A 30-day clinical investigation of the safety and efficacy of kollaGen II-xs, a new avian sternal collagen type II hydrolysate

Andrey Pereira Lopes[1,2], Bianca Souza Bagatela[1,2], Fernando Luiz Affonso Fonseca[1], Scott Morten[2], Jennifer Gu[3], Fabio Ferreira Perazzo[1]

[1] Department of Exact and Earth Sciences, Federal University of Sao Paulo, Diadema, Sao Paulo, Brazil,
[2] Department of Clinical Medicine, Mortec Scientific, Cambridge, Ontario, Canada,
[3] Department of Research and Development, Los Angeles, California, United States of America.

Abstract

The present prospective and single-center investigated the safety and efficacy of KollaGen II-xs™, an avian sternal collagen type II hydrolysate. The range of motion, general pain, and muscle strength were evaluated. The results indicated that administration of 1500 mg/day of collagen type II hydrolysate for 30 days improved essential symptoms in individuals suffering from joint diseases, including range of motion, general pain, and muscle strength. These data support the view that collagen type II hydrolysate may be administered to patients suffering from joint diseases. No adverse effects were observed during the trial. These data support its use for patients suffering from degenerative joint diseases, including cartilage injuries, connective tissue disorders, polychondritis, joint defects, osteoarthritis, and rheumatoid arthritis.

Key words: avian sternal collagen type II hydrolysate, joint diseases, range of motion, general pain, muscle strength.

Introduction

KollaGen II-xs™, an avian sternal collagen type II hydrolysate, is a dietary supplement that may be beneficial for patients suffering from degenerative joint diseases, including cartilage injuries, connective tissue disorders, polychondritis, joint defects, osteoarthritis, and rheumatoid arthritis. Its use in the treatment of degenerative joint diseases has increasingly gained support in medical community and among consumers[1].

It has an average molecular weight of between about 45 and 65 kilodaltons (kDA). It is obtained from desiccated young avian sternal cartilage. Preferably, the avian sternal cartilage is collected from 4 to 8 week-old chicks. It is partially water-soluble and the composition comprises 20% to 30% of mucopolysaccaride, 65% to 70% of collagen type II and 1% to 3% of lipids. It may provide a method of helping cartilage formation in humans[2].

In preclinical studies, it has been demonstrated that orally administered collagen type II hydrolysate is thoroughly absorbed by the intestine and circulated in the blood stream, remaining in the gastrointestinal tract. These studies also revealed that that a significant amount of collagen type II hydrolysate-derived peptides reach cartilage tissue[3]. In addition, it was exposed that treatment of cultured chondrocytes induced a statistically significant dose-dependent increase in type II collagen synthesis of the chondrocytes in cell culture experiments[4].

Based on the findings that collagen type II hydrolysate is absorbed in its high molecular form, accumulating in cartilage, and is able to stimulate chondrocyte metabolism, it might be reasonable to use collagen type II hydrolysate as a nutritional supplement to activate collagen biosynthesis in chondrocytes in humans, especially patients suffering from degenerative joint diseases. Thus, the aim of this prospective and single-center investigation is to extend these earlier findings with KollaGen II-xs™, an avian sternal collagen type II hydrolysate.

Materials and methods

Study design

This prospective and single-center clinical trial was approved by the Ethics Committee of Mortec Scientific, Inc. (Cambridge, ON, Canada) and managed in its Department of Clinical Medicine.

According to study schedule, the consent form was discussed, signed and a complete physical examination was executed at screening. Activity level, diet history, medication/supplement use and medical history were recorded.

Subjects' complaints of joint discomfort were recorded using pre- and post-treatment questionnaires to evidence personal data and issues related to an individual's functional quality. A goniometer was used to measure the range of motion[5], a pain scale (Borg) was applied to subjectively percept the pain[6], and a properly calibrated sphygmomanometer was utilized to evaluate muscle strength[7].

Urine was collected for a pregnancy test for women of childbearing potential. A blood sample was taken for determination of alanine transaminase (ALT), aspartate transaminase (AST), bilirubin, blood urea nitrogen (BUN) and creatinine. Upon review of blood test results, eligible subjects were instructed to get an X-ray of the affected joints to confirm diagnosis.

