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THE EFFECT OF AN INNOVATIVE CREAM ON PAIN, MOBILITY, FUNCTIONAL ABILITY AND QUALITY OF LIFE IN PATIENTS WITH NON-SPECIFIC LOW BACK PAIN

UČINAK INOVATIVNE KREME NA BOL, POKRETLJIVOST, FUNKCIONALNU SPOSOBNOST I KVALITETU ŽIVOTA U BOLESNIKA S NESPECIFIČNOM KRIŽOBOLJOM

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Abstract

Introduction. Non-specific low back pain is defined as pain between the rib cage and the lower fold of the buttocks, which cannot be associated with a specific pathology, but probably is of mechanical cause. The empirical use of a cream intended for the ease of mobility of the spine, called Beaute Vitale® (BV) which was used approximately 40 years ago in Southeastern Europe, showed a significant reduction in the symptoms of many diseases of the locomotor system, especially in non-specific low back pain. The main active ingredients of the cream are brown algae extract and turmeric. The aim of this study was to investigate the effect of the BV cream on pain intensity, mobility, functional capacity and quality of life in patients with non-specific low back pain. *Patients and methods.* The cream was applied to the skin of the lumbar and sacral region through 4 treatments during the course of one year, on the basis of 20 consecutive patients with acute and subacute non-specific low back pain. Each treatment lasted for 7 days. Before and after each treatment, including after the end of the entire treatment cycle, spinal mobility indices (Thomayer's test), Schober's test and lateral flexion of the spine to the left and right were measured. In addition to that, the subjects filled out the validated Rolland-Morris Disability Questionnaire (RMDQ) as a standard measure of functional ability of patients with low back pain and the EQ-5D-5L as a validated measure of quality of life. To compare the results, depending on the data distribution, the T-test or the Wilcoxon test for dependent samples were used. *Results.* After one year (a total of 4 treatments), a significant difference was found in the clinical tests of lateral flexion ($p<0.0001$) and EQ-5D-5L, in the domains of pain ($p<0.001$) and mobility ($p<0.01$), as well as the VAS scale of overall health ($p=0.05$), and all of these changes revealed improved scores. No significant change was found in the measures of sagittal mobility (Thomayer's test and Schober's test), in the total value of the RMDQ, and in the EQ-5D-5L domains of activity, self-care and anxiety/depression. No significant skin changes or other side effects were observed when using the product. *Conclusion.* In our sample of subjects with acute and subacute non-specific low back pain, the BV cream showed positive effects on reducing the sense of pain, increasing spinal mobility and improving the general feeling of well-being. The BV cream can be recommended as supportive conservative therapy in these patients. Further research is needed in terms of additional assessment of the effect of this preparation.

Keywords: pain, function, quality of life, cream, lumbar pain, unspecific, muscle relaxation

Sažetak

Uvod. Nespecifična križobolja se definira kao bol između rebrenog luka i donje glutealne brazde, koja se ne može povezati sa specifičnom patologijom, a vjerojatno je mehaničkog uzroka. Empirijskim korištenjem kreme za olakšanu pokretljivost kralježnice, imenom *Beaute Vitale*® (BV), posljednjih četrdesetak godina u jugoistočnoj Europi pokazalo se značajno smanjenje simptoma sa strane mnogih bolesti lokomotornog sustava, osobito u nespecifičnoj križobolji. Osnovni aktivni sastojci kreme su ekstrakt smeđe alge i kurkuma. Cilj ove studije bio je istražiti učinak kreme BV na intenzitet boli, pokretljivost, funkcionalnu sposobnost i kvalitetu života u bolesnika s nespecifičnom križoboljom. *Ispitanici i metode.* Krema se nanosila na kožu lumbalne i sakralne regije kroz četiri tretmana tijekom jedne godine, na uzorku od 20 konsekutivnih bolesnika s akutnom i subakutnom nespecifičlnom križoboljom. Svaki tretman trajao je sedam dana. Prije i nakon svakog tretmana, uključivo i nakon završetka cjelokupnog ciklusa liječenja, mjereni su indeksi pokretljivosti kralježnice (Thomayerova mjera), Schoberov klinički test te laterofleksija kralježnice ulijevo i udesno. Također, ispitanici su ispunili validirane upitnike *Rolland-Morris Disability* (RMDQ) kao standardnu mjeru funkcionalne sposobnosti bolesnika s križoboljom i EQ-5D-5L kao validiranu mjeru kvalitete života. Za usporedbu rezultata, ovisno o distribuciji podataka, korišteni su T- test ili Wilcoxonov test za zavisne uzorke. *Rezultati.* Nakon jedne godine (ukupno četiri tretmana) nađena je značajna razlika u kliničkim testovima laterofleksije ($p<0,0001$) i EQ-5D-5L i to u domenama za bol ($p<0,001$), mobilnost ($p<0,01$), kao i VAS skale ukupnog zdravlja ($p=0,05$), sve promjene u smislu poboljšanja rezultata. Nije nađena značajna promjena u mjerama sagitalne gibljivosti (Thomayerova i Schoberova mjera), u ukupnoj vrijednosti RMDQ, te EQ-5D-5L domeni aktivnosti, samozbrinjavanja i anksioznosti/depresije. Nisu primijećene značajne kožne ili druge nuspojave pri primjeni preparata. *Zaključak.* U našem uzorku ispitanika s akutnom i subakutnom nespecifičnom križoboljom krema BV je pokazala pozitivne učinke smislu smanjenja boli, povećanja pokretljivosti kralježnice te poboljšanja općeg osjećaja zdravlja. Krema BV može se preporučiti kao suportivna konzervativna terapija u tih bolesnika. Potrebna su daljnja istraživanja u smislu dodatne ocjene učinka ovog preparata.

