ЭФФЕКТИВНОСТЬ И БЕЗОПАСНОСТЬ КУРКУМИНА У ПАЦИЕНТОВ С МЕТАБОЛИЧЕСКИМ ФЕНОТИПОМ ОСТЕОАРТРИТА: ПИЛОТНОЕ ИССЛЕДОВАНИЕ

Ширинский И.В.[1], Ширинский В.С.[1], Филатова К.Ю.[2]

[1] ФГБНУ«Научно-исследовательский институт фундаментальной и клинической иммунологии», г. Новосибирск, Россия
[2] Новосибирский областной клинический диагностический центр, г. Новосибирск, Россия

Резюме. Целью исследования была оценка эффективности и безопасности куркумина при остеоартрите, ассоциированном с метаболическим синдромом (МетС-ОА). Перед включением в исследование все пациенты подписали форму добровольного информированного согласия. Диагноз ОА ставился в соответствии с критериями Американской Коллегии Ревматологов, МетС – в соответствии с критериями Российского общества кардиологов.

Дизайн исследования: до, после. Основными критериями включения были наличие ОА и МетС, уровень оценки общего состояния здоровья и боли более 50 мм с использованием 100 мм визуальной аналоговой шкалы (ВАШ). Основными конечными точками были ВАШ общего здоровья. Другими исходами были ВАШ боли, различные подкатегории шкалы повреждения и ОА коленного сустава, Knee injury and Osteoarthritis Outcome Score (KOOS): подкатегория боли (KOOS боль), подкатегория другие симптомы (KOOS симптомы), подкатегория повседневных активностей (KOOS ПА), подкатегория активностей при спорте отдыхе sport and recreation (KOOS спорт и отдых) и подкатегория качества жизни (KOOS КЖ). Выраженность депрессии оценивалась с помощью опросника PHQ-9. Оценивалась доля пациентов, достигших минимального клинически значимого различия в изменении боли (МКЗР). Точкой разделения для МКЗР для боли было (а) 15 из 100 для абсолютного улучшения и 20% для относительного улучшения.

Пациенты принимали экстракт C. longa в дозе 1000 мг/день в течение 4 недель. Оценка параметров проводилась до лечения и через 4 недели терапии.

В исследование были включены 18 женщин с МетС-ОА. К концу терапии выявлялось достоверное уменьшение ВАШ общего здоровья в среднем на 33,9 мм (p = 0,001), ВАШ боли на 25 мм (p = 0,001). Наблюдалась тенденция к улучшению показателя PHQ-9 на 2,9 (p = 0,05). Среднее уменьшение KOOS боли было 11 (p = 0,001). KOOS симптомом – 9 (p = 0,025), KOOS ПА – 12,4 (p 0,001), KOOS спорт и отдых – 10,3 (p = 0,044), KOOS КЖ – 14,4 (p = 0,009). МКЗР боли и общего здоровья выявлено у 9 (56%) пациентов. Нежелательных событий не было.

Результаты этого исследования указывают на безопасность и эффективность экстракта C. Longa при МетС-ОА. Для подтверждения этих данных необходимы крупные контролируемые исследования.

Ключевые слова: куркумин, ревматология, минимальное клинически значимое различие, метаболический синдром, депрессия, остеоартрит, коморбидность

Адрес для переписки:

Ширинский Иван Валерьевич
ФГБНУ«Научно-исследовательский институт фундаментальной и клинической иммунологии»
630047, Россия, г. Новосибирск, ул. Залесского, 6.
Тел.: 8 (923) 107-51-00.
Факс: 8 (383) 228-25-47.
E-mail: valery.shirinsky@gmail.com

Address for correspondence:

Ivan V. Shirinsky
Research Institute of Fundamental and Clinical Immunology
6 Zalessky St
Novosibirsk
630047 Russian Federation
Phone: +7 (923) 107-51-00.
Fax: +7 (383) 228-25-47.
E-mail: valery.shirinsky@gmail.com

Образец цитирования:

И.В. Ширинский, В.С. Ширинский, К.Ю. Филатова «Эффективность и безопасность куркумина у пациентов с метаболическим фенотипом остеоартрита: пилотное исследование» // Медицинская иммунология, 2023. Т. 25, № 5. С. 1099-1102.
doi: 10.15789/1563-0625-EAS-2771

© Ширинский И.В. и соавт., 2023
Эта статья распространяется по лицензии Creative Commons Attribution 4.0

For citation:

I.V. Shirinsky, V.S. Shirinsky, K.Yu. Filatova "Efficacy and safety of curcumin in patients with metabolic phenotype of osteoarthritis: A pilot study", Medical Immunology (Russia)/Meditsinskaya Immunologiya, 2023, Vol. 25, no. 5, pp. 1099-1102.
doi: 10.15789/1563-0625-EAS-2771

