffler SG, Mosure JC, Kim P D. Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double-blind, placebo-controlled pilot study. *Mil Med*. 1999; 164(2): 85-91
25. Perez Busquier M, Calero E, Rodríguez M, et al. Comparison of aceclofenac with piroxicam in the treatment of osteoarthritis. *Clin Rheumatol (Belgium)*. 1997;16(2):154-159
26. Bocanegra TS, Weaver AL, Tindall EA, et al. Diclofenac / misoprostol compared with diclofenac in the treatment of osteoarthritis of the knee or hip: a randomized, placebo controlled trial. *Arthritis Rheumatism Study Group*. *J Rheumatol (Canada)*. 1998; 25(8): 1602-1611.
27. Gramajo RJ, Cutroneo EJ, Fernandez DE, et al. A single-blind, placebo-controlled study of glycosaminoglycan-peptide complex ('Rumalon') in patients with osteoarthritis of the hip or knee. *Curr Med Res Opin*. 1989;11(6): 366-373.
28. Uebelhart D, Thonar EJ, Delmas PD, Chantraine A, Vignon E. Effects of oral chondroitin sulfate on the progression of knee osteoarthritis: a pilot study. *Osteoarthritis Cartilage*. May 1998;6 suppl A:39-46.
29. Conrozier T. Anti-arthritis treatments: efficacy and tolerance of chondroitin sulfates (CS 4&6). *Presse Med*. 1998; 27(36): 1862-1865.
30. Kim JM. The effect of Plorotherapy for osteoarthritis of the knee. *J Korean Acad Rehabil Med* 2009;26(4):445-448.
31. Hashemi SM, Madadi F, Razavi S, Nikooseresht M, Hassanzadeh Kiyabi F, Nasiripour S. Intra-articular hyaluronic acid injections Vs. dextrose Plorotherapy in the treatment of osteoarthritic knee pain. *Tehran University Medical Journal* 2012;69(2): 872-877.

32. Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. *Arthritis Rheum* 2001;4:384–391.
33. Tubach F, Wells GA, Ravaud P, et al. Minimal clinically important difference, low disease activity state, and patient acceptable symptom state: Methodological issues. *J Rheumatol* 2005;32:2025–2029.
34. GyoryAN, Chao EY, Stauffer RN. Functional evaluation of normal and pathologic knees during gait. *Arch Phys Med Rehabil* 1976;57:571–577.
35. Brinkmann JR, Perry J. Rate and range of knee motion during ambulation in healthy and arthritic subjects. *Phys Ther* 1985;65:1055–1060
36. Messier SP, Loeser RF, Hoover JL, et al. Osteoarthritis of the knee: Effects on gait, strength, and flexibility. *Arch Phys Med Rehabil* 1992;73:29–36.
37. Yelland MJ, Sweeting KR, Lyftogt JA, et al. Plorotherapy injections and eccentric loading exercises for painful Achilles tendinosis: A randomised trial. *Br J Sports Med* 2011;45:421–428
38. Banks A. A rationale for Plorotherapy . *J Orthop Med* 1991;13:54–59.
39. Jensen K, Rabago D, Best TM, et al. Early inflammatory response of knee ligaments to Plorotherapy in a rat model. *JOrthop Res* 2008;26:816–823.
40. Jensen KT, Rabago D, Best TM, et al. Longer term response of knee ligaments to Plorotherapy in a rat injury model. *Am J Sports Med* 2008;36:1347–1357.
41. Kim SR, Stitik TP, Foye PM. Critical review of Plorotherapy for osteoarthritis, low back pain, and other musculoskeletal conditions: A physiatric perspective. *J Phys Med Rehab* 2004;83:379–389.
42. Felson DT. Epidemiology of osteoarthritis. In: Brandt KD DM, Lohmander LS, eds. *Osteoarthritis*. Oxford, England: Oxford University Press, 2003:9–16.
43. Felson DT. Osteoarthritis: New insights, part 1. The disease and its risk factors. *Ann Intern Med* 2000;133:635–646.
44. Samson DJ, Grant MD, Ratko TA, et al. Treatment of primary and secondary osteoarthritis of the knee. Agency for PLOROTHERAPY FOR KNEE OSTEOARTHRITIS 413Healthcare Research and Quality (Publication No. 07-E012):
Evidence Report/Technology Assessment. Rockville, MD:Blue Cross and Blue Shield Association Technology Evaluation Center Evidence-Based Practice Center under Contract No. 290-02-0026). 2007;157.