Ključne riječi: bol, funkcija, kvaliteta života, krema, križobolja, nespecifična, relaksacija mišića

INTRODUCTION

Low back pain is most often defined as pain between the rib cage and the lower fold of the buttocks, which can (but does not have to) spread to the legs (1). If this pain is caused by a specific pathophysiological mechanism, we speak of specific low back pain. However, in cases where we are talking about pain without a clear nociceptive-specific cause, that is the case of non-specific low back pain (2).

A preparation called Beaute Vitale® (BV) is a cream that has been empirically used for the past 40 years to relieve symptoms of the locomotor system, especially non-specific low back pain. The aforementioned preparation started to be used in northern Macedonia in the 1980s, and over time, its use has spread to the whole of Southeastern Europe and beyond, mainly through word-of-mouth recommendations. In 2020, the cream was submitted for analysis to the Croatian Institute of Public Health (CIPH), where its composition was defined, and it consists of water, petrolatum, propylene glycol, caprylic/capric triglyceride, PEG 30 glyceryl stearate, glycerine, cetyl alcohol, brown algae *Fucus vesiculosus* extract, *Curcuma longa* extract, camphor, benzyl alcohol, and dehydroacetic acid preservative. After the analysis carried out at the Croatian Institute of Public Health (CIPH), the BV cream was registered as a cosmetic product. By looking at the composition of the cream, it is evident that the active substances are brown algae *Fucus vesiculosus* extract, and *Curcuma longa* extract, curcumin.

UVOD

Križobolju najčešće definiramo kao bol između rebrenog luka i donje glutealne brazde, s propagacijom na nogu ili bez nje (1). Ako je ta bol uzrokovana specifičnim patofiziološkim mehanizmom, govorimo o specifičnoj križobolji, dok, ako se radi o boli bez jasnog nociceptivno-specifičnog uzroka, govorimo o nespecifičnoj križobolji (2).

Preparat imenom *Beaute Vitale*® (BV) je krema koja se posljednjih četrdesetak godina empirijski koristi za ublažavanje simptoma sa strane lokomotornog sustava, osobito nespecifične križobolje. Navedeni preparat se počeo koristiti u sjevernoj Makedoniji 1980-ih godina prošloga stoljeća te se s vremenom, uglavnom preko usmene predaje korisnika, proširio i na cijelu jugoistočnu Europu pa i dalje. Godine 2020. krema je data na analizu u Hrvatski zavod za javno zdravstvo (HZJZ), gdje je definiran njezin sastav, a sastoji se od vode, petrolatuma, propilen-glikola, triglicerid caprylic/capric, PEG 30 glyceryl stearata, glicerina, cetil alkohola, ekstrakta smeđe alge *Fucus vesiculosus*, ekstrakta *Curcuma Longa*, kamfora, benzilnog alkohola te konzervansa dihidrooctene kiseline. Nakon analize u HZJZ-u, BV je registrirana kao kozmetički proizvod. Uvidom u sastav kreme, vidljivo je da su aktivne tvari ekstrakt smeđe alge, *Fucus vesiculosus*, te ekstrakt kurkumin iz *Curcume longe*.

Fucus vesiculosus je smeđa morska alga koja se dulji niz godina koristi u biljnoj medicini kao dodatak pre-

Fucus vesiculosus is a brown seaweed that has been used in herbal medicine for many years as a dietary supplement for joint swelling (3), but it is increasingly being used for relieving the symptoms of osteoarthritis (4) by the probable mechanism of reducing the fibrosis of the synovial membrane (5), and it also indirectly leads to the reduction of joint stiffness, muscle relaxation, and ease of mobility. *Fucus vesiculosus* is also used locally, however previous papers on local activity have mainly examined the role of this product as an antioxidant used in the cosmetic industry (6). On the other hand, *Curcuma longa*, which belongs to the ginger family, has been used for many years as an anti-inflammatory substance that systemically affects the symptoms of osteoarthritis (7), but it also has a local effect in the form of volatile oils (9) that are used for muscle relaxation (8), and, in addition to that it indirectly improves mobility.

Non-specific low back pain is a major public health problem (1), and one of the known methods of treatment includes perorally applied muscle relaxants (10) or, for example, massage (11), with the end result of reducing pain and improving mobility.

The aim of this study was to evaluate the effect of the BV preparation on pain, mobility of the lumbar spine, functional capacity and quality of life in patients with acute and subacute non-specific low back pain.