© Shirinsky I.V. et al., 2023
The article can be used under the Creative Commons Attribution 4.0 License

DOI: 10.15789/1563-0625-EAS-2771

EFFICACY AND SAFETY OF CURCUMIN IN PATIENTS WITH METABOLIC PHENOTYPE OF OSTEOARTHRITIS: A PILOT STUDY

Shirinsky I.V.[a], Shirinsky V.S.[a], Filatova K.Yu.[b]

[a] *Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russian Federation*
[b] *Novosibirsk Regional Clinical Diagnostic Center, Novosibirsk, Russian Federation*

Abstract. The aim of this study was to assess efficacy and safety of curcumin in metabolic syndrome-associated osteoarthritis (MetS-OA). All patients provided written informed consent. Knee OA was diagnosed according to American College of Rheumatology criteria; MetS was diagnosed according to Russian Scientific Society of Cardiology Guidelines. The study had before-and-after design. The main inclusion criteria were presence of knee OA and MetS, levels of global health assessment and pain assessment more than 50 mm using 0-100 visual analogue scale (VAS). The main outcome was VAS global. The other outcomes were VAS pain, Knee injury and Osteoarthritis Outcome Score (KOOS) consisting of five subscales: pain (KOOS pain), other symptoms (KOOS symptoms), activities in daily living (KOOS ADL), function in sport and recreation (KOOS Sport/Rec) and knee related Quality of life (KOOS QoL). The level of depression was measured using PHQ-9. For pain, proportion of patients achieving minimal clinically important improvement (MCII) was assessed using the cut-offs of (a) 15 of 100 for absolute improvement and 20% for relative improvement.

The treatment consisted of C. longa extract 1000 mg/day for 4 weeks. The assessments were performed on baseline and 4 weeks thereafter. Eighteen women with MetS-OA of the knee were included in the study.

At the end of treatment, there were significant improvements in the VAS global scale by an average 33.9 mm ($p = 0.001$), VAS pain by 25 mm ($p = 0.001$). There was a trend towards improvement in PHQ-9 by 2.9 ($p = 0.05$). The mean improvement in KOOS pain was 11 ($p = 0.001$). KOOS symptoms improved by 9 ($p = 0.025$), KOOS ADL – by 12.4 ($p = 0.001$), KOOS Sport/Rec by 10.3 ($p = 0.044$), and KOOS QOL by 14.4 ($p = 0.009$). The proportion of patients achieving clinically significant improvement (MCII) were nine (56%) for both global health and pain. There were no adverse events during the study. The findings of this study suggest clinical efficacy and safety of C. Longa in MetS-associated knee OA. There is a need for large controlled studies to confirm these results.

Keywords: curcumin, rheumatology, minimal clinically important difference, metabolic syndrome, depression, osteoarthritis, comorbidity

Introduction

The World Health Organization (WHO) declares prevention and treatment of chronic non-communicable diseases (NCDs) as a priority of the third decade of the 21st century. Common NCDs are heterogeneous in terms of their pathogenesis and clinical manifestations. This heterogeneity is manifested as different endotypes (distinct patho-biological mechanisms of a disease) and phenotypes (observable characteristics or traits of a disease) of NCD [4, 8]. It now becomes evident that further improvements in the prevention, diagnostics, and treatment of NCDs are possible only in case of better understanding of the differences in various endotypes and phenotypes of asthma, rheumatoid arthritis, osteoarthritis and other NCDs.

Metabolic syndrome (MetS) – associated OA, also called metabolic OA, occurs as a result of metabolic disturbances caused by obesity, diabetes mellitus, insulin resistance, dyslipidemia, hyperuricemia, and arterial hypertension [8]. The prevalence of MetS ranges from 10 to 34% in people older than 18 years. In Russia, the estimated prevalence of MetS varies from 20% to 35% [5, 8].

A promising way to treat comorbidity is to use pleiotropic phytotherapeutic agents aimed at various pathogenetic pathways [3]. One of the popular phytomedicines, Curcuma longa (CL) and its active components (curcuminoids) has been shown to exert anti-inflammatory, immunomodulatory, and lipid lowering effects [1]. There have been many studies assessed the effects of CL in OA. In a meta-analysis treatment with CL was associated with clinically significant improvements of pain in knee O [6]. It should be noted that the studies on CL included patients with OA irrespective of their comorbidities or phenotype of OA.

There is a lack of studies evaluating effects of CL in a selected group of patients with particular phenotype of OA. Therefore, we undertook this exploratory study to assess efficacy and safety of CL in patients with MetS-associated OA.

