**Long-term Effectiveness of Occlusal Splint Therapy Compared to Placebo in Patients with Chronic Temporomandibular Disorders**

**Usporedba dugotrajne učinkovitosti stabilizacijske i placebo udlage u terapiji kroničnih temporomandibularnih poremećaja**

**Abstract**

**Purpose:** The aim of this study was to compare long-term effectiveness of stabilization splint (SS) with that of placebo splint (PS) in chronic TMD patients and to investigate differences in treatment outcomes based on diagnostic subgroups [Disc displacement (DD)/myofascial pain (MP)].

**Materials and Methods:** Thirty-four female participants, diagnosed with chronic TMD, were classified in groups: one provided with SS and other with PS and were followed for six months. Treatment outcomes included spontaneous pain [visual analogue scale (VAS)], self-perceived quality of life (OHIP-14), pain-free maximal mouth opening (MCO), maximal mouth opening (MMO), level of perceived stress (PSS), characteristic pain intensity [graded chronic pain scale (GCPS)], and functional jaw limitation [jaw functional limitation scale (JFLS)].

**Results:** Baseline characteristics did not differ significantly between the two groups (p>0.05). After six months of treatment the changes in spontaneous pain and OHIP-14 scores differed significantly between treatment groups (p=0.004, p=0.02 respectively), with greater reduction in SS compared to the PS group. Pain-free maximal mouth opening did not change significantly over time, however MCO values differed significantly between the two treatment groups, with greater overall values in the SS compared to the PS group (p=0.046), as well as between TMD subgroups, with greater overall values in MP compared to DD patients (p=0.03). In the SS group, significant difference in JFLS categories was found between baseline and after 6 months of treatment in all except emotional and verbal expression (mastication p=0.00015; vertical jaw mobility p=0.00018). No such changes in JFLS categories were observed in the PS group.

**Conclusions:** During 6-month period, SS was more effective than PS in reducing spontaneous pain and improving self-perceived quality of life and functional limitations of the lower jaw. Moreover, significantly higher values of pain-free mouth opening were observed in patients treated with stabilization splint. While placebo might be partly responsible for improving the symptoms of TMD, it seems that it cannot maintain a continual long-term positive therapeutic effect.

**Introduction**

Temporomandibular disorders (TMDs) is a term covering neuromuscular and musculoskeletal conditions that affect masticatory muscles and temporomandibular joints (TMJ) as well as surrounding structures (1). The most common TMD diagnoses are myofascial pain and disc displacement (2,3). Temporomandibular disorders can affect anyone, however women aged 20 – 50 years are most affected (4). The most common symptoms for which patients seek help are pain in orofacial region and limited lower jaw movements, which are often aggravated by function. In addition, patients are often worried about the sounds that appear in the TMJ (clicking or popping sounds, or crepitations) (5). The complexity of the etiopathophysiology of disorders and its effect on patients’ quality of life, as it is frequently stated in various research studies, requires thorough and careful therapeutic approach (1-5).

**Uvod**

Temporomandibularni poremećaji (TMP) obuhvaćaju neuromuskularna i musculoskeletna bolna stanja koja zahvataju zvučne ili nezvučne bolesti (TMZ) i okoline strukture (1). Najčešći oblik poremećaja je tzv. miofascijalna bol, a najčešći intraartikularni oblik TMP-a jest pomak zglobove (2, 3). TMP se može pojaviti u svim populacionim skupinama, no najčešći je kod žena između 20 i 50 godina (4). U karakteristični trijar simptoma TMP-a, zbog kojih pacijenti najčešće traže pomoć, ubrajaju se orofacijalna bol, ograničenja u kretnjama donje čeljusti te zvukovi u zglobu (kliktaj, pucketanja, krepi- tacijski) (5). Kako su etiologija i patofiziologija poremećaja složene, a utjecaj na kvalitetu pacijentova života prilično velik, pristup kliničara dijagnostici i terapiji TMP-a treba biti po- najprije biti temeljit (1 – 5).
Therapy of Chronic Temporomandibular Disorders

Vrbanović i sur.

U liječenju TMP-a preferiraju se neinvazivni, reverzibilni terapijski postupci kojima je svrha poboljšati cjelokupnu funkciju žvačnog sustava. Ipak, u studijama u kojima su se promatrane razlike u liječenju uglavnom se ne upućuje na prednost pojedine neinvazivne terapijske opcije u usporedbi s drugom, pa zato ne možemo sa sigurnošću tvrditi koja od njih ima prioritet u liječenju TMP-a (6).

Veličom broju pacijenata najbolje odgovara kombinacija behirolla i fizikalne terapije, a u kliničkom radu najčešće se preporučuje popularna okluzijska udlaga (7). U literaturi se spominju razne udlage čiji oblik uglavnom ovisi o indikaciji, no široko je prihvaćena i uspješna u liječenju stabilizacijska udlaga (SU) izrađena od tvrdog akrilata tako da omogućuje do-ticaje u centričnoj relaciji (CR-u) (8). Terapijski učinak SU-a pripisuje se različitim čimbenicima, pa se tako smatra da on mijenja položaj kondila u zglobnoj jamici, uklanja okluzijske interferencije, održava stabilne okluzijske odnose i jedanako-mjerne kontakte, smanjuje neuromuskularnu aktivnost i podiţe vertikalnu dimenziju okluzije, što vjerojatno pridonosi opuštanju muskulature i rasterećenju TMZ-a (7, 9). Ipak, još nije sasvim jasno kako i zašto se stabilizacijskom udlagom postiţe olakšanje simptoma TMP-a. Znanstvenici se uglavnom slaţu da je učinak vjerojatno posljedica kombinacije spomenutih čimbenika, ali i placebo učinka. Istraţivanja o placebo učinku udlage nude proturječne zaključke. Naime, diuo znanstvenika ističe kako ne postoji razlika između terapijskih ishoda između SU-a, neokludirajuće nepčane ploče i fizikalne terapije (7, 10), a drugi da se tvrdom stabilizacijskom udlagom postiţu bolji rezultati u liječenju negoli pri primjeni placebo udlage (11, 12). Nameće se pitanje je li terapijski učinak postignut SU-om dugotrajniji od terapijskog učinka naprave čiji oblik ne omoguće uspostavljanje meĎučeljusnih odnosa u CR-u i ima zane-mariv učinak na vertikalnu dimenziju okluzije.