MATERIALS AND METHODS

The study was conducted at the Special Hospital for Medical Rehabilitation "Daruvarske toplice" during the course of one year. The study was conducted in accordance with the 1967 Declaration of Helsinki and its subsequent amendments, as well as with the principles of good clinical practice. All subjects signed an informed consent before any procedure related to the study, and were previously informed in detail about the study, its goals and risks. The approval for this study was given by the Ethics Committee of the Special Hospital for Medical Rehabilitation "Daruvarske toplice" at the session held on March 9th, 2021. The inclusion criteria were non-specific/mechanical low back pain (12), lasting up to 12 weeks in the acute/subacute phase) (1), without the so-called red flags (13), and without an indication for diagnostic radiology, which is not routinely recommended (1,14). The following patient were excluded: patients with febrile conditions of any genesis, patients who previously had surgery on the lumbar spine or hips, patients with neurological diseases and conditions that could affect the conduct and results of the study, and those who for any reason could not follow the study protocol either due to somatic or psychosocial reasons. According to the already empirically determined protocol, standardised by the manufacturer, the BV cream was applied to the skin of the lumbar

hrani za otekline zglobova (3), ali sve više i za simptome osteoartritisa (4) vjerojatnim mehanizmom smanjenja fibroze sinovijalne membrane (5), te posredno utječe i na smanjenu ukočenost zglobova, relaksaciju muskulature te olakšanu pokretljivost. *Fucus vesiculosus* se također koristi i topički, međutim dosadašnji radovi o lokalnom djelovanju uglavnom su ispitivali njegovu ulogu u kozmetičkoj industriji, kao antioksidansa (6). S druge strane, *Curcuma longa*, koja spada u skupinu đumbira, već se dulji niz godina koristi kao protuupalna supstanca koja djeluje sistemski na simptome osteoartritisa (7), ali i lokalno u obliku isparljivih ulja (9) na opuštanje muskulature (8) te posredno na poboljšanje pokretljivosti.

Nespecifična križobolja velik je javnozdravstveni problem (1), a jedan od poznatih načina liječenja su peroralno primijenjeni miorelaksansi (10) ili npr. masaža (11), a s krajnjim rezultatom smanjenja boli i poboljšanja pokretljivosti.

Cilj ovog istraživanja bio je evaluirati učinak preparata BV na bol, pokretljivost slabinske kralježnice, funkcionalnu sposobnost i kvalitetu života u bolesnika s akutnom i subakutnom nespecifičnom križoboljom.

MATERIJALI I METODE

Istraživanje je provedeno u Specijalnoj bolnici za medicinsku rehabilitaciju „Daruvarske toplice" tijekom jedne godine. Istraživanje je provedeno u skladu s Helsinškom konvencijom iz 1967. godine i njezinim kasnijim dopunama, kao i s načelima dobre kliničke prakse. Svi ispitanici su potpisali su informirani pristanak prije bilo kakvog postupka u vezi studije, a prethodno su detaljno bili informirani o samom istraživanju, ciljevima i rizicima. Odobrenje za ovo istraživanje donijelo je Etičko povjerenstvo Daruvarskih toplica, na sjednici održanoj 9. 3. 2021. godine. Uključni kriteriji bili su nespecifična/mehanička križobolja (12), trajanja do 12 tjedana u akutnoj / subakutnoj fazi (1), bez tzv. crvenih zastava (13), kao i bez indikacije za radiološku dijagnostiku koja se i inače rutinski ne preporučuje (1,14). Isključeni su bolesnici s febrilnim stanjima bilo kakve geneze, bolesnici s prethodnim kirurškim zahvatima na slabinskoj kralješnici ili kukovima, bolesnici s neurološkim bolestima i stanjima koja bi mogla utjecati provođenje i na rezultate istraživanja, te oni koji iz bilo kojeg razloga nisu mogli slijediti protokol istraživanja, bilo zbog somatskih ili psihosocijalnih razloga. Prema već empirijski utvrđenom protokolu, standardiziranom od strane proizvođača, krema BV se nanosila na kožu slabinske i sakralne regije u tankom sloju (da se izbjegne efekt masaže), svakodnevno, kroz sedam dana, u razmacima od četiri mjeseca (nulti, četvrti, osmi i dvanaesti mjesec). Svaki dan u isto vrijeme, tijekom sedam dana, ispitanika se namazalo preparatom količine 90 – 120 g, ovisno o konstituciji bole-

and sacral region in a thin layer (to avoid the massage effect), daily, for 7 days, at intervals of 4 months (zero, fourth, eighth and twelfth month). Every day at the same time, for 7 days, the preparation was applied to the subject's skin in the amount of 90 – 120 g, depending on the constitution of the patient. To avoid the effect of heat, the cream was at room temperature (about 21 °C), and an air-permeable cotton gauze with 4 – 5 layers was used in the treatment, to keep the preparation on the skin, and to cancel out the effect of heat. When it comes to the active ingredients, *Fucus vesiculosus* (brown algae) was present in the amount of approximately 3% (3 g), while curcumin was present in the amount of approximately 1% (1 g). During each treatment, the subjects were not allowed to remove the gauze, wash the treated area, or perform activities that would lead to significant sweating, and thus to the loss of the active substance of the preparation from the surface of the skin. During the entire treatment, there was no change in pharmacological therapy, and only paracetamol could be used as the "rescue medication" in the amount of 1 to a maximum of 2 500 mg tablets. It was administered for a maximum of 2 days during an individual treatment, and it was not administered the day before the end of the treatment and on the very last day of the treatment when the evaluation was carried out. During the first treatment, 36 subjects were included. Due to the reduction of low back pain symptoms, but also due to some objective reasons such as the inability to avoid sweating in certain occupations (working conditions), a total of 20 subjects completed all 4 treatments, and the main outcomes were measured precisely in these patients. In the statistical analysis of the research power with the requested number of variables, a sufficient number of subjects was included for this study of the differences in average values between dependent groups using the Wilcoxon signed-rank test with two-tailed hypothesis testing using a beta error of 20% (80% power) and 5% for an alpha error. In the study, the following parameters were measured before and immediately after each treatment, after which a questionnaire (Euro-Quol) EQ-5D-5L, a validated questionnaire for the quality of life assessment with all its domains (15) was used: the Rolland-Morris Disability Questionnaire (RMDQ) was used to assess the quality of life, as a standardised instrument of functional ability in patients with low back pain (16), and measures for spine mobility, Thomayer's fingertips-to-floor distance test at maximum trunk inclination angle and arms extended towards the floor (17), modified Schober's test as a standard measure of sagittal mobility for the lumbar spine (18) and the lateral flexion test of the spine, all of which are measured in cm (with one decimal place for mm). During the lateral flexion test, the subject stands upright with his legs

