Orthomolecular Therapy for Gonarthrosis: A Case Series

Bernhard G. Welker, MD[1]

[1] Gynecologist, Outpatient clinic, Koenigstrasse 29, 53115 Bonn, Germany, Tel: 0049-228-265410
Fax: 0049-228-222515, email: welker-bonn@t-online.de

Abstract *Nine patients suffering from gonarthrosis were administered ascorbic acid, L-lysine, grape seed extract, and broad-spectrum nutrients orally. Over the course of three to four weeks, five patients became pain-free and four experienced significant pain relief. All gained mobility. Neither surgery nor analgesics were required during follow-up periods up to more than three years. This therapy for osteoarthritis should be studied further, as it might be an effective and convenient primary treatment. It might also be useful to prevent osteoarthritis.*

Introduction

Osteoarthritis is a widespread disease of unknown causes. It is described as disparity between burden and loading capacity of the cartilage. Degeneration of cartilage generates pain and thus immobility. The balanced condition between construction and reduction of cartilage is disturbed, and the latter prevails. In an article about collagen, Eyre et al. noted the following:

"…there appears to be little capacity for articular chondrocytes to recapitulate the overall collagen architecture if the mature tissue is mechanically injured or goes through advanced stages of degeneration. The ability of chondrocytes to remodel the collagen at ultrastructural and molecular levels is poorly understood. There may be greater capacity than previously thought."[1]

Even though the turnover rate of collagen increases following injury or damage, it appears to be very slow.[2,3] In contrast, using isotopes which were "probably incorporated into the protein polysaccharide", Mankin observed "a half-life of about eight days accounting for over one fourth of the polysaccharide present in the tissue."[4] Hence, cartilage is not inert metabolically.[5] Insufficient remodelling capacity could depend on oxidative stress[6] or lack of substrates like L-lysine, ascorbic acid, and copper which cannot be synthesized by the body.[7] Over the last two decades studies both *in vitro* and *in vivo* "have confirmed that articular chondrocytes are able to respond to mechanical injury, joint instability due to genetic factors, and biological stimuli such as cytokines and growth and differentiation factors that contribute to structural changes in the surrounding cartilage matrix."[5]

Besides glycine and proline, L-lysine is an important component of collagen fibrils whose sufficient intake must be guaranteed. Ascorbic acid is crucial as a cofactor of prolyl hydroxylase and lysyl hydroxylase to generate hydroxyproline and hydroxylysine. After glycosylation with monosaacharides that occurs on hydroxy groups of L-lysine only, three propeptides will form a triple helix known as procollagen. In the golgi apparatus oligosaccharides are added. In being secreted out of the cell, collagen peptidases remove the ends of the procollagen molecule, and thereby tropocollagen is built. Lysyl oxidase produces aldehyde groups, which enable covalent bonding between tropocollagen mol-

ecules resulting in a polymer called collagen fibril.[8] Lysyl oxidase is an extracellular copper enzyme, therefore copper supply should be sufficient.

In vitro and animal studies support the idea that the properties of grape seed extract (GSE) may have beneficial effects on cartilage integrity.[9-12] GSE contains polyphenols such as resveratrol, phenolic acids, oligomeric proanthocyanidins (OPC), and flavonoids. Bioflavonoids and OPC show an initial increase in capillary resistance as they inhibit catecholamine O-methyl transferase resulting in a prolonged action of adrenalin which decreases capillary permeability.[13] Nevertheless, blood pressure remains normal and even mild hypertension gets normalized.[14] Masquelier's experiments also discovered that OPC, but not bioflavonoids, reduce dehydroascorbic acid to ascorbic acid with glutathione as a cofactor, thus establishing a long term effect on increased capillary resistance by ascorbic acid mediated reconstruction of collagen.

Arthrosis is frequently accompanied by episodes of arthritis leading to exacerbation of cartilage damage. Therefore, GSE's effective antioxidant properties[15,16] and anti-inflammatory qualities, for example by inhibiting histamine release,[17] are helpful. GSE is well absorbed,[14,18] plays a role in the prevention of degenerative diseases,[19] and decreases low-density lipoprotein-cholesterol oxidation and platelet aggregation. Another study showed that catechin treated collagen became resistant to mammalian, but not to bacterial collagenase. It was concluded catechin binds tightly to collagen and modifies its structure sufficiently to make it resistant to enzyme degradation.[20] Altogether, these effects make OPC much more effective compared to bioflavonoids.

Methods

Orthomolecular therapy with L-lysine, ascorbic acid, and GSE (Polyphenolics, Madera, CA) was offered to nine female patients who were suffering from chronic pain due to gonarthrosis (**Table 1**, opposite). Gonarthrosis is a degenerative, non-infectious disease of the knee joint, of which the arthrosis is morphologically characterized by a progressive loss of cartilage, sclerosis of the subchondral osseous structures, and partial involvement of the synovia.[21] The OPC content of GSE was significant at 94 %.[22] All patients were treated orthopedically for many years. Their knees did not have any major axial deviations. In addition to these substances a mixture of broad-spectrum nutrients was recommended to guarantee basic nutrient availability. The clinical focus was on pain relief. Pain levels were recorded before and during treatment using a 4-point Likert-type scale ranging from no or almost no pain (denoted as "0") to severe pain (denoted as "3").

Results

Significant pain relief was observed in four cases and five cases became pain-free (**Table 2**, p. 182; sign test, $p<0.05$). No analgesics were needed and mobility improved in all cases.