A total of 15 subjects were recruited using the inclusion and exclusion criteria outlined in Table 1. At the first visit, selected subjects, properly informed by the Consent Term approved by the Scientific Committee of the Institute, were assigned to receive 1500 mg kollaGen II-xs™ (Certified Nutraceuticals, Inc., San Diego, CA) daily. At the final visit, subjects were required to come to the clinical division for clinical assessment. A subject treatment diary was completed by each patient throughout the study period to determine product compliance, side effects, and supplementation use.

Statistical method

For comparing non-parametric values, the Wilcoxon's test was used, and for comparing parametric values, the variance analysis (ANOVA) test were used. A significance level of 5% was adopted in all comparisons and statistically significant results were marked with an asterisk (*).

Table 1. Inclusion and exclusion criteria

Inclusion criteria
Males and females 45-75 years old
Females of childbearing potential must agree to use a medically approved form of birth control and have a negative urine pregnant test result
Disorder of the knee for more than three months
Able to walk
Availability for duration of study
Subject agrees not to start any new therapies during the course of the study
Able to give informed consent
Exclusion criteria
History of asthma, history of diabetes
Hyperuricemia
Hypersensitivity to NSAIDs
Abnormal liver or kidney function tests
Abnormal findings on complete blood count
Uncontrolled hypertension
History of allergic reaction to any ingredients in the test product
Hyperkalemia (potassium > 6.2 mmol/L)
History of cancer as well as gastrointestinal, renal, hepatic, cardiovascular, hematological, or neurological disorders
Anticipated problems with product consumption
High alcohol intake (>2 standard drinks per day)
History of psychiatric disorder that may impair the ability of subjects to provide written informed consent
Use of concomitant prohibited medication (narcotics, NSAIDs)
Any other condition that, in the opinion of the investigator, would adversely affect the subject's ability to complete the study or its measures

Results

Baseline characteristics of patients are summarized in Table 2. Where applicable, values are expressed as mean ± standard deviation.

Table 2. Baseline characteristics of patients.

Characteristics of patients	Values
Age (years)	53.7 ± 8.72
Sex (male/female)	8/7
Height (cm)	168.3 ± 9.74
Weight (kg)	82.9 ± 16.3
Systolic blood pressure (mm)	121.8 ± 8.92
Diastolic blood pressure (mm)	80.6 ± 7.71
Heart rate (bpm)	69.4 ± 7.56

The results are presented in Table 3 and Table 4 listing values for average, and standard deviation for each analyzed variable. Statistically significant results are marked with an asterisk (*)

Table 3. Range of motion, pain and muscle strength.

Treatment	Range of motion[5]		General pain[6]		Muscle strength[7]	
	Pre	Post	Pre	Post	Pre	Post
Average	105,22	169,87	8,73	2,36	58,43	102,89
Standard deviation	13,46	10,54	10,54	13,15	10,54	11,46
Standard error	4,22	4,76	4,76	5,37	4,76	5,21

Table 4. Pre- and post- treatment groups.

Comparison	P
Range of motion	0,021*
General pain	0,007*
Muscle strength	0,005*

These results indicate that administration of 1500 mg/day of collagen type II hydrolysate for 30 days improved essential symptoms in individuals suffering from joint diseases, including range of motion, general pain, and muscle strength. No adverse effects occurred during the 30-day trial period. The treatment was reported to be well tolerated by subjects.

Discussion

In the last few years, various nutritional supplements, including chondroitin, glucosamine, soybean unsaponifiables and diacerein have emerged as new treatment options for joint disorders[8]. The aim of this prospective and single-center investigation is to evaluate the safety and the efficacy of KollaGen II-xs™, an avian sternal collagen type II hydrolysate, which is a complex structural protein that may provide strength and flexibility to connective tissues.

An observational study investigated the use of collagen type II hydrolysate as a nutritional supplement to reduce symptoms of joint damage, with the hope that this change would reflect improvements in joint health. In that study, individuals were recruited who had not been diagnosed with degenerative joint disease but who complained about joint pain that both the treating physician and the subjects interpreted as being a result of stressful exercising. It was reported that 78% of individuals at the end of the study noticed substantial improvement of their joint symptoms, including range of motion, pain, and muscle strength[9].

The evaluation of muscle strength is an important technique to diagnose the etiology of the disease, and to define rehabilitation strategies. The muscle weakness, which was observed in our study during the pre-treatment assessments, is directly associated with knee joint pain and joint disability[10].

Osteoarthritis results in changes that affect not only intracapsular tissue, as well as periarticular tissues, such as ligaments, capsules, tendons and muscles. Osteoarthritis patients compared to healthy individuals of the same age had muscle weakness, reduced knee proprioception, reduced balance and position sense[11].

The presence of joint effusion, even in small amounts, is a potent inhibitory mechanism reflex muscular activity of the joints. A reduced reflex muscular activity causes hypotrophy and weakness early, with the resultant associated mechanical damages, such as decreased range of motion[12].

Muscle strength declines rapidly during the detention of a member by decreasing the size of the muscle and stress per unit of the muscle cross-sectional area. The largest absolute loss of muscle mass occurs at the beginning of hypotrophy pro-

cess[13]. The pain inhibits reflex muscular activity, causing atrophy, and muscle weakness. The painful process is prior to the muscular weakness[14].

This prospective and single-center investigation suggests that KollaGen II-xs™, an avian sternal collagen type II hydrolysate, may be beneficial for patients suffering from degenerative joint diseases, including cartilage injuries, connective tissue disorders, polychondritis, joint defects, osteoarthritis, and rheumatoid arthritis.

Conclusion

The purpose of this study was to determine whether administration of 1500 mg of avian sternal collagen type II hydrolysate daily would reduce joint pain in patients suffering from joint diseases. The design of the clinical trial was appropriate to reveal that collagen type II hydrolysate as a nutritional supplement ingested over 30 days was safe and efficacious in reducing symptoms of joint discomfort. The results of the trial provide data supporting the view that collagen type II hydrolysate may be administered to patients suffering from joint diseases. Further research will elucidate additional benefits from collagen type II hydrolysate.

Acknowledgements

This research was supported by Certified Nutraceuticals, Inc., San Diego, CA.

References

1. *Oesser S, Seifert J. Impact of collagen fragments on the synthesis and degradation of the extracellular matrix (ECM) of cartilage tissue. Orthopaedische Praxis 2005: 565-568.*

2. *Stiles TL. Kolla2-desiccated avian sternal cartilage powder. U.S. Patent 6,838,440 B2. January 04, 2005.*

3. *Oesser S, Adam M, Babel W, Seifert J. Oral administration of (14)C labeled gelatin hydrolysate leads to an accumulation of radioactivity in cartilage of mice (C57/BL). J Nutr 1999; 129: 1891-1895.*

4. *Oesser S, Seifert J. Stimulation of collagen type II biosynthesis and secretion in bovine chondrocytes cultured with degraded collagen. Cell Tissue Res 2003; 311: 393-399.*

5. *Lequesne M, Mery C, Sanson M, Gerard P. Indexes of severity for osteoarthritis of the hip and knee. Validation-value in comparison with other in comparison. Scand J Rheumatol 1987; 65: 85-89.*

6. *Borg G. Borg's perceived exertion and pain scales. Champaign: Human Kinects; 1998; 120.*

7. *Helewa A, Goldsmith CH, Smythe HA. The modified sphygmomanometer, an instrument to measure muscle strength: a validation study. J Chronic Dis 1981; 34: 353-361.*

8. *Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, et al. Glucosamine, chondroitin sulfate, and the two in combination for pain knee osteoarthritis. N Engl J Med 2006; 354: 795-808.*

9. *Flechsenhar K, Alf D. Ergebnisse einer Anwendungsbeobachtung zu Kollagen-Hydrolysat CH-Alpha. Orthopaedische Praxis 2005; 9: 486-494.*

10. *O'Reilly SC, Jones A, Muir KR, Doherty M. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. Ann Rheum Dis 1998; 57: 588-594.*

11. *Hassan BS, Mockett S, Doherty M. Static postural sway, proprioception, and maximal voluntary quadriceps contraction in patients with knee osteoarthritis and normal control subjects. Ann Rheum Dis 2001; 60: 612-618.*

12. *Wilson CH, Mayer WP. Exercise and mobilization techniques in principles of physical medicine and rehabilitation in the muscles diseases. Orlando: Grune & Stratton; 1986.*

13. *Booth FW. Physiologic and biochemical effects of immobilization on muscle. Clin Orthop Relat Res 1987; 219: 15-20.*

14. *Silva ALP, Imoto DM, Croci AT. Comparison of cryotherapy, exercise and short waves in knee osteoarthritis treatment. Acta Ortop Bras 2007; 15: 204-209.*

Corresponding Author
Fabio Ferreira Perazzo,
Department of Exact and Earth Sciences,
Federal University of Sao Paulo,
Diadema,
Sao Paulo,
Brazil,
E-mail: ffperazzo@gmail.com