snika. Da se izbjegne efekt topline, krema je bila na sobnoj temperaturi (oko 21°C), te se u tretmanu koristila pamučna gaza s 4 – 5 slojeva s propusnošću, da se preparat zadrži na koži, a opet da se anulira efekt topline. Od aktivnih sastojaka, količina *Fucus vesiculosus* (smeđih algi) je oko 3% (3 g), dok je količina kurkumina oko 1% (1 g). Tijekom svakog tretmana ispitanici nisu smjeli uklanjati gazu, prati tretirano područje niti izvoditi aktivnosti koje bi dovele do značajnog znojenja, a time i do gubitka aktivne supstance preparata s površine kože. Tijekom cijelog tretmana nije bilo promjene farmakološke terapije, a kao „lijek spasa" mogao se koristiti samo paracetamol, jedna do maksimalno dvije tablete od 500 mg do najviše dva dana tijekom pojedinog tretmana i to ne dan prije završetka tretmana i na sam zadnji dan tretmana, kada se provodila evaluacija. Tijekom prvog tretmana bilo je uključeno 36 ispitanika. Zbog smanjenja simptoma križobolje, ali i zbog nekih objektivnih razloga kao što je nemogućnost izbjegavanja znojenja u određenim zanimanjima, sva četiri tretmana završilo je ukupno 20 ispitanika, a glavni ishodi su mjereni upravo u tih bolesnika. U statističkoj analizi snage istraživanja s traženim brojem varijabli, za ovu studiju razlika u prosječnim vrijednostima između zavisnih skupina pomoću Wilcoxonova *signed-rank* testa s dvosmjernim testiranjem hipoteze koristeći beta pogrešku od 20% (80% snage) te 5% za alfa grešku uključen je dovoljan broj ispitanika. U ispitivanju su prije i neposredno nakon svakog tretmana mjereni sljedeći parametri nakon smo za ocjenu kvalitete života koristi upitnik (Euro-Quol) EQ-5D-5L, validirani upitnik ocjene kvalitete života sa svim svojim domenama (15), Rolland Morris upitnik (RMDQ) kao standardizirani instrument funkcionalne sposobnosti u bolesnika s križoboljom (16) te mjere za mobilnost kralježnice, Thomayerovu mjeru udaljenosti prsti – pod kod maksimalne inklinacije trupa i ruku ispruženih prema podu (17), modificiranu Schoberovu mjeru kao standardnu mjeru sagitalne gibljivosti za slabinsku kralješnicu (18) i mjeru laterofleksije kralježnice, sve u centimetrima (s jednim decimalnim mjestom za milimetre). Prilikom ispitivanja laterofleksije ispitanik stoji uspravno sa skupljenim nogama, flektira trup u jednu pa u drugu stranu, povlačeći ispruženi dlan uz tijelo (nogu), te se mjeri udaljenost između vrška srednjeg prsta i poda (19).

antefleksije (Thomayerova mjera), sagitalna gibljivost u području slabinske kralješnice (Schoberov klinički test) te laterofleksija kralježnice ulijevo i udesno. Također, ispitanici su ispunili validirane upitnike Rolland-Morris Disabilitiy (RMDQ) kao standardnu mjeru funkcionalne sposobnosti bolesnika s križoboljom i EQ-5D-5L kao validiranu mjeru kvalitete života. Sva mjerenja te ispunjavanje upitnika učinjeni su neposredno prije prve svake aplikacije preparata i

Table 1 Results of measures and questionnaires before and after the entire treatment period with Beaute Vitale® cream in patients with nonspecific low back pain (N=20).

Tablica 1. Rezultati mjera i upitnika prije i nakon cjelokupnog perioda liječenja primjenom kreme Beaute Vitale® u bolesnika s nespecifičnom križoboljom (N=20).

Testovi / Tests	Before treatment / Prije treatmana†	After treatment / Poslije tretmana†	Absolute difference / Apsolutna razlika§	Average relative difference / Prosječna relativna razlika (%)
Schober (cm)	6,425	6,5	0,075	3,02
Thomayer (cm)	10	3,5	0	–13,04
Lateral flexion / Laterofleksija (cm) right / desna left / lijeva	 51,95 53,075	 47,5 48,175	 –8,24**** –4,9****	 –4,45 –8,99
EQ-5D-5L (1–5) mobility / pokretljivost self-care / samozbrinjavanje activity / aktivnost pain / bol anxiety / depression tjeskoba / depresija	 3 2 2 3 1	 2 1 2 2 1	 –0,5* 0 0 –1** 0	 –12,5 0 0 –33,33 0
VAS for health state / zdravlja (1–100)	60,25	68,85	8,6*	23,67
RMDQ (1–100)	5	3,5	–1	–25

† Mode or median of results / Mod ili medijan rezultata

§ Mode or median of the difference in results (before-after) / Mod ili medijan razlike rezultata (prije-poslije)

*P-value of the dependent t-test or Wilcoxon's test marked as *(p<=0.05), **(p<0.01), ****(p<0.0001), and without a symbol if the result is not significant (p>0.05). / P-vrijednost zavisnog t-testa ili Wilcoxonovog testa označenog kao *(p<=0,05), **(p<0,01), ****(p<0,0001) i bez simbola ako rezultat nije značajan (p>0,05).*

together, flexes his torso to one side and then to the other, pulling the outstretched palm against the body (leg), and the distance between the tip of the middle finger and the floor is measured (19).

Anteflexions (Thomayer's test), sagittal mobility in the area of the lumbar spine (Schober's test) and lateral flexion of the spine to the left and right are also measured. In addition to that, the subjects filled out the validated Rolland-Morris Disability Questionnaire (RMDQ) as a standard measure of functional ability of patients with low back pain and the EQ-5D-5L as a validated measure of quality of life. All measurements and questionnaires were completed immediately before the first application of the preparation and two days after the last application, for each of the 4 treatments.

All measurements were performed by two specialists in physical medicine and rehabilitation (DK, AK). They took turns at each measurement, and the data for each individual visit was entered in separate parts of the questionnaire, without any insight into previous measurements. Measurements were always made in the same room and at the same time of day.

The Shapiro-Wilk's test was used for statistical testing of normal distribution, and all tests considered an alpha error < 0.05 for a significant difference. After determining the distribution of the data, the T-test or Wilcoxon test for dependent samples was used in statistics. Exploratory data analysis and statistical analysis was performed using the R v.4.1.2 software (R core team 2021) (20).

dva dana nakon zadnje aplikacije, za svaki od četiri tretmana.

Sva mjerenja provodila su dva specijalista fizikalne i rehabilitacijske medicine (DK, AK). Izmjenjivali su se pri svakom mjerenju, podatke za svaku pojedinu vizitu upisivali u posebne dijelove upitnika, a bez uvida u prethodna mjerenja. Mjerenja su vršena uvijek u istoj prostoriji i u isto doba dana.

Za statističko ispitivanje normalne distribucije korišten je Shapiro-Wilksov test, a svi testovi su za značajnu razliku uzeli da je alfa pogreška < 0,05. Nakon određivanja distribucije podataka, u statistici se koristio T-test ili Wilcoxonov test za zavisne uzorke. Za eksplorativnu i statističku analizu korišten je R softver v.4.1.2 (*R core team 2021*) (20).

REZULTATI

Prosječna dob ispitanika bila je 55,6 godina uz udio ženskih ispitanika oko 60% (20/36; 12/20). Sumarni rezultati mjerenja i upitnika na početku i na kraju promatranog razdoblja prikazani su u tablici 1. Nakon prvog tretmana na 36 ispitanika, sve varijable osim EQ-5D-5L anksioznosti/depresije pokazale su značajne promjene u smislu smanjenja simptoma nespecifične križobolje, uz povećan opseg pokreta. Nakon drugog i trećeg tretmana na uzorku od 24 ispitanika u kretnjama nije došlo do značajne promjene u onima sagitalne gibljivosti, kao ni u pojedinim varijablama u EQ-5D-5L upitniku, ali je tretman i dalje značajno dovodio do smanjenja boli te poboljšanja pokretljivo-

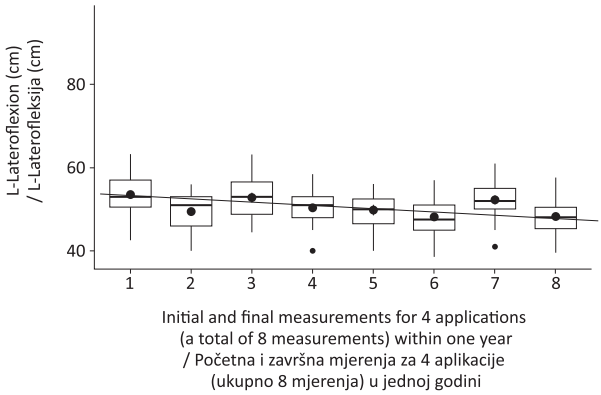

Figure 1 Measurement results of left-sided lateroflexion during the study

Slika 1. Rezultati mjerenja ljevostrane laterofleksije tijekom istraživanja

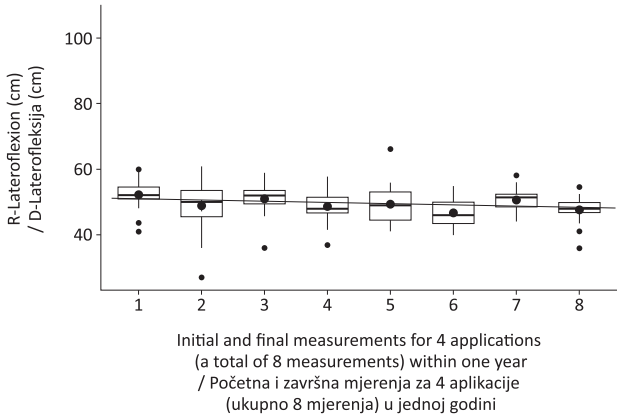

Figure 2 Measurement results of right-sided lateroflexion during the study

Slika 2. Rezultati mjerenja desnostrane laterofleksije tijekom istraživanja

RESULTS

The average age of the subjects was 55.6 years. with the share of female respondents around 60% (20/36; 12/20). The summary results of measurements and questionnaires at the beginning and at the end of the observed period are shown in Table 1. After the first treatment that was applied to 36 subjects, all variables except EQ-5D-5L in the domains of anxiety/depression showed significant changes in terms of reduction of symptoms of non-specific low back pain, with increased range of motion. After the second and third treatment applied to a sample of 24 subjects, there was no significant change in movements in those of sagittal mobility, and in individual variables in the EQ-5D-5L questionnaire, but the treatment still significantly reduced pain and improved mobility. Finally, after the fourth treatment was applied to a total of 20 subjects, significant differences were found in the clinical tests of bilateral lateral flexion (p<0.0001) (Figures 1 and 2) and EQ-5D-5L – pain domain (p<0.001) (Figure 3) and mobility (p<0.01) (Figure 4), as well as the VAS (visual analogue scale) scale of overall health (p=0.05)

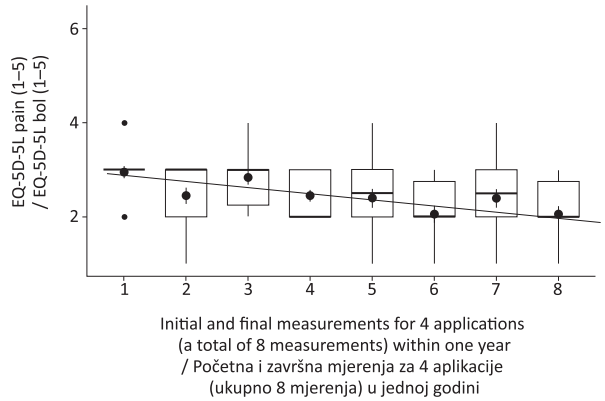

Figure 3 EQ-5D-5L results – pain domain, during the study

Slika 3. Rezultati EQ-5D-5L – domena boli, tijekom istraživanja

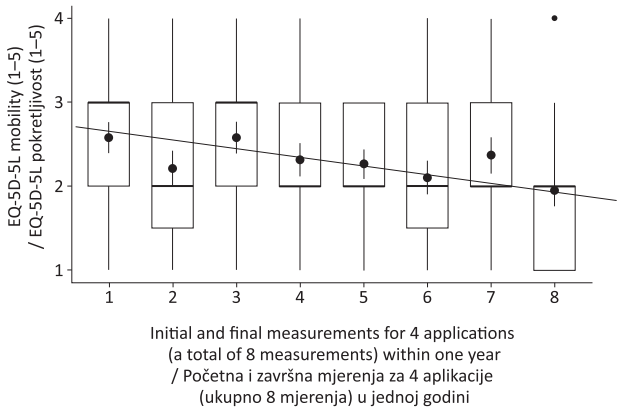

Figure 4 EQ-5D-5L results – mobility domain during the study

Slika 4. Rezultati EQ-5D-5L – domena pokretljivosti tijekom istraživanja

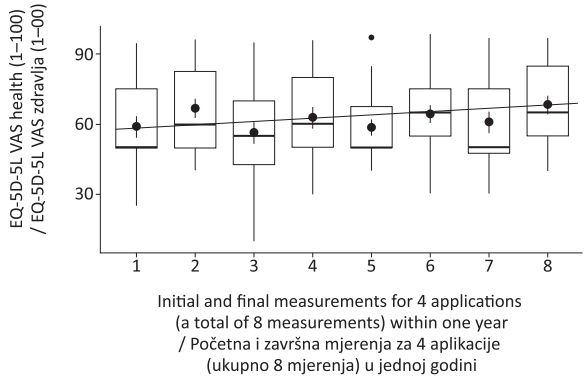

Figure 5 EQ-5D-5L results – health domain, during the study

Slika 5. Rezultati EQ-5D-5L – domena zdravlja, tijekom istraživanja

sti. Konačno, nakon četvrtog tretmana kod ukupno 20 ispitanika nađena je značajna razlika u kliničkim testovima obostrane laterofleksije (p<0,0001) (slike 1 i 2) i EQ-5D-5L – domeni za bol (p<0,001) (slika 3) i mobilnost (p<0,01) (slika 4), kao i VAS (engl. *visual analog scale*) skale ukupnog zdravlja (p=0,05) (slika 5), a sve su promjene bile u smislu poboljšanja. Nakon jedne

(Figure 5), and all of these changes revealed improved scores. After one year, no significant change was found in Thomayer's (p=0.2926) and Schober's tests (p=0.7963), total RMDQ value (p=0.11), and EQ-5D-5L – activity domains (p=0, 1676), self-care (p= 0.0708) and anxiety/depression (p=0.7693).

DISCUSSION

In this study conducted on patients with acute and subacute non-specific low back pain, a positive effect of the preparation/cream BV was shown, the topical application of which reduced the symptoms and signs of non-specific low back pain after the very first treatment, while after four treatments applied during the course of one year the positive effect in terms of pain reduction, improvement in spinal mobility in the frontal plane, and in the EQ-5D-3L questionnaire, in the domains of pain, mobility and overall health and well-being was achieved and maintained.

During the long-term use of this preparation, it was noticed that the paravertebral muscles become extremely relaxed after the treatment and acquire a "softer" consistency, are less painful on palpation, with improved mobility in the lumbar spine. Muscle relaxation, which consequently leads to increased mobility, is one of the important elements in the treatment of non-specific low back pain, which was proven in numerous studies (10,21,22). When we cover the topic of non-specific low back pain, although by definition it refers to an unknown origin, it is considered that in the majority of patients, the so-called mechanical causes are underlying, (12,23) and that the relaxation of the paravertebral muscles is extremely important in their treatment. The active substances of the BV cream obtained by analysis are the brown algae, *Fucus vesiculosus* extract, and *Curcuma longa* extract, curcumin, which have been used for many years in the treatment of symptoms of the locomotor system. Although *Fucus vesiculosus* is used systemically to alleviate the symptoms of osteoarthritis (4), which is associated with some cases of non-specific low back pain, the said extract has so far been tested as an oral preparation and not as a topical preparation for degenerative joint diseases. Brown algae extract was also investigated as an anti-inflammatory substance (24), and it could also be associated with non-specific low back pain in a broader context. On the other hand, curcumin, an extract of *Curcuma longa*, has been examined in several papers as an anti-inflammatory systemic preparation (7,25,26), but also as a local preparation (8), which could explain its beneficial effect on the symptoms of non-specific low back pain. In our study, during the first seven-day treatment, there was a change in almost all variables in terms of improved results, while after the third treatment (26 subjects), there was no significant change in 5 of the observed variables. Nevertheless, the positive results that were achieved in some of the key variables that are im-

godine nije nađena značajna promjena u Thomayerovoj (p=0,2926) i Schoberovoj mjeri (p=0,7963), ukupnoj vrijednosti RMDQ (p=0,11), te EQ-5D-5L – domenama aktivnosti (p=0,1676), samozbrinjavanja (p= 0,0708) i anksioznosti/depresije (p=0,7693).

RASPRAVA

U ovoj studiji na bolesnicima s akutnom i subakutnom nespecifičnom križoboljom pokazan je pozitivan učinak preparata/kreme BV čijom je topičkom primjenom već nakon prvog tretmana došlo do smanjenja simptoma i znakova nespecifične križobolje, dok je nakon četiri tretmana tijekom jedne godine zadržan pozitivan učinak u smislu smanjenja boli, poboljšanja pokretljivosti kralježnice u frontalnoj ravnini, te u domenama EQ-5D-3L upitnika: bol, mobilnost i ukupno zdravlje.

Tijekom dugogodišnjeg korištenja ovoga preparata primijetilo se da paravertebralni mišići nakon tretmana postaju izrazito opušteni i dobivaju „mekšu" konzistenciju, manje su bolni na palpaciju, uz poboljšanje pokretljivosti u slabinskoj kralježnici. Mišićna relaksacija koja posljedično dovodi do povećane pokretljivosti, kao jedan od važnih elemenata u liječenju nespecifične križobolje, dokazana je u brojnim studijama (10,21,22). Kada govorimo o nespecifičnoj križobolji, premda se ona po definiciji odnosi na nepoznato podrijetlo, smatra se da su u podlozi u najvećem dijelu bolesnika tzv. mehanički uzroci (12,23) u čijem je tretmanu relaksacija paravertebralnih mišića izrazito važna. Aktivne supstance kreme BV dobivene analizom jesu ekstrakt smeđe alge *Fucus vesiculosus* te ekstrakt *Curcume longe*, kurkumin, koji se dulji niz godina koriste u tretmanu simptoma lokomotornog sustava. Premda se *Fucus vesiculosus* sistemski koristi za ublažavanje simptoma osteoartritisa (4), s čime se i povezuju pojedini slučajevi nespecifične križobolje, navedeni ekstrakt do sada je ispitivan kao peroralni preparat, a ne kao topički pripravak za degenerativne bolesti zglobova. Ekstrakt smeđe alge također je ispitivan i kao protuupalna supstanca (24), s čime bismo također u širem kontekstu mogli povezivati nespecifičnu križobolju. Kurkumin, ekstakt *Curcume longe*, s druge strane, u više je radova ispitivan kao protuupalni sistemski (7,25,26), ali kao i lokalni pripravak (8), te bismo i tako mogli objasniti njegov utjecaj na simptome nespecifične križobolje. U našoj je studiji tijekom prvoga sedmodnevnog tretmana došlo do promjene u skoro svim varijablama u smislu poboljšanja rezultata, dok nakon trećeg tretmana (26 ispitanika) u 5 promatranih varijabli nije bilo značajne promjene. Ipak, pozitivni rezultati nakon jedne godine i to u nekim ključnim varijablama važnima za kvalitetu života tih bolesnika nakon jedne godine, odnosno četiri tretmana ukazuju na učinkovitost navedene kreme. Mora se

portant for the quality of life of these patients after one year, i.e. after 4 treatments, confirm the effectiveness of the mentioned cream. One should bear in mind that in the third and fourth treatment, only people with more "stubborn" low back pain were treated, whose low back pain was probably unresponsive to other conservative treatments as well. In addition to that, it is worth noting that there was no significant difference in the EQ-5D-5L anxiety/depression variable after any of the treatments, and due to this fact, it could be concluded that during the treatment there was no change in the mental status of the subject or the effect of that component to other study results. The average age of the subjects was 55.6 years, with a higher share of female subjects. In terms of demographics, this is also the most common age (45 – 60) when patients visit the physician for an examination for acute or subacute non-specific low back pain (27). Working conditions were not included in the analysis, although they may certainly have an impact on low back pain symptoms (27), unlike socioeconomic ones, which are still questionable (1). No systemic or local side effects were noted during the study.

This study has certain limitations. The first of these limitations is the relatively small number of subjects who underwent all 4 treatments (20 people), even though that number is sufficient for a valid statistical analysis of the variables of interest. Another limitation is the issue of standardisation of the preparation, given that the ingredients of the cream are manually titrated. Besides that, although we monitored the patients during the course of one year, we have no data on the status of non-specific low back pain after the last treatment. Finally, an important limitation of the study is the absence of a control group. There are certain methodological difficulties for the inclusion of a control group, although in the future one could introduce a comparison with another physical therapy modality.

CONCLUSION

In our sample of patients with acute and subacute non-specific low back pain, the Beaute Vitale® (BV) cream, applied through four seven-day treatments during the course one year, showed effectiveness in terms of improving the mobility of the lumbar spine, and reducing the intensity of pain, improving mobility and the feeling of general health and well-being, without local or systemic side effects. The aforementioned preparation can be used as supportive conservative therapy, along with other methods of conservative treatment of non-specific low back pain. Additional research is needed in terms of comparison with the control group, as well as long-term monitoring of the examined variables in subjects treated with this preparation.

Author's contribution: Responsible for the concept: all authors; responsible for the methodology: D.K., A.K.; responsible for the formal analysis, D.K., imati na umu da su se u trećem i četvrtom tretmanu zadržale samo osobe s „tvrdokornijom" križoboljom, inertnijom vjerojatno i na druge konzervativne tretmane. Također, značajno bi bilo naglasiti da niti nakon jednog tretmana nije došlo do značajne razlike u varijabli EQ-5D-5L anksioznosti/depresije, iz čega bi se moglo zaključiti da tijekom tretmana nije došlo do promjene psihičkog statusa ispitanika, pa tako ni utjecaja te komponente na ostale rezultate ispitivanja. Prosječna dob ispitanika bila je 55,6 godina uz veći udio ženskih ispitanika. U demografskom smislu to je i najčešća dob (45 – 60) kada se bolesnici javljaju liječniku na pregled radi akutne ili subakutne nespecifične križobolje (27). Radni uvjeti nisu bili uključeni u analizu, premda sigurno mogu imati utjecaj na simptome križobolje (27), za razliku od socioekonomskih koji su još uvijek upitni (1). Tijekom ispitivanja nisu zabilježene sistemske ili lokalne nuspojave.

Ovo istraživanje ima ograničenja. Na prvom mjestu je relativno mali broj ispitanika koji su prošli sva četiri tretmana (20 osoba), iako je i taj broj dovoljan za valjanu statističku analizu varijabli od interesa. Također, tu je pitanje standardizacije pripravka, s obzirom na to da se sastojci kreme ručno titriraju. Osim toga, premda smo bolesnike pratili tijekom jedne godine, nemamo podatke o stanju nespecifične križobolje nakon zadnjeg tretmana. Na kraju, važno ograničenje istraživanja jest nepostojanje kontrolne skupine. Za uključivanje kontrolne skupine postoje određene metodološke poteškoće, iako bi se u budućnosti moglo razmišljati o usporedbi s nekim drugim fizikalno-terapijskim modalitetom.

ZAKLJUČAK

U našem uzorku bolesnika s akutnom i subakutnom nespecifičnom križoboljom krema *Beaute Vitale*® (BV), primijenjena kroz četiri sedmodnevna tretmana tijekom jedne godine, pokazala je učinkovitost u smislu poboljšanja pokretljivosti slabinske kralježnice te smanjenja intenziteta boli, poboljšanja mobilnosti i osjećaja općeg zdravlja, a bez lokalnih ili sistemskih nuspojava. Navedeni preparat može se primijeniti kao suportivna konzervativna terapija, uz ostale metode konzervativnog liječenja nespecifične križobolje. Potrebna su dodatna istraživanja u smislu usporedbe s kontrolnom skupinom, kao i dugoročno praćenje ispitivanih varijabli u osoba liječenih ovim preparatom.

Doprinos autora: Koncept – svi autori; metodologija – D.K., A.K.; formalna analiza, D.K., I.S., E.R., Z.V.; provođenje istraživanja – D.K., A.K.; priprema originalnog teksta – D.K., A.K., Z.V.; pisanje prve inačice teksta – D.K.; uređivanje i revizija – svi autori.

Izjava o sukobu interesa: Tvrtka Osteoart d.o.o., licencirana za *Beaute Vitale*® (BV), financirala je istra-

I.S., E.R., Z.V.; responsible for conducting research: D.K., A.K.; responsible for the preparation of the original text: D.K., A.K., Z.V.; responsible for writing the first version of the text (draft): D.K.; responsible for the editing and revision: all authors.

Conflict of interest statement: The company Osteoart d.o.o., which is licensed for the sale of the Beaute Vitale® (BV) cream, provided funding for the research. However, that company had no influence on the design, implementation, results and interpretation of any part of this paper. Therefore, the authors have no conflict of interest regarding this paper.

živanje. Međutim, ta tvrtka nije imala nikakav utjecaj na nacrt, provođenje, rezultate i njihovu interpretaciju ni na bilo koji dio ovog rada. Stoga u vezi ovog rada autori nemaju sukob interesa.

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