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Vitamin C May Help to Reduce the Knee's Arthritic Symptoms. Outcomes Assessment of Nutraceutical Therapy

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ABSTRACT

Introduction: Osteoarthritis (OA) is a chronic joint disease characterized by degeneration of the articular cartilage, changes in the physico-chemical properties of the synovial fluid and macroscopical modifications of the joint. Patients with Classes I and II of Knee OA can be treated with pharmacologic therapy. Vitamin C is key for both preventing inflammatory arthritis and maintaining healthy joints with OA. **Aim:** The aim of our paper is to verify the effectiveness of the addition of vitamin c in nutraceutical drugs for the therapy of the knee arthritis in the young adult. **Results:** Group B has a lower VAS score at 6 and 12 months with $p < 0.05$. Not statistical difference we found in KSS during all follow up. A better quality of life was founded in Group B at 12 months in group B ($p < 0.05$) and less use of pain killers/monthly ($p < 0.05$). **Conclusion:** There is no denying that vitamin C benefits everybody, whether they have arthritis or not. Therefore, it is a good idea to maintain a healthy balance of vitamin C. Without a doubt, vitamin C benefits most people with early OA.

Keywords: Vitamin C, Knee, Adult, Arthritis, Joint, Outcomes, Quality Life.

1. INTRODUCTION

Osteoarthritis (OA) is a chronic joint disease characterized by degeneration of the articular cartilage, changes in the physico-chemical properties of the synovial fluid and macroscopical modifications of the joint (1). OA is the most frequent: it is estimated that 25–30% of people over 45 years old are affected by it (2). While age is a major risk factor for osteoarthritis of the knee, young people can get it, too. For some individuals, it may be hereditary. For others, osteoarthritis of the knee or in another joints can result from injury or infection or even from being overweight. Here are answers to your questions about knee osteoarthritis, including how it's treated and what you can do at home to ease the pain (3-14). Estimates of incidence and prevalence of OA of the knee vary considerably among 29 studies from 14 countries and 4 ethnic groups (incidence: 10 to 2230 per 100000 person-years, prevalence: 0.5% to 36% (15).

Many different therapies are available nowadays for the treatment of early OA ranging from non-pharmacologic therapy to pharmacological approaches, but a flawless treatment is still to be found (1). Patients with

Classes I and II of Knee OA can be treated with pharmacologic therapy but Patients with severe symptomatic early OA who have pain and a progressive limitation in ADL should be referred to an orthopaedic surgeon for evaluation. They needs a medical therapy. Treatments with enhanced safety margins and that offer chondroprotective effects are unmet needs. Nutraceuticals derived from foods and herbs have been long used in traditional medicine, and many have wide-ranging biologic effects suggesting novel mechanisms of action. Some of these have shown promise in controlled clinical trials in OA patients. Whether these approaches could offer safe symptom relief and possibly mediate beneficial joint remodeling in early OA are possibilities that merit further investigation (16).

Though the study reports reflected both ends of the C spectrum, they show that getting the right amount of vitamin C is key for both preventing inflammatory arthritis and maintaining healthy joints with OA (17).

2. AIM

The aim of our paper is to verify the effectiveness of the addition of

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vitamin C in nutraceutical drugs for the therapy of the knee arthritis in the young adult.

3. METHODS

This study is a prospective work of orthopedic and rehabilitation medicine ambulatory for the patients that suffered of OA's knee Class II. This is not double randomized blind trial. It's carried from January 2015 to December 2018. Exclusion criteria to include patients in this study: alcohol or drug abuse, systemic treatment with anticoagulants and steroids ongoing or suspended for less than 1 month; presence of rheumatoid arthritis, BMI>30; hematological or oncological pathologies; mineral or bone metabolism diseases; the age more than 65; patients who did not adhere to a minimum follow-up of 12 months, intra-joint injection therapy.

According the exclusion criteria we enrolled 120 patients were treated with oral nutraceutical drus.