Cilji ove studije bi je usporediti šestomjesečnu učinkovitost stabilizacijske udlage rezultate s onima postignutima placebo udlagom. Nulta hipoteza bila je da neće biti razlika izmeĎu tih terapijskih skupina tijekom šest mjeseci.

Materials and methods

The study was approved by the Ethics Committee of the School of Dental Medicine, University of Zagreb (01-PA-26-6/15, item 3.2). All participants were informed about the study protocol and provided with written informed consent. All experimental procedures were conducted in accordance with ethical standards of the Helsinki Declaration.

Participants

This randomized controlled clinical trial was carried out at the Department of Removable Prosthodontics, School of Dental Medicine, University of Zagreb from June 2016 to June 2019. The participants were recruited from patients seeking treatment for chronic TMD pain and/or limited lower jaw movements. In the research period, the only patients who met the inclusion criteria were women, therefore exclusively female participants were included in the study. The inclusion criteria were as follows: the report of chronic pain, lasting more than 6 months, spontaneous pain >30 mm on visual analogue scale (VAS), and diagnosis of myofascial pain (MP) or disc displacement. The participants were randomized to either the stabilization splint (SS) group or the placebo splint (PS) group. The SS group received a custom-made stabilizing splint, whereas the PS group received a placebo splint. The SS splint was fabricated from a hard acrylic material and was designed to provide centric relation positioning and has a negligible influence on vertical dimension of occlusion. The aim of this study was to compare a 6-month effectiveness of stabilization splint with that of placebo splint. The null-hypothesis was that there would be no difference between treatment groups in a 6-month treatment period.

Materijali i metode

Studiju je odobrio Etički odbor Stomatološkog fakulteta Sveučilišta u Zagrebu (01-PA-26-6/15, item 3.2). Svi ispitani bili su informirani o njezinu protokolu i dali su svoj pristanak. Eksperimentalni postupci primjenjeni u studiji ni na koji način nisu u sukobu s etičkim načelima Helsinške deklaracije.

Sudionici

Kontrolirano randomizirano kliničko istraţivanje provedeno je u Zavodu za mobilnu protetiku Stomatološkog fakulteta u Zagrebu od lipnja 2016. godine do lipnja 2019.

Tijekom trajanja studije jedino su žene zadovoljile kriterije za uključivanje u istraţivanje pa su zato samo one uvrštene u istraţivačku skupinu. Kriteriji za sudjelovanje bili su: kronična bol koja traje dulje od šest mjeseci, spontana bol veća od 30 mm prema procjeni na vizualno-analognoj lje-stvici (VAS-u) te dijagnoza bolnog miofascijalnog poremećaja ili pomaka zglobove pločice. Kriteriji za isključivanje bili su: ostala orofojalna bolna stanja nevezana za TMP, degene-
ment (DD). Exclusion criteria were orofacial pain not related to TMD, degenerative joint disease, oral lesions, periodontal disease, systemic diseases, pregnancy, as well as previous active treatment for painful TMD. Patients with combined MP and DD were not considered for the study.

Sample size estimation

A statistical power analysis was performed for sample size estimation based on data from Michelotti et al. (12). The minimum difference in VAS and maximal comfortable mouth opening (MCO) scores between treatment groups was estimated to be 8.8 mm and 3.4 mm, respectively, with the standard deviation of 7.5 mm and 2.5 mm, respectively. With an alpha = .05 and power set at 80%, the projected sample size was approximately N = 26 (13 per group).

Study protocol

Out of 38 female patients that met the inclusion criteria, 2 of them declined to participate in the study due to travel complications, thus 36 participants were included in the study. The randomization was performed using Microsoft Excel software after the codification of each patient. Two of the participants dropped out before they were provided with a splint. Eventually, 34 patients were randomized in SS group, and placebo splint (PS) group. The number of subjects was 19 in the SS group, and 15 in the PS group. Two of the patients in each treatment group withdrew before the completion of the therapy, thus 17 patients in the SS group and 13 patients in the PS group completed the 6-month treatment (Figure 1).

At the baseline (T0) all patients were evaluated by the expert in TMD (IA). The patients were diagnosed using Diagnostic criteria for temporomandibular disorders (DC/TMD) (13). After the patients had been provided with a splint, they were followed during a 6-month period with follow-up appointments at 1st (T1), 3rd (T2) and 6th (T3) month. The study included patients with a minimum of 18 years of age, signs and symptoms of chronic TMD, who had been treated previously with miofacial treatment for 3 months, who had experienced at least a 30% decrease in the intensity of pain, who were unable to stretch the mouth to a normal position, and who were experiencing increased difficulties in eating, speaking, and yawning. The exclusion criteria were orofacial pain not related to TMD, degenerative joint disease, oral lesions, periodontal disease, systemic diseases, pregnancy, as well as previous active treatment for painful TMD. Patients with combined MP and DD were not considered for the study.