After a few months of therapy four patients lowered their daily doses of L-lysine and Case #7 took L-lysine (2 g) from the beginning and no GSE. Two of these became pain-free and three experienced pain relief. The only one patient who did not take GSE did not become pain-free. All pain-free patients took 4-8 g (mean 6.4 g) ascorbic acid; those who still had little pain were taking 2-6 g (mean 4.0 g). It is concluded that for complete and lasting pain relief 4-6 g of ascorbic acid is advisable combined with GSE and a sufficient amount of L-lysine (0.3-2.5 g).

Knee prosthesis was recommended to Case #1 in August, 2008. Following explanations of biochemical pathways she decided to attempt orthomolecular treatment. In January 2009, she ordered another prescription. Consulting in March she reported running out of her medication and realized just a couple of weeks later that her pain had relapsed. She continued taking her medication and reduced L-lysine some months later to 500 mg, staying pain-free with just little discomfort during winter, and of course

Table 1. Nutrients and prescribed daily doses (Ascorbic acid, GSE, L-lysine, arginine, carnitine, cysteine, and proline were taken orally in twice daily divided doses; all other substances once daily)

Nutrient	Dosage
Ascorbic acid	6-8 g
GSE	500 mg
L-lysine	2,500 mg
Vitamin A	500 IU
Vitamin B_1	1.0 mg
Vitamin B_2	1.2 mg
Vitamin B_3	12 mg
Vitamin B_6	1.2 mg
Vitamin B_{12}	3 µg
Vitamin D_3	5 µg
Vitamin E	34 mg
Folic Acid	0.4 mg
Chromium	60 µg
Copper	1.0 mg
Magnesium	200 mg
Molybdenum	80 µg
Selenium	33 µg
Zinc	8 mg
Beta-carotene	0.167 mg
Lutein	1.3 mg
Lycopene	1.3 mg
L-arginine	250 mg
L-carnitine	50 mg
L-cysteine	30 mg
L-proline	375 mg
Biotin	70 µg
Coenzyme Q10	10 mg

without prosthesis.

Case #5 experienced little improvement in December 2009, taking less than 2 g of ascorbic acid. After increasing the dose to 8 g she became pain-free. In June, 2010, she could lower the dose of L-lysine to 500 mg without relapse of pain.

Besides arthrosis, Case #9 had arthroscopic surgery two times to repair the menisci of her right knee. She was pain-free after one month of therapy and lowered her daily L-lysine and GSE from 500 to 300 mg, respectively, but continued taking 4 g ascorbic acid and the other nutrients.

Discussion

Mobility itself leads to an improvement of cartilage metabolism.[23] Even if many microbiological pathways are not well understood, the relief of pain correlates to a remodelling and thickening of the cartilage layer, to improvements of cartilage quality, to diminished inflammation, or to a combination of these. Cartilage thickness could be measured by radiography or magnetic resonance tomography which was not done because these patients recovered and there was no need for extended diagnostic procedures. Furthermore, radiography would not explain

Table 2. Pain levels before and after therapy (0: No or almost no pain, 1: little pain, 2: moderate pain, 3: severe pain)

Case	Age	Score Before Treatment	Score After 3-4 Weeks of Treatment	Ascorbic (g)* Acid	L-lysine(g)*	GSE (g)*
1	64	3	0	8	2.5	0.5
2	75	3	1	2	1.0	0.5
3	57	3	0	6	2.5	0.5
4	60	2	0	6	2.5	0.5
5	75	2	0	8	0.5	0.5
6	87	2	1	4	0.5	0.5
7	43	2	1	4	2.0	0
8	66	3	1	6	2.5	0.5
9	70	2	0	4	0.3	0.3

*Long-term daily dosages patients have remained on to sustain their improvements

the underlying microbiological mechanisms.

The daily demand for L-lysine in healthy people is estimated to be 30 mg/kg bodyweight[24] (i.e. 2.1 g/70 kg). The demand in arthritic disease is unknown even though it is a major substrate for collagen production. This study suggests that supplemental L-lysine has therapeutic effects. Cartilage is supplied with nutrients by the synovial fluid under anaerobic conditions. Ascorbic acid concentration in synovial fluid and in blood plasma is at comparable levels.[25] As seen among the present cases, raising the dose of ascorbic acid improved the results (case #5), and those taking less ascorbic acid did not get pain-free completely. This indicates the importance of the dose of ascorbic acid, which suggests that higher synovial fluid concentrations are more therapeutic.

Prior to this study, such fast recoveries of osteoarthritis could not be observed in patients who only took ascorbic acid for other reasons. Adding GSE enhanced the efficacy by augmenting anti-inflammatory and antioxidative mechanisms. As Case #7 demonstrated, GSE might be necessary to achieve painlessness; without GSE and despite sufficient ascorbic acid intake, pain relief was not complete.

In order to elucidate which nutrient contributes to pain relief, they could be prescribed consecutively. This data suggests that the combination of ascorbic acid, L-lysine, and GSE yields the best achievable results.

Conclusion

The cause of primary osteoarthritis is not unknown. It is an imbalance between mechanical forces that have the potential to damage cartilage and the collagen remodelling capacity of the chondrocytes. As arthrosis progresses with age, even if just minor physical burdens are present, chondrocyte function seems to be crucial. The present study proves that it is possible to ease and to resolve gonarthrotic pain by means of nutrients in appropriate doses which assist chondrocytes' ability to maintain cartilage integrity. These findings are in accordance with what we know about biochemical mechanisms in osteoarthritis. Additional studies are warranted to confirm these preliminary results.

Statement of Informed Consent

Verbal consent was obtained from all patients for publication of this report. All

identifying details have been removed to protect anonymity. The author and editor provide their assurance that these alterations have not distorted the scientific meaning.

Competing Interests

The author declares that he has no competing interests.

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