We divided the patients into two groups. The two patient groups were formed based on the patient's choice to undergo such treatment. Group A was 60 patients(30 male and 30 female) were treated by oral nutraceutical therapy with a a common oral drud based by Collagen Peptide and Hyaluronic acid and Group B was 30 patient (30 male and 30 female) were treated by oral nutraceutical therapy with ZETA ARTRO-CUR Flex[®] (Erbozeta[™], Chiesanuova, Republic of San Marino).

All patients were informed in a clear and comprehensive way of the two types of treatment and other possible surgical and conservative alternatives. Patients were treated according to the ethical standards of the Helsinki Declaration and were invited to read, understand and sign the informed consent form.

All patients used Etoricobix 90 mg 1 pill/day for 7 days and after 1 pill/day if it's necessary like killer pain and anti-inflammatory, after the first visit in ambulatory. All patients after the first visit in ambulatory do physiokinesis therapy according Vad et al. (18). Physiokinesis therapy was not performed in the same center for all patients.

The chosen criteria to evaluate the two groups during the clinical and radiological follow-up were: Pain levels were measured using a 0-10 cm Visual Analogue Scale (VAS) (19); the objective quality of life and the knee function measured by Knee Society Score (KSS) (19) while the subjective quality of life by the Short Form 12 Health Survey (SF-12) (19); and the number of pain killer's pill taken monthly.

To try to eliminate a possible "placebo effect"(20), We decided to give the oral therapy at the first visit orthopedical examination. In follow up we have three endpoints at the first month, the third month and sixth month, to evaluate the pain and function of Knee.

Statistical analysis

Descriptive statistics were used to summarize the characteristics of the study group and subgroups, including means and standard deviations of all continuous variables. The t test was used to compare continuous outcomes. The Fisher, in this groups are smaller than 10 patients, exact test were used to compare Categorical variables. The statistical significance was defined as $p < 0.05$.

We used Pearson correlation coefficient (r) was used to compare the predictive score of outcomes and quality of life. The predictive score of outcomes and quality of life and their standard deviations were approximated at the first decimal while at the second decimal was approximated Pearson correlation coefficient (r).

4. RESULTS

The average age of patient was 39.6 (± 12.3 ; range 18-64) in Group A and 40.1 in Group B (± 11.8 ; range 18-64). Patients in group A were tall on average 173.36 cm (± 18.6 ; range 147-202), weigh on average 74.6 kg (± 16.42 ; range 45-105) with an average Body Max Index (BMI) 23.79 (± 3.53 ; range 20.1-29.9), while patients in group B were high an average of 172.89 cm (± 17.89 ; range 144-200), weighed on average 75.84 kg (± 17.48 range 47-106) with an average BMI 24.74 (± 4.13 ; range 20.1-29.9).

Null hypothesis between the two populations was rejected, $p > 0.05$ between group A and Group B.

Group A started with Average VAS 5.3 and Group B 5.5 there was no statistically significant difference ($p > 0.05$). At three months VAS of Group A was 4.8 and Group B 3.6 there was no statistically significant difference ($p > 0.05$). Instead six months VAS of Group A was 4.3 and Group B 2.7 there was statistically significant difference ($p < 0.05$) for Group B. At last endpoints, 12 months, VAS of Group A was 2.9 and Group B 1.6 there was statistical significant difference ($p < 0.05$) for Group B (Figure 1).

There was not statistical difference between the two groups in the objective quality of life and the knee function measured by Knee Society Score (KSS) during the entire follow up (Figure 2).

When studying the trends of the subjective quality of life by SF-12, we reported a statistically significant difference at 6 and 12 months for group B (Figure 3).

At moment of the pain in Group A patients took an average of 18.7 pain killer's pill/monthly while in Group B 18.8, $p > 0.05$. At the three months in Group A the average was 10.3 pain killer's pill/monthly while in Group B was 9.9 pain killer's pill/monthly, $p > 0.05$. At six months in Group A the average was 5.6 pain killer's pill/monthly while in Group B was 5.4 pain killer's pill/monthly, $p > 0.05$. At the last endpoint, 12 months, in Group A the average was 3.2 pain killer's pill/monthly while in Group B was 1.2 pain killer's pill/monthly, $p < 0.05$.

At 12 months the regression between pain killers taken and VAS scores showed a p value of 0.064 for Group A and $p = 0.052$ for group B, $p > 0.05$.