Materials and methods

The study protocol, patient information sheet, and case report form were approved by the Local Ethics Committee attached to the Scientific Research Institute of Fundamental and Clinical immunology. The main inclusion criteria were as follows:

– The diagnosis of knee OA made in accordance with ACR 1986 criteria [2].

– MetS diagnosed according to criteria of Russian Society of Cardiology:

Presence of abdominal obesity [waist circumference (WC) > 80 cm in women and > 94 cm in men] and two of the following criteria:

1) Arterial hypertension (arterial blood pressure ≥ 140/90 mm hg);

2) Triglycerides (TG) ≥ 1.7 mmol/L;

3) High density lipoprotein (HDL) cholesterol < 1.0 mmol/L in men and < 1.2 mmol/L in women;

4) Low density lipoprotein (LDL) cholesterol > 3.0 mmol/L;

5) Fasting hyperglycemia (blood glucose ≥ 6.1 mmol/L) or impaired glucose tolerance (plasma glucose ≥ 7.8 but ≤ 11.1 mmol/L 2 hours after meal).

– Pain level more than 50 mm on Visual Analogue Scale (VAS).

– Not taking non-steroidal anti-inflammatory drugs due to poor tolerability or lack of effect.

All patients underwent knee x-ray and assessment according to Kellgren-Lawrence classification. The study design was before-and-after study. Each participant was given oral curcumin 1000 mg daily in two doses for four weeks. The patients were not allowed to take non-steroidal anti-inflammatory drugs during the study. Paracetamol up to 3 g/day could be used as a rescue therapy.

The assessments and blood sampling were made on baseline visit (W0) and 4 weeks thereafter (W4). The primary end point was global assessment of health by the patient using 100 mm VAS. The secondary endpoints were:

– Knee injury and Osteoarthritis Outcome Score (KOOS) consisting of five subscales: pain (nine items), other symptoms (seven items), activities in daily living (ADL) (17 items), function in sport and recreation (Sport/Rec) (five items) and knee related Quality of life (QoL) (4 items). Likert scale was used so all items had five possible answer options scored from 0 (No Problems) to 4 (Extreme Problems). Each of the five scores was calculated as the sum of the items included. The scores were transformed to a 0-100 scale, with zero representing extreme knee problems and 100 representing no knee problems [7].

– Patient Health Questionnaire (PHQ-9) for the assessment of depression presence and severity. The PHQ-9 has nine Likert (0 to 3) questions. After the completion all items are summed thus giving range from 0 to 27, with 0 – indicating no depression, 27 – maximal depression. In accordance with PHQ-9, depressive symptomatology is classified as no depression (0-4), mild depression (5-9), moderate depression (10-14).

– Pain on 100 mm VAS.

We assessed the proportion of patients achieving minimal clinically important improvement (MCII) in global scale assessment and in VAS pain. The cut-offs for MCII changes were (a) 15 of 100 for absolute improvement and 20% for relative improvement [9]. The descriptive statistics is presented with mean and standard deviation/median and interquartile range for continuous variables, absolute number (percentage) for dichotomous variables. The differences between means before and after the treatment were assessed using paired t-test.

Results and discussion

Eighteen women with knee OA and concomitant MetS were included in the study. The baseline demographic and clinical characteristics of the included patients are presented in Table 1. All patients had obesity and have had diagnoses of knee OA or hypertension for 8-10 years. All patients had radiographic knee OA, grades II-III according to Kellgren-Lawerence classification. The majority (88%) of patients had symptoms of mild to moderate depression.

Table 2 shows changes in VAS global, VAS pain, and PHQ-9 before and after the treatment. There

TABLE 1. BASELINE CHARACTERISTICS OF PATIENTS WITH KNEE OA AND MetS

	Patients with knee OA and MetS, n = 18
Age (years)	65 (61-71)
Body mass (kg)	90 (85-100)
Waist circumference (cm)	107.5 (103.5-116.0)
Body mass index (kg/m²)	34 (31.5-36.8)
Time since the diagnosis of OA (years)	8 (5-11)
Time since the diagnosis of hypertension (years)	10 (4-14)

TABLE 2. VAS GLOBAL, VAS PAIN AND PHQ-9 BEFORE AND AFTER THE TREATMENT

	Before treatment (W0)	After treatment (W4)	p
VAS global, mm	57.6 (15.8)	23.7 (20.5)	0.001
VAS pain, mm	65.3 (19.4)	40.3 (22.9)	0.001
PHQ-9	9.4 (4.9)	6.5 (4.1)	0.05

Note. The values represent mean (SD).

TABLE 3. KOOS SUBSCALES BEFORE AND AFTER THE TREATMENT WITH CURCUMIN

	Before treatment (W0)	After treatment (W4)	p
KOOS symptoms	49 (13.5)	58 (14.9)	0.025
KOOS pain	49.2 (12.1)	60.9 (11.5)	0.001
KOOS function in daily living	47.6 (10.2)	60 (13.9)	0.001
KOOS function in sport and recreation	24.3 (13.5)	34.6 (13.6)	0.044
KOOS knee related Quality of life	22.5 (13.6)	36.9 (19.1)	0.009

were statistically significant improvements in VAS global (-33.9 mm) and VAS pain (-25 mm) at the end of treatment. The proportion of patients achieving clinically significant improvement (MCII) were nine (56%) for both global health and pain. There was a trend towards improvement of depressive symptoms.

The mean values of KOOS subscales before and after treatment are shown in Table 3. There were significant improvements in all subcategories: KOOS symptoms, KOOS pain, KOOS function in daily living, KOOS function in sport and recreation, and KOOS knee related Quality of life.

No adverse event was registered during the study.

Conclusion

In conclusion, we found significant improvement of global assessment of health, pain, function, and quality of life after treatment with curcumin of patients with MetS-associated knee OA. These results support efficacy and safety of curcumin in OA patients with comorbidity. However, as our findings were obtained in a non-controlled study, larger randomized double-blind controlled studies comparing curcuminoids with active control or placebo are needed.

References

1. Akaberi M., Sahebkar A., Emami S.A. Turmeric and Curcumin: From Traditional to Modern Medicine. *Adv. Exp. Med. Biol., 2021, Vol. 1291, pp. 15-39.*
2. Altman R., Asch E., Bloch D., Bole G., Borenstein D., Brandt K., Christy W., Cooke T.D., Greenwald R., Hochberg M., Howell D., Kaplan D., Koopman W., Longley S. III, Mankin H., McShane D.J., Medsger T. Jr., Meenan R., Mikkelsen W., Moskowitz R., Murphy W., Rothschild B., Segal M., Sokoloff L., Wolfe F. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum., 1986, Vol. 29, pp. 1039-1049.*
3. Harvey A.L., Edrada-Ebel R., Quinn R.J. The re-emergence of natural products for drug discovery in the genomics era. *Nat. Rev. Drug Discov., 2015, Vol. 14, pp. 111-129.*
4. Kazygasheva E., Shirinsky V., Shirinsky I. Diabetes-associated osteoarthritis: a syntropy? *Medical Immunonogy (Russia), 2016, Vol. 18, no. 4, pp. 317-330.* (In Russ.) doi: 10.15789/1563-0625-2016-4-317-330.
5. Liu X., Machado G.C., Eyles J.P., Ravi V., Hunter D.J. Dietary supplements for treating osteoarthritis: a systematic review and meta-analysis. *Br. J. Sports Med., 2018, Vol. 52, pp. 167-175.*
6. Roos E.M.,Lohmander L.S. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes, 2003, Vol. 1, 64.* doi: 10.1186/1477-7525-1-64.
7. Shirinsky V., Kalinovskaya N.Y., Filatova K.Y., Shirinsky I. Clinical and immunological features of metabolic phenotype of osteoarthritis. *Medical Immunonogy (Russia), 2020, Vol. 22, no. 2, pp. 327-334.* (In Russ.) doi: 10.15789/1563-0625-CAI-1881.
8. Tubach F., Ravaud P., Baron G., Falissard B., Logeart I., Bellamy N., Bombardier C., Felson D., Hochberg M., van der Heijde D., Dougados M. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. *Ann. Rheum. Dis., 2005, Vol. 64, pp. 29-33.*

Авторы:

Ширинский И.В. *– д.м.н., ведущий научный сотрудник, заведующий лабораторией клинической иммунофармакологии ФГБНУ «Научно-исследовательский институт фундаментальной и клинической иммунологии», г. Новосибирск, Россия*

Ширинский В.С. *– д.м.н., профессор, главный научный сотрудник лаборатории клинической иммунофармакологии ФГБНУ «Научно-исследовательский институт фундаментальной и клинической иммунологии», г. Новосибирск, Россия*

Филатова К.Ю. *– врач-ревматолог, Новосибирский областной клинический диагностический центр, г. Новосибирск, Россия*

Authors:

Shirinsky I.V., *PhD, MD (Medicine), Leading Research Associate, Head, Laboratory of Clinical Immunopharmacology, Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russian Federation*

Shirinsky V.S., *PhD, MD (Medicine), Professor, Consultant Rheumatologist, Chief Research Associate, Laboratory of Clinical Immunopharmacology, Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russian Federation*

Filatova K.Yu., *Rheumatologist, Novosibirsk Regional Clinical Diagnostic Center, Novosibirsk, Russian Federation*

Поступила 14.04.2023
Принята к печати 20.04.2023

Received 14.04.2023
Accepted 20.04.2023