ORIGINAL ARTICLE

Safety and Efficacy KollaGen II-xs: A 60-day Clinical Trial

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ABSTRACT

Objective: *To investigate the safety and efficacy of an avian sternal collagen type II hydrolysate, KollaGen II-xs™.*

Methods: *A goniometer was used to measure the range of motion, a pain scale (Borg) was applied to subjectively percept the pain, and a properly calibrated sphygmomanometer was utilized to evaluate muscle strength.*

Results: *The results indicated that the administration of 2000 mg/day of collagen type II hydrolysate for 60 days improved essential symptoms in individuals suffering from joint diseases, including the range of motion, general pain and muscle strength. No adverse effects were observed during the trial.*

Conclusion: *The results support the view that collagen type II hydrolysate may be administered to patients suffering from joint diseases. These data encourage its use for patients suffering from degenerative joint diseases, including cartilage injuries, connective tissue disorders, polychondritis, joint defects, osteoarthritis and rheumatoid arthritis.*

Keywords: Dietary supplement, efficacy, joint diseases, KollaGen II-xs, safety

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 been verified in preclinical studies that orally administered collagen type II hydrolysate is thoroughly absorbed by the intestine and circulated in the blood stream, remaining in the gastrointestinal tract. It was also revealed that a significant amount of collagen type II hydrolysate-derived peptides reached cartilage tissue (2). Additionally, 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 (3).

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 (4), 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 single-centre investigation is to extend these earlier findings with KollaGen II-xs™, an avian sternal collagen type II hydrolysate.

SUBJECTS AND METHODS

This single-centre 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 the study schedule, the consent form was discussed and signed, and a complete physical examination was executed at screening. Activity level,

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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 the determination of alanine transaminase, aspartate transaminase, bilirubin, blood urea nitrogen 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 20 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 Mortec Scientific, Inc. (Cambridge, ON, Canada), were assigned to receive 2000 mg KollaGen II-xs™ (Certified Nutraceuticals, Inc., San Diego, CA, USA) 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.

For comparing non-parametric values, Wilcoxon's test was used, and for comparing parametric values, the analysis of variance test was performed by GraphPad InStat 3.1. 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 of 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 3 months
Able to walk
Availability for the duration of the 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
Hyperuricaemia
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
Hyperkalaemia (potassium > 6.2 mmol/L)
History of cancer as well as gastrointestinal, renal, hepatic, cardiovascular, haematological 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

NSAIDs = non-steroidal anti-inflammatory drugs.

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)	55.9 ± 7.91
Sex (male/female)	10/10
Height (cm)	168.1 ± 8.52
Weight (kg)	81.3 ± 14.6
Systolic blood pressure (mm)	120.5 ± 7.84
Diastolic blood pressure (mm)	80.6 ± 8.33
Heart rate (bpm)	68.9 ± 7.42

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

Table 3: Range of motion, pain and muscle strength

	Range of motion[5]		**General pain**[6]		**Muscle strength**[7]	
Treatment	Pre	Post	Pre	Post	Pre	Post
Average	105.22	172.53	8.73	1.92	58.43	104.97
Standard deviation	13.46	10.81	10.54	12.73	10.54	11.73
Standard error	4.22	4.93	4.76	5.48	4.76	5.68

Table 4: Pre- and post-treatment groups

Comparison	***p* value**
Range of motion	0.011*
General pain	0.001*
Muscle strength	0.004*

These results indicate that the administration of 2000 mg/day of collagen type II hydrolysate for 60 days improved essential symptoms in individuals suffering from joint diseases, including the range of motion, general pain and muscle strength. No adverse effects occurred during the 60-day trial period. The treatment was reported to be well tolerated by subjects.

DISCUSSION

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

In an observational study, the use of collagen type II hydrolysate as a nutritional supplement to reduce symptoms of joint damage was investigated, with the expectation that this change would reflect improvements in joint health. 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 the range of motion, pain and muscle strength (9).

The evaluation of muscle strength is an important technique to diagnose the aetiology 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 but also periarticular tissues, such as ligaments, capsules, tendons and muscles. Compared with healthy individuals of the same age, osteoarthritis patients 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 the 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 process (13). The pain inhibits reflex muscular activity, causing atrophy and muscle weakness. The painful process is prior to the muscular weakness (14).

This single-centre investigation suggests that the avian sternal collagen type II hydrolysate, KollaGen II-xs™, 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 define whether the administration of 2000 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 60 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.

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