In both groups we have had no adverse effects related to the use of the two drugs. Furthermore, it was noted no miscellaneous complications.

5. DISCUSSION

OA is a widespread chronic disease, By the year 2020, osteoarthritis will become the fourth leading cause of disability worldwide; and today, it accounts for nearly the 3% of total years of living with disability globally (1, 21). Several pharmacological approaches are used for the treatment of OA, like intra-articular hyaluronan or corticosteroid, NSAIDs, oral supplements (e.g., glucos-

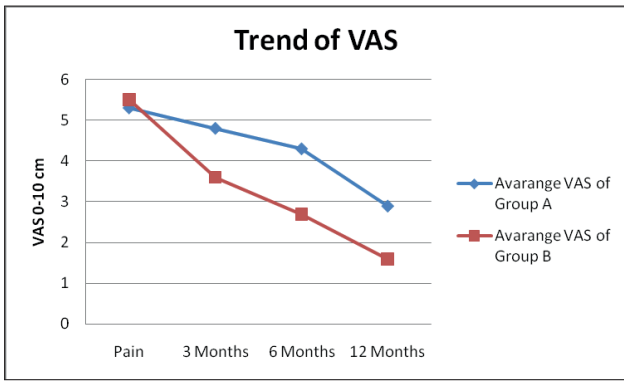


Figure 1. The trends of pain measured by VAS in the Group A and Group B in the 12 months of follow-up. At 6 and 12 months there was statistically significant difference ($p < 0.05$) for Group B.

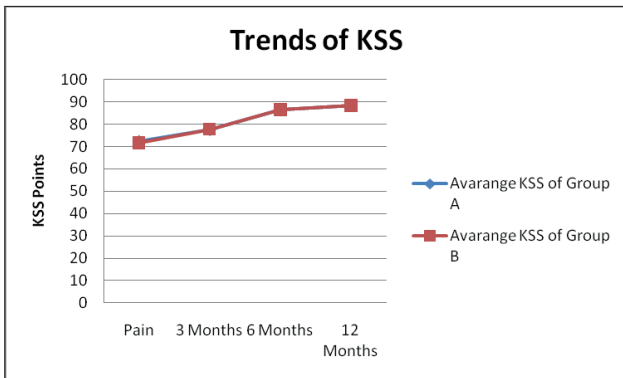


Figure 2. The trends of objective quality of life and the knee function measured by Knee Society Score in the Group A and Group B in the 12 months of follow-up. There was not statistically significant difference between the two groups in entire follow up.

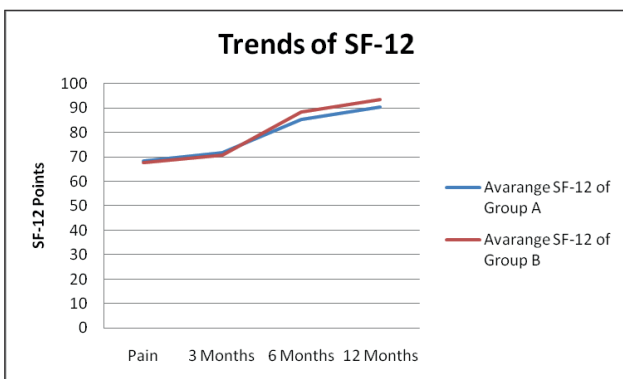


Figure 3. The trends of the subjective quality of life by the Short Form 12 Health Survey (SF-12) in both groups. At 6 and 12 months there was statistically significant difference ($p < 0.05$) for Group B.

amine or chondroitin (1, 21) and topical treatments (e.g., capsaicin) (1, 21). For some of these therapies, a considerable amount of clinical data is available, often claiming a substantial efficacy in dealing with osteoarthritis symptomatology (1, 21). The Dietary Supplement Health and Education Act (DSHEA) defined dietary supplements as products – not conventional foods – containing vitamins, minerals, amino acids, intended to supplement the diet by increasing the total daily intake of these substances (22). The “active aging” is one of the main targets of dietary supplements, as showed by the increasing sales of multivitamins, minerals, and vitamins B targeting this specific population. Iolascon et al founded in their re-

view that selected micronutrients in appropriate doses might have an ancillary role in musculoskeletal health and cognitive functions in older people. Therefore, they recommend that older people have an adequate nutrition or intake of nutraceuticals and/or dietary supplements, as supported by EBM, in order to maintain or achieve good health status (22). In 2017, Lubis et al (23) reported their double blind experience in the comparison of Glucosamine-Chondroitin Sulfate (GCM) with and without Methylsulfonylmethane (GC) in 147 patients suffered Grade I-II Knee Osteoarthritis, at their chosen criteria they found in the three groups: a statistical analysis it was found that at the 12th week, there are significant difference between three treatment groups on the WOMAC score ($p = 0.03$) and on the VAS score ($p = 0.004$). When analyzed between weeks, GCM treatment group was found statistically significant on WOMAC score ($p = 0.01$) and VAS score ($p < 0.001$). Comparing the score difference between weeks, WOMAC score analysis showed significant difference between GC, GCM, and placebo in week 4 ($p = 0.049$) and week 12 ($p = 0.01$). In addition, VAS score also showed significant difference between groups in week 8 ($p = 0.006$) and week 12 ($p < 0.001$) (23). Recently, it was hypothesized an association between bone mineral density and oxidative stress (22). Considering the known role of vitamins C and E as antioxidants. The use of Vitamine C for a 12-month period a significantly lower decrease of lipoperoxides (LPO) ($p < 0.05$), linked with hip bone loss, than the placebo group (22). Li et al (24) had examined the cross-sectional associations between dietary antioxidants (carotenoid, vitamin C, E, and selenium) intake and radiographic knee osteoarthritis (OA) in 4685 participants. Radiographic knee OA was grade 2 in at least one leg. Radiographic knee OA was not significantly associated with dietary carotenoid, vitamin E, and selenium. Among dietary antioxidants, dietary vitamin C intake was positively correlated with the prevalence of radiographic knee OA, while no significant association was found between dietary intake of carotenoid, vitamin E, and selenium and the prevalence of radiographic knee OA (24). Overall, vitamin C appears to be a safe and effective adjunctive therapy for acute and chronic pain relief in specific patient groups (25). In turn, infections can significantly impact on vitamin C levels due to enhanced inflammation and metabolic requirements (22-25). In fact the severity of knee pain lower prevalence of severe knee pain by affecting pain perception in the knee joint. Therefore, we investigated the relationship between self-reported knee pain and the consumption of fruits vegetables, carotenoids and vitamin C and self-reported knee pain (26). So we explain why the group that also took vitamin C had long-term better results on pain. However, we have not found in the literature that there is evidence that the intake of Vitamin C reduces the use of painkillers. Therefore empirically we can state that the significant reduction of pain in group B led to the lower monthly intake of painkillers. But vitamin C and E supplementation interfered with the acute cellular response to heavy-load resistance exercise and demonstrated tentative long-term negative effects on adaptation to

strength training (27). Most likely for the explanation provided by Paulsen et al (27) did not have functional improvements in group B evaluated with long distance KSS. Other authors suggested daily intake of vitamin C showed no statistical significance with lessened disability for knee (28). Instead they found that supplementary vitamin D was strongly associated with lessened disability for knee OA patients (28). Some studies report in oncology that the use of Vitamin C improves the quality of life of the oncological patient (29, 30). However, the reduction in quality of life is led to the reduction of pain.

The principal limitation of this study is represented by the not double blind randomize trial of this study. Another limitation of this study is represented by the population all people had a good life and the second class of OA.

6. CONCLUSION

There is no denying that vitamin C benefits everybody, whether they have arthritis or not. Therefore, it is a good idea to maintain a healthy balance of vitamin C. Without a doubt, vitamin C benefits most people with early OA.

- **Author's contribution:** U.R., P. M.A., S. G.L., J.U.G., A.D.M.D.L. and M.A.R. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work, The same authors had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they are agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Declaration of patient consent:** For this type of study is not required any statement relating to studies on humans and animals. All patients gave the informed consent prior being included into the study. All procedures involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.
- **Conflict of interest:** All authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.
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