Procjena potrebne veličine testiranog uzorka

Za procjenu veličine uzorka obavljena je analiza snage statističkog testa prema podatcima istraživanja Michelotti i su-radnika (12). Minimalne razlike u iznosu VAS-a bile su 8,8 mm sa standardnom devijacijom koja je iznosila 7,5 mm, a maksimalnog bezbolnog otvaranja (MCO-a) 3,4 mm sa standardnom devijacijom koja je iznosila 2,5 mm. S alfa = 0,05 i snagom testa na 80 %, predviđena veličina uzorka bila je N = 26 (s 13 ispitanika u skupini).

Protokol istraživanja

Od 38 pacijenica koje su zadovoljile sve kriterije, dvije su odbile sudjelovati u studiju zbog poreškoća s prijevozom. Od preostalih 36 pacijenica uključenih u studiju, dvije su odu-stale prije nego što im se izradila udlaga. Naposljetku, u aktivnu i placebo skupinu slučajnim odabirom raspoređene su 34 pacijentice – 19 u skupinu sa SU-om i 15 u skupinu s PUom. Po dvije pacijentice povukle su se prije završetka terapije, tako da je šestomjesечно praćenje završilo 17 pacijentica u skupini sa SU-om i 13 u skupini s PU-om (slika 1.). Nakon što su pacijenticama priključeni kodovi, napravljena je ran-andomizacija s pomoću softvera Microsoft Excela. Početni pregled i procjenu (T0) obavio je stručnjak iz podrucja TMP-a (I. A.). Dijagnostika je provedena s pomoću dijagnostičkog kriterija za temporomandibularne poremećaje (DC/TMD-om) (13). Pacijenticama je dodijeljeno terapijsko sredstvo nakon čega su praćene šest mjeseci s kontrolnim pregledima i procjenom nakon prvoga (T 1), trećeg (T 2) i šestog mjeseca (T 3). Kliničarka koja nije znala početnu diagnozu, početni intenzitet boli i vrstu terapije, obavljala
follow-up evaluations (T1, T2, T3) were carried out by a clinician (EV) blinded for the type of treatment, the initial diagnosis and the pain intensity.

Treatment procedure

Both treatment groups were equally informed and counseled about their condition prior to splint therapy, in terms of explanation of the origin and prognosis of the disease.

The maxillary stabilization splint was fabricated on stone cast in ARTEX articulator. It was a hard acrylic splint (Resilit-S, Erkodent, Siemensstraße 3, 72285 Pfalzgrafenweiler, Germany), with a 2 mm thickness at the level of the first molar. The clinician (IA) adjusted the splint so that that the opposing teeth occluded uniformly and simultaneously with the occluding surface of the splint in centric relation. The same clinician adjusted the splint at follow-up appointments if it was needed.

The placebo splint was made of a thin thermoforming foil (Erkodent, 0.5 mm) fabricated on the patient’s maxillary stone cast. All contacts that interfered with maximal intercuspation have been removed. The increase in vertical dimension was less than 0.5 mm, thus providing negligible influence on occlusion and condylar position. (Figure 2 and 3).

The same dental technician made all splints. Patients in both treatment groups were instructed to wear their splints only during sleep.

Treatment outcomes

Changes in spontaneous pain were assessed by VAS, changes in oral health quality of life were assessed by the Oral health impact profile (OHIP-14), and the level of perceived stress by Perceived stress scale (PSS). Moreover, the study followed the impact profile (OHIP-14), and the level of perceived stress by PSS. Također

Ishodi liječenja

Promjene u spontanoj boli pruženih su s pomoću ljestvice VAS, kvaliteta života ovisna o oralnom zdravlju procijenjena je upitnikom Oral health Impact Profile (OHIP-14), a stres upitnikom o percipiranom stresu (PSS-om). Također su pružene promjene u ishodima ljestvice kronične boli (GCPS-om). Svi spomenuti ishodi procjenjivani su na svakom kontrolnom pregledu, a ljestvicu ograničenja funkcije čeljusti pacijentice su ispunjavale samo na početnom (T 0) i završnom pregledu (T 3). Upitnici GCPS i JFLS dio su protokola DC/TMD-a (13).
Maximal mouth opening
Maximal mouth opening was defined as the maximum distance the participant could open their mouth regardless of the pain they felt, measured as the distance between the upper and lower central incisors.

Maximal comfortable mouth opening
Maximal comfortable mouth opening (pain-free maximal mouth opening) was measured as the distance between the upper and lower central incisors, and was defined as the maximum distance the participant could open their mouth without experiencing pain or discomfort (12).

Perceived stress
Perceived stress scale is a 10-item questionnaire that evaluates subjective perceptions of stress over the previous month. Response options form a 5-point Likert scale: 0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, 4 = very often. Possible scores ranged from 0–40, with higher scores indicating higher stress levels. The questionnaire was previously translated and validated by Hudek-Knežević et al. (15).

Oral health - related quality of life
The OHIP-14 questionnaire was used to evaluate how TMD-related pain and disability influence patients’ quality of life. Patients status was expressed throughout 14 questions, by choosing 1 of the 5 possible answers: 0 = never, 1 = hardly ever, 2 = sometimes, 3 = fairly often, and 4 = very often. Possible scores ranged from 0–56. The questionnaire, previously validated for the evaluation of TMD patients (16), was translated into and validated in Croatian (17).

