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Ozone (O_2 - O_3) Has SYSADOA (Symptomatic Slow Acting Drug for Osteoarthritis) and DMDOA (Disease Modifying Drug for Osteoarthritis) Effect in Knee Osteoarthritis Patients

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1. Introduction

Knee osteoarthritis (OA) is the most common cause of knee pain and disability in Western societies (1, 2). It is so prevalent that 50% of the population over 60 to 75 years old has radiological signs and 80% of people over 80 years have radiological signs and clinical symptoms (3).

Knee OA is characterized by cartilage destruction, joint space narrowing, subchondral sclerosis, and osteophyte formation (1, 2). As a consequence, pain, loss of function, and reduced quality of life appear in knee OA patients (3). In Spain, knee OA affects almost four million people and it is the cause of 50% of cases of disability. The economic impact due to direct costs is about 4738 million euros per year, which represents 0.5% of gross domestic product (GDP) (4).

The pathogenesis of knee OA is multifactorial. Risk factors include biomechanical factors, trauma, obesity, age and gender and recently, chronic inflammation (1-5). Therefore, the pathological process of knee OA includes inflammation and structural changes (1). To date, conventional medicine has no cure for OA. The definitive treatment for knee OA is total arthroplasty replacement, which has a 95% rate of success at ten years, yet the procedure is not exempt from risks (1, 3). Conservative treatment includes non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, physical medicine, and intra articular infiltrations (1, 4).

The objectives on the short-term are to reduce symptoms such as pain, stiffness, and swelling and to improve function. On the long-term, the objectives are to reduce or revert damage and destruction of the articulation (1, 4). As far as the authors are concerned, symptomatic slow acting drug for osteoarthritis (SYSADOA) effect has been reported for glucosamine and chondroitin sulfate (6), yet the disease modifying drug for osteoarthritis (DMDOA) effect is still controversial (7).

Recent recommendations of the osteoarthritis research society international (OARSI) proposed 25 recommendations for OA management (twelve are non-pharmacological, eight are pharmacological, and five are surgical). None of the recommendations suggested intra articular infiltration of ozone (O_2 - O_3) (8). Similarly, the European clinical practice guidelines for the management of knee OA does not include ozone (O_2 - O_3) therapy (8).

For the management of knee OA, there is the necessity to evaluate biomarkers for diagnosis, monitoring and progression of the disease (9). Those biomarkers should evaluate clinical, biochemical (laboratorial), and radiographic outcomes (9).

In order to determine the SYSADOA and DMDOA effect of ozone (O_2 - O_3) in the management of knee OA, three prospective studies of level 2b of medicine-based-evidence have been designed by the study group.

2. Arguments

Firstly, Fernandez-Cuadros et al. demonstrated that four intra articular infiltrations of ozone (O_2 - O_3) were capable of improving clinical parameters; these were pain, function, stiffness, and quality of life in 119 knee OA patients. The improvement reported in the mid-term follow-up (two months after treatment) was significant ($P < 0.001$) (8).

Secondly, Fernandez-Cuadros et al. reported that four intra articular infiltrations of ozone (O_2 to O_3) were ca-

pable of decreasing laboratorial biomarkers of inflammation; namely, C-reactive protein, erythrocyte sedimentation rate, and serum uric acid in 33 patients with knee OA (9). Ozone was both capable of decreasing inflammation biomarkers and improving clinical symptoms (pain, function, stiffness, and quality of life) in a two-month follow-up period, and with a level of significance of $P < 0.05$ (9).

Finally, Fernandez-Cuadros et al. demonstrated that in the long-term follow-up period of 10 to 28 months that ozone was capable of increasing medial and lateral minimal joint space at the knee in 52 OA patients (10). Ozone was also capable of delaying knee arthroplasty replacement to an extent that none of the patients went to definitive surgical procedure (10). This is a proof of evidence that ozone (O_2 - O_3) might reduce and might even overcome radiographic impairment in knee OA patients. This study suggests that for the first time ozone would be capable of modifying the natural history of the disease.

The arguments of this article are based on three previous quasi-experimental before-and-after studies published by the study group and with a level of evidence 2b (6, 9, 10). Scientists are encouraged to replicate the current promising findings for the management of knee OA.

Ozone (O_2 - O_3) is a cheap and safe treatment with no reported adverse effects as the case of NSAIDs (1), and the symptoms are observed sooner than SYSADOA drugs (7). The DMDOA effect may modify the natural history of knee OA and therefore delay knee arthroplasty replacement. The SYSADOA (6, 8) and DMDOA (10) effect of ozone (O_2 - O_3) may reduce direct/indirect costs and ozone (O_2 - O_3) may have a direct impact on patient's economy and government's policies, because of the prevalence and burden of knee OA.

3. Conclusions

As previously stated and referenced by Level 2b medicine-based-evidence studies, Fernandez-Cuadros et al. recently demonstrated that ozone (O_2 - O_3) has SYSADOA and DMDOA effects, reflected by the improvement in clinical, biochemical, and radiographic variables in the management of knee OA. The researchers suggest that it is time for government policies, Public and private hospitals and clinical guidelines to consider ozone (O_2 - O_3) as a suitable option for the management of knee OA based on the medicine-based-evidence results.

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Footnotes

Conflict of Interests: The authors note that there was no commercial relationship giving rise to a conflict of interest in conducting this study.

Ethical Approval: The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Institution's Human Research Committee.

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Patient Consent: Informed consent was obtained from the patients included in the study.

References

1. Fernandez-Cuadros ME. *[Analisis de la Calidad de Vida en pacientes con protesis de rodilla] [Dissertation]*. Spain: Universidad de Salamanca; 2013. Spanish.
2. Fernandez-Cuadros ME, Perez-Moro OS, Miron-Canelo JA. Age and comorbidities affect quality of life in patients with osteoarthrtitis and knee replacement. *Middle East J Rehab Health*. 2016;**3**(4). doi: 10.17795/mejrh-40247.
3. Fernandez-Cuadros ME, Perez-Moro OS, Miron-Canelo JA. Knee osteoarthritis: Impact on quality of life and effectiveness of total knee arthroplasty. *Divers Equal Health Care*. 2016;**13**(4):278–83.
4. Fernandez-Cuadros ME. *Ozone fundamentals and effectiveness on knee pain: Chondromalacia and knee osteoarthritis*. Germany: Lambert Academic Publishing; 2016.
5. Fernandez-Cuadros ME, Perez-Moro OS, Alonso-Sardon M, Iglesias-de-Sena H, Miron-Canelo JA. Age and sex affect osteoarthritis and the outcome on knee replacement. *MOJ Orthoped Rheumatol (MOJOR)*. 2017;**9**(3). doi: 10.15406/mojor.2017.09.00362.
6. Fernandez-Cuadros ME, Perez-Moro OS, Albaladejo-Florin MJ, Miron-Canelo JA. Ozone improves pain, function and quality of life in patients with knee osteoarthritis: A prospective quasi-experimental before-after study. *Middle East J Rehab Health*. 2017;**4**(1). doi: 10.17795/mejrh-41821.
7. Raynauld JP, Pelletier JP, Abram F, Dodin P, Delorme P, Martel-Pelletier J. Long-term effects of glucosamine and chondroitin sulfate on the progression of structural changes in knee osteoarthritis: Six-year followup data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken)*. 2016;**68**(10):1560–6. doi: 10.1002/acr.22866. [PubMed: 26881338].
8. Fernandez-Cuadros ME. Does glucosamine/chondroitin sulfate have a long-term effect on the progression of structural changes in knee osteoarthritis? Comment on the article by Raynauld et al. *Arthritis Care Res (Hoboken)*. 2018;**70**(1):167. doi: 10.1002/acr.23313. [PubMed: 28686811].
9. Fernandez-Cuadros ME, Perez-Moro OS, Albaladejo-Florin MJ, Algarra-Lopez R. Ozone decreases biomarkers of inflamation (C-reactive protein and erytrocyte sedimentation rate) and improves pain, function and quality of life in knee osteoarthrtitis patients: A before-and-after study and review of the literature. *Middle East J Rehab Health*. 2018;**5**(2). doi: 10.5812/mejrh.64507.
10. Fernandez-Cuadros ME, Perez-Moro OS, Albaladejo-Florin MJ. Knee osteoarthritis: Condroprotector action and symptomatic effect of ozone on pain, function, quality of life, minimal joint space and knee arthroplasty delay. *Middle East J Rehab Health*. 2017;**4**(1). doi: 10.17795/mejrh-43200.