Graded chronic pain scale - characteristic pain intensity
Graded chronic pain scale was used to evaluate two dimensions of chronic pain severity: pain intensity and pain-related disability. Subscale scores for pain intensity and disability are combined to calculate a chronic pain grade that allows classification of chronic pain patients into 5 categories: grades 0 (pain-free) to IV (high disability-severely limiting). All items are scored on a scale, with responses ranging from 0–10. Scores are computed and divided into 3 subscales: the characteristic pain intensity scale calculated as the mean intensity ratings for reported current, worst, and average pain; the disability score is calculated as the mean rating for difficulty performing daily, social, and work activities; and the disability points score is derived from a combination of ranked categories of number of disability days and disability score (13, 18). In our study we evaluated only the changes related to characteristic pain intensity scores.

Jaw functional limitation scale
Jaw functional limitation scale questionnaire is a reliable and valid form that assesses global limitations caused by TMD. The questionnaire consist of 52 items in groupations as follows: a) mastication (20 items), b) vertical jaw mobility (9 items), c) verbal and emotional expression (14 items), and miscellaneous (9 items) (19). In this study we followed the changes in 3 JFLS categories: mastication, vertical jaw mobility and verbal and emotional expression.

Maksimalno neasistirano otvaranje usata
Maksimalno neasistirano otvaranje usata mjerno je kao udaljenost između maksilarnih i mandibularnih centralnih inciziva, a definirano je kao najveći iznos otvaranja koji pacijent može postići bez obzira na bol i nelagodu.

Maksimalno bezbolno otvaranje usata
Maksimalno bezbolno otvaranje mjerno je kao udaljenost između maksilarnih i mandibularnih centralnih inciziva, a definirano je kao najveći iznos pri otvaranju usata koji pacijent postigne otvarajući ih bez boli i nelagode (12).

Prcipirani stres
PSS is a standard 10-item questionnaire which measures perceived stress as perceived stress over the previous month. Response options form a 5-point Likert scale: 0 = never, 1 = hardly ever, 2 = sometimes, 3 = fairly often, and 4 = very often. Possible scores ranged from 0–40. The questionnaire has been validated and shown to be a reliable and valid measure of perceived stress (19).

Kvaliteta života ovisna o oralnom zdravlju
Kratka verzija upitnika OHIP-14 korištena je kako bi se pokazao utjecaj ishoda terapije (stupanj boli i ograničenja) na kvalitetu pacijentova života ovisnu o oralnom zdravlju. Pacijenti su odgovorili na 14 pitanja odabirom jednog od sljedećih odgovora: 0 = nikad, 1 = gotovo nikad, 2 = katkad, 3 = često, 4 = vrlo često. Mogući rezultati se oduzimaju od 0 do 40. Upitnik je validiran i preveden na hrvatski jezik (15).

Graduirana ljestvica kronične boli - karakteristični intenzitet boli
Upitnik GCPS upotrebjava se za procjenu dviju dimenzija ozbiljnosti kronične boli: intenziteta boli i ograničenja povezanih s boli. Rezultati karakterističnog intenziteta boli i rezultata nesposobnosti kombiniraju se kako bi se izračunao stupanj kronične boli koji omogućuje klasifikaciju pacijenata u pet kategorija – od 0 (nema boli) do IV (obzljena i nesposobni). Sve točke sastoje se od ljestvice koja ima vrijednosti od 0 do 10. Rezultati pojedinih točaka bazuju se na uvažavanju rezultata ljestvice – karakterističan intenzitet boli izračunava se kao aritmetička sredina rezultata intenziteta kronične boli ovisna na oralnom zdravlju. Rezultati nesposobnosti izračunava se kao aritmetička sredina rezultata nesposobnosti ovisne o oralnom zdravlju. Rezultat izračunava se kao aritmetička sredina rezultata nesposobnosti rezultata ovisne o oralnom zdravlju.

Ljestvica funkcijalnih ograničenja čeljusti
Upitnik JFLS pouzdany je i valjan alat kojim se procjenjuju ograničenja i uzrokovana temperomandibularnim poremećajima. Sastoji se od 52 točki grupirane na sljedeći način: a) ograničenje žvakanja (20 točaka), b) ograničenje pokretljivosti (9 točaka), c) ograničenje komunikacije (14 točaka), d) druga ograničenja (9 točaka) i e) druga ograničenja (9 točaka). U ovom istraživanju pratili smo promjene u trima kategorijama JFLS-a – u ograničavanju žvakanja, ograničavanju pokretljivosti i ograničavanju komunikacije.
Statistical Analysis

Data analyses were performed using the Statistica 13.4.0 software package (1984-2018 TIBCO Software Inc.). The distribution of data was tested using the Shapiro-Wilk test. The baseline and 6-month follow-up data (JFLS scores, percentage change of MCO values and MMO values) were analyzed using Student's t-test. The changes in the means of measured variables (VAS, OHIP-14, PSS, GCPS, MCO and MMO scores) were analyzed using repeated measures analysis of variance (ANOVA) with time (baseline, 1st, 3rd, 6th month of therapy) as the within factor and diagnostic subgroups (MP and DD) and type of treatment (SS and PS) as the between factors. Bonferroni's post hoc test was used to show where the differences were found. Eta squared (η²) was used to estimate the effect size. A value of p < 0.05 was considered statistically significant.

Results

Baseline characteristics did not differ significantly between the two treatment groups when observed in general, as well as when observed in each diagnostic subgroup (p>0.05). No significant age difference was found between both treatment groups (SS 38.89 ± 11.79; PS 32.66 ± 11.48; t=1.54, p=0.13) nor in both treatment groups when divided into diagnostic subgroups: MP group (SS 42.25 ± 10.06; PS 36.37 ± 12.86; t=1.017, p=0.33), DD group (SS 36.36 ± 12.88; PS 28.28 ± 8.81 t=1.45, p=0.16). Table 1 shows participants' baseline data in both treatment groups.

PSS scores did not differ significantly between diagnostic subgroups (p>0.05). However, PSS scores changed significantly over time (p=0.049, effect size=0.11) and differed significantly between the two treatment groups (F=6.89, p=0.014) with significantly lower values in SS compared to PS group at all follow up appointments (Figure 4).

VAS scores for spontaneous pain showed significant reduction over time (Wilks Lambda = 0.19, F=32.70; p=0.0001, effect size=0.56). Changes in spontaneous pain differed significantly between treatment groups, with greater reduction in the SS compared to the PS group (interaction time x treatment group; Wilks Lambda = 0.58, F=5.78; p=0.004, effect size=0.22) (Figure 5). The post hoc analysis showed that in the SS group the mean VAS values were significantly lower at the 1st, 3rd and 6th month of the treatment compared to the baseline (p=0.0007, p=0.0001 and p=0.0001 respectively), while in the PS group a significant difference in mean VAS values was found only between 6th month of treatment compared to the baseline (p=0.006). No statistical significance in VAS scores was present between TMD subgroups.

OHIP-14 scores also showed significant reduction over time (Wilks Lambda = 0.47, F=8.80; p=0.0004, effect size=0.29). Changes in OHIP-14 scores differed significantly between treatment groups, with reduced values only in the SS group during a 6-month period (interaction time x treatment group; Wilks Lambda = 0.62, F=4.32; p=0.02, effect size=0.15) (Figure 6). The post hoc analysis showed that in the SS group the mean OHIP-14 scores were significantly lower at the 3rd and 6th month of the treatment compared to the baseline (p=0.0009, p=0.0001 respectively), while in the PS group no significant difference in mean OHIP-14 scores was considered statistically significant.

Statistička analiza

Podatci su analizirani u statističkom paketu (TIBCO Software Inc., 2018.) Statistica, verzija 13. Za testiranje distribucije podataka korišten je Shapiro-Wilkov test. Početne vrijednosti i vrijednosti tijekom šestomjesечnog kontrola (rezultati upitnika JFLS-a i postotna promjena vrijednosti MCO-a i MAM-a) analizirane su s pomoću Studentova t-testa.

Promjene u prosječnim vrijednostima (VAS, OHIP-14, PSS, GCPS, MCO i MMO) proučene su s pomoću analize ponovljenih mjerenja (ANOVOA om) s čimbenikom vrijeme (T 0, T 1, T 2, T 3) kao izvorom varijabilnosti unutar subjekta te čimbenicima dijagnostička podskupina (MP-om i DD-om) i vresta terapije (SU-om i PU-om) kao izvorima varijabilnosti između subjekata, nakon čega su slijedili post hoc Bonferronije-vi testovi. Eta kvadrat (η²) služio je u procjeni veličine efekta. Statistički značajnom smatra se vrijednost p < 0.05.

Rezultati

Nisu zabilježene statistički značajne razlike među terapijskim skupinama prije početka liječenja, ali ni među terapijskim skupinama kada su bile podijeljene u dijagnostičke podskupine (p > 0.05). Također nije bilo značajne razlike u dobi pacijentica između dviju terapijskih skupina (SU 38.89 ± 11.79; PU 32.66 ± 11.48; t=1.54, p=0.13), ni između dijagnostičkih podskupina s TMP-om: u podskupini s MP-om (SU 42.25 ± 10.06; PU 36.37 ± 12.86 t=1.017, p=0.33) i u podskupini s DD-om (SU 36.36 ± 12.88; PU 28.28 ± 8.81 t=1.45, p=0.16). Osnovne karakteristike pacijentica pri po- djeli u terapijske skupine nalaze se u tablici 1.

Rezultati PSS-a nisu se značajno razlikovali između dijagnostičkih podskupina (p > 0.05). Međutim, rezultati PSS-a s vremenom su se značajno smanjili (p = 0.049, veličina efekta = 0.11), a u skupini SU na svim su kontrolnim pregledima zabilježene značajno niže PSS vrijednosti u usporedbi s SU skupinom (F = 6.89, p = 0.014) (slika 4.).

Vrijednosti boli, procjenjivane prema ljestvici VAS, značajno su se smanjile tijekom vremena (Wilksova lambda = 0.19, F = 32.70; p = 0.0001, veličina efekta = 0.56). Promje- ne u spontanoj boli značajno su se razlikovali između terapijskih skupina, pri čemu je veće smanjenje bilo zabilježeno u skupini sa SU-om negoli u onoj s PU-om (interakcija vrijeme x terapijska skupina; Wilksova lambda = 0.58, F = 5.78; p = 0.004, veličina efekta = 0.22). Post hoc analiza pokazala je da su u skupini sa SU-om srednje vrijednosti VAS-a bile značajno niže u prvom, trećem i šestom mjesecu terapije u odno- su prema početnim vrijednostima (p = 0.0007, p < 0.0001 i p < 0.0001 respektivno), a značajna je razlika u odnosu prema početnom mjerennju pronađena u skupini s PU-om samo na posljednjem mjerenu (šesti mjesec terapije) (p = 0.006). Ni- je bilo značajnih razlika u vrijednostima VAS-a između dija- nostičkih podskupina (slika 5.).

Rezultati upitnika OHIP-14 također su se smanjili tije- kom vremena (Wilksova lambda = 0.47, F = 8.80; p = 0.0004, veličina efekta = 0.29). Promjene u OHIP-14 u vrijednosti- ma su se značajno razlikovale između terapijskih skupina, sa značajno nižim vrijednostima tijekom terapijskog razdoblja u skupini sa SU-om (interakcija vrijeme x terapijska skupina; Wilksova lambda = 0.62, F = 4.32; p = 0.02, veličina efekta = 0.15). Post hoc analiza pokazala je da su u skupini sa SU-om
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PSS, perceived stress scale/samo-percipienti stres; GCPS, graded chronic pain scale/scala gradijacije kronične bol; OHIP-14, oral health impact factor/profil za procjenu oralnog zdravlja; JFLS, jaw function limitation scale/scala ograničenja funkcije done čeljusti; MCO maximal comfortable mouth opening/maximalno bezbolno otvaranje; MMD maximal mouth opening/ maksimalno moguće otvaranje usta; VAS, visual analogue scale/visualno-analogni skala; TO, baseline variables/početne variablene

**Table 1**

| Variable | Stabilization splint | Placebo splint | t | p |
|----------|----------------------|----------------|---|---|
| deb • age | 34.89 ± 11.79 | 32.66 ± 11.48 | 1.54 | 0.13 |
| PSS | 17.63 ± 9.03 | 20.73 ± 6.22 | -0.92 | 0.36 |
| GCPS | 49.42 ± 29.08 | 46.20 ± 15.89 | 0.49 | 0.62 |
| OHIP-14 | 26.31 ± 9.99 | 22.19 ± 11.76 | 1.11 | 0.27 |
| JFLS žvakanje • mastication | 3.87 ± 2.34 | 2.91 ± 1.80 | 1.28 | 0.20 |
| JFLS pokretnost done čeljust • jaw mobility | 4.85 ± 1.73 | 3.96 ± 1.67 | 1.50 | 0.14 |
| JFLS verbalna i neverbalna komunikacija • verbal and emotional expression | 1.75 ± 1.66 | 1.28 ± 1.28 | 0.90 | 0.37 |
| MCO (mm) | 27.57 ± 9.88 | 27.93 ± 6.18 | -0.12 | 0.90 |
| MMD (mm) | 35.78 ± 9.12 | 36.86 ± 6.41 | -0.38 | 0.70 |
| VAS | 6.52 ± 2.03 | 5.53 ± 1.72 | 1.50 | 0.14 |

**Figure 4** Changes in self-perceived stress (PSS) from baseline to 6th month of the therapy. SS stabilization splint; PS placebo splint; MP myofascial pain subgroup; DD disc displacement subgroup

**Figure 5** Changes in spontaneous pain (VAS) from baseline to 6th month of the therapy. SS stabilization splint; PS placebo splint; MP myofascial pain subgroup; DD disc displacement subgroup

**Figure 6** Changes in oral health-related quality of life (OHIP-14) from baseline to 6th month of the therapy. SS stabilization splint; PS placebo splint; MP myofascial pain subgroup; DD disc displacement subgroup

**Figure 7** Changes in maximal comfortable mouth opening (MCO) from baseline to 6th month of the therapy. SS stabilization splint; PS placebo splint; MP myofascial pain subgroup; DD disc displacement subgroup

Slika 4. Promjene percipiranog stresa (PSS) od polaznih rezultata do 6. mjeseca liječenja. SU stabilizacijska udlaga; PU placebo udlaga; MP podgrupa miofascijalna bol; DD podgrupa pomak zglobne pločice

Slika 5. Promjene spontane bile (VAS) od polaznih rezultata do 6. mjeseca liječenja. SU stabilizacijska udlaga; PU placebo udlaga; MP podgrupa miofascijalna bol; DD podgrupa pomak zglobne pločice

Slika 6. Promjene u kvaliteti života povezanoj s oralnim zdravljem (OHIP-14) od polaznih rezultata do 6. mjeseca liječenja. SU stabilizacijska udlaga; PU placebo udlaga; MP podgrupa miofascijalna bol; DD podgrupa pomak zglobne pločice

Slika 7. Promjene u maksimalnom bezbolnom otvaranju usta (MCO) od polaznih rezultata do 6. mjeseca liječenja. SU stabilizacijska udlaga; PU placebo udlaga; MP podgrupa miofascijalna bol; DD podgrupa pomak zglobne pločice
was present between baseline and follow-up appointments. No statistical significance in OHIP-14 scores was found considering the TMD subgroups.

MCO values did not change significantly over time, however pain-free maximal mouth opening differed significantly between the two treatment groups ($F=4.37$, $p=0.046$) with greater overall values in the SS group (Figure 7). Also, a significant difference was found when comparing the MP group to the DD group with greater overall values in the MP group ($F=5.42$, $p=0.03$). Significant difference in percentage change in MCO between the two treatment groups with greater increase in the SS group was found ($SS 28.54 $; $PS 1.64 $; $t=2.11, p=0.043$).

MMO values did not differ significantly between the two treatment groups or the diagnostic subgroups ($p>0.05$) but they changed significantly over time (Wilks Lambda = 0.72, $F=3.16; p=0.042$, effect size = 0.12). Although the changes in MMO values did not differ significantly between the two treatment groups, a tendency of constant increase of MMO was present in the SS group (Figure 8). Also, a significant
difference in percentage change in MMO between the two treatment groups with greater increase in the SS group was found (SS 23.82%; PS 0.73%; t = 2.32, p = 0.028).

GCPS scores did not differ significantly between treatment groups or the diagnostic subgroups but decreased significantly over time (Wilks Lambda = 0.45, F=9.52; p=0.0003, effect size=0.35) (Figure 9).

All JFLS categories, except emotional and verbal expression, showed significant decrease between baseline measurements (T0) and the last time-point measurements (T3) in the SS group (mastication t=4.92, p=0.00015; vertical jaw mobility t=4.82, p=0.00018; emotional and verbal expression t=1.82, p=0.086). No such changes in JFLS categories were observed in the PS group (mastication t=0.24, p=0.81; vertical jaw mobility t=1.26, p=0.23; emotional and verbal expression t=-0.24, p=0.56) (Figure 10).

Discussion

Studies that tried to compare the effect of placebo therapy with stabilization splint have sometimes yielded conflicting results. Some researchers attempted to equate the effect of stabilization with that of placebo devices encouraging the debate on the real value of the specific design of the stabilization splint. In these studies, the placebo splint is often a “nonsplit” designed as non-occluding device (20, 21).

In our research, starting with the assumption that patients may recognize non-occluding device as placebo, we took a slightly different approach. Since it is speculated that therapy value of SS lies in increasing of vertical dimension and changing of condylar position (22, 23, 24, 25), we used very thin thermoforming foil that covered occlusal surfaces and changing of condylar position (22, 23, 24, 25), we used very thin thermoforming foil that covered occlusal surfaces but did not provide occlusion in CR position. In addition, the effect on the vertical dimension wasn’t notable, therefore when biting patients were in their habitual occlusion position vertically increased for less than 0.5 mm. With Michelotti et al. pointing out that counselling may be as successful modality as splint therapy (12), we informed both patients treated with stabilization splint as compared to patients treated with placebo splint, with greater reduction through all 6 months found in the SS group. In addition, significant improvement in the SS group after 6th month of treatment compared to baseline was present in all JFLS categories, except emotional and verbal expression.

We may say that SS provided better continuous, long-term therapeutic effect. PS performed very well in reduction of spontaneous pain in the short term, however reduction of OHIP-14 and JFLS scores was found only in the SS group.
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It is interesting to note that the graphic representation of PS performance during 6-month treatment in Figures 5, 6 and 9 resemble the graphic representation of SS but after 3rd month it is followed by either plateau or even mild deterioration towards the higher values. Regardless of the potentially negligible effect of the slightly increased vertical dimension of less than 0.5 mm, the design of the placebo device should be taken into consideration when interpreting these results since all the changes in vertical positioning of the lower jaw might affect the treatment outcomes. We may conclude that both SS and PS were effective in management of spontaneous pain. This could be attributed to prior education of patients on the disorder (12) or the fact that even a slight increase in vertical dimension can provide the muscle rearrangement leading to a relaxation of the elevator muscles and consequently, reduction of the pain. Significant differences between the treatment groups in improvement of pain and quality of life could be due to the fact that SS was thicker (providing a greater increase in vertical dimension of occlusion), as well as constructed to provide CR occlusion and specific condylar position, thus contributing to the relief of the TMJ (7, 9).

An interesting finding was that most of the mentioned parameters did not differ significantly between the TMD subgroups except the MCO with better results in the MP group. The reason for better improvement of the MCO results in the MP when comparing to the DD subgroup is probably the fact that in the DD group the biological barrier (displaced disc) is blocking the condyle without the possibility for restoring its position (26), thus limiting the full range of opening.

PSS scores differ significantly between treatment groups, and changed significantly over time. The decreased PSS scores showed that psychological stress, considered the predisposing factor for TMD (27), was positively affected by treatment duration.

Similar long-term effectiveness of SS was found by Ekberg et al. They monitored patients over 6 and 12 months and recommended the SS appliance for further use in TMD management (28). Moreover, Alajbeg et al. found that, when compared to placebo and amitriptyline therapy, SS showed a significantly greater change in the MCO (29). Still, in studies with the goal to compare TMD treatment options, patients have been monitored over different time periods, hence the inconsistent results can be attributed to different therapy duration. Furthermore, the design of occlusal or nonocclusal devices differ to a great extent and it is difficult to provide comparable results (20, 21, 28, 29).

The limitation of the present study lies in the fact that only female experiencing chronic, moderate to severe pain, whose response to the therapy may be different than in those with mild pain, were included in the study. However, the main advantage of the study was that we carefully selected and followed the subjects for a longer period of time with validated and widely accepted TMD diagnostic questionnaires and protocols, whereby our results showed that the specific design of the stabilization splint contributes to the treatment of TMD.

Stabilization appliance imala je značajan utjecaj na smanjenje simptoma i pružala je kontinuirani, dugotrajni terapijski učinak. Placebo usklađala je kratkoročan učinak na smanjenje spontanog boli, no smanjenje vrijednosti OHIP-a 14 te iznosa pojedinih kategorija JFLS-a tijekom šestomjesečne terapije bilo je zabilježeno samo u skupini sa SU-om. Zanimljivo je primijetiti kako se grafički prikaz trajanja liječenja PU-a na slikama 5., 6. i 9. kreće jednako kao i kod SU- a, no nakon trećeg mjesečnog priljeva blago pogoršanje prema većim iznosima. Bez obzira na potencijalno zanemariv učinak površine vertikalne dimenzije okluzije za manje od 0,5 mm pri oblikovanju placebo usklađenja, pri interpretaciji rezultata treba uzeti u obzir svaku promjenu u vertikalnom odnosu gornje i donje čelosti zbog njezina potencijalnog utjecaja na ishod terapije. Početno smanjenje simptoma TMP-a, vidljivo u objema terapijskim skupinama, može biti posljedica informiranja pacijenata o poremećaju za koji je dokazano da pozitivno utječe na smanjenje simptoma (12) ili činjenice da se čak i zbog vrlo diskretnog povišenja vertikalne dimenzije okluzije može dogoditi promjena u mišićima koja za posljedicu ima opuštanje mišića podizajno čelosti i naposljetku smanjenje boli.

Razlike koje postoje kada promatramo odnose između terapijskih skupina možda se pojavljuju zbog specifičnog dizajna operativne uklanjanja načina u kojem je deblji od PU-a i zbog toga značajnije povisanje vertikalnu dimenziju okluzije. Također je oblikovan tako da donju čelost šmješta u CR, a kondile u položaj koji rezultira zračenjem TMJ-a (7, 9).

Zanimljivo je da se većina mjerenih parametara nije značajno razlikovala između dijagnostičkih podskupina TMP-a, osim vrijednosti MCO-a koje su bile značajno više u skupini s MP-om. Razlog za razliku u vrijednostima MCO-a između skupina s MP-om i DD-om je podudarnost u podskupini s DD-om koji čini biološku barijeru i najvjerojatnije ne postoji mogućnost da se vrati u prijašnje fiziološko stanje (26). Na taj način ograničeno je vranje punog raspona otvaranja usta u podskupini s DD-om.

Vrijednosti PSS-a razlikovale su se između terapijskih skupina, te se dogodio značajniji pad tijekom vremena. Značajan pad vrijednosti PSS-a pokazuje kako je na psihološki stres, rizični čimbenik TMP-a (27), terapijsko razdoblje od šest mjeseci imalo pozitivan učinak.

Ekberg i suradnici pratili su pacijente tijekom šest i dva naesta mjeseca te uočili sličan dugotrajni terapijski uspjeh SU-a. Preporučili su SU za daljnje korištenje u terapiji TMP-a (28). Alajbeg i suradnici uspoređivali su terapijski učinak amitriptilina, placebo lijeka i SU-a, te pokazali da se jedino u skupini liječenoj SOU-zmno značajno poveća MCO (29). Poteškoće u interpretaciji usporedbi rezultata ovoga i sličnih istraživanja proizlaze iz činjenice da su istraživanja provedena u različitim vremenskim razdobljima, stoga su inkonsistentni rezultati vjerovatno posljedica različitog trajanja terapije, a posljedica konstrukcija istraživanih uskladlja koje se razlikuju u velikoj mjeri i onemogućuju kvalitetnu usporedbu rezultata (20, 21, 28, 29).

Ispitno i kontrolnu skupinu činile su samo žene s kroničnim, srednje jakim do jakim boli. Kako ishodi terapije mogu biti značajni različiti u skupini s blagom bolesti, spomenuto se može smatrati otežajućim čimbenikom u istraživanju.

Kao najveći prednost istraživanja istaknuli bismo pažljivost biranja i početna ispitanika tijekom duljeg razdoblja, pri

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Svrha istraživanja: Cilj ove studije bio je procijeniti dugoročnu učinkovitost stabilizacijske udlage u liječenju pacijenata s kroničnim temporomandibularnim poremećajima (TMP-om) te usporediti ishode liječenja s onima postignutima placebo udlagom kod pacijenata s dijagnozom miofascijalne boli i većim aktivnim terapijskim uputama.

Materijali i metode: U dvije terapijske skupine bile su podijeljene 34 pacijentice s kroničnim TMP-om – u prvoj su se skupini, kao terapijskim sredstvom, koristile stabilizacijska udlaga (SU-om), a u drugoj placebo udlaga (PU-om). Ishodi liječenja (bol procijenjen prema graduiranoj ljestvici kronične boli) i funkcija čeljusti (prema ljestvici ograničenja funkcije čeljusti – JFLS-u) prateće šest mjeseci.

Rezultati: U skupini s SU-om nije bilo značajnih promjena u pojedinim kategorijama JFLS-a, osim u emocionalnoj i verbalnoj ekspresiji (žvakanje p = 0,00015; okomita pokretljivost čeljusti p = 0,00018). U skupini s PU-om nije bilo značajnih promjena u pojedinim kategorijama JFLS-a.

Zaključak: Tijekom šestomjesečnog liječenja stabilizacijska udlaga pokazala je učinkovitiji od placebo udlage, a u skupini liječenoj stabilizacijskom udlagom također su uočene veće vrijednosti maksimalnoga bezbolnog otvaranja usta. Iako bi placebo mogao biti dijelom odgovoran za poboljšanje simptoma TMP-a, vjerojatno ne može zadržati kontinuirani dugoročni pozitivni terapijski učinak.

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Conflict of interest
The authors report no conflict of interest

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Ključne riječi: temporomandibularni poremećaji, okulzijska udlaga, kronična bolesnost, facijska boli.

Sažetak
Svrsna istraživanja: Cijeli ovaj rad željimo koristiti u kliničkoj praksi kod terapijskog učenja pacijenata s kroničnim temporomandibularnim poremećajima. U cilju procijeniti učinkovitost stabilizacijske udlage u terapiji kroničnih temporomandibularnih poremećaja, provedena je studija koja je pokušala procijeniti učinkovitost stabilizacijske udlage u usporedbi s placebo udlagom.

Materijali i metode: U dvije terapijske skupine (SU i PU) bile su podijeljene 34 pacijentice s kroničnim temporomandibularnim poremećajima. U skupini SU, kao terapijsko sredstvo, koristili su stabilizacijsku udlagu, dok u skupini PU oni koristili placebo udlagom.

Rezultati: U skupini SU nije bilo značajnih promjena u pojedinim kategorijama učinaka (JFLS), osim u emocionalnoj i verbalnoj ekspresiji. U skupini PU nije bilo značajnih promjena u pojedinim kategorijama učinaka.

Zaključak: Tijekom šestomjesečnog liječenja stabilizacijska udlaga pokazala je učinkovitiji od placebo udlage, a u skupini liječenoj stabilizacijskom udlagom također su uočene značajne veće vrijednosti maksimalnoga bezbolnog otvaranja usta. Iako bi placebo mogao biti dijelom odgovoran za poboljšanje simptoma TMP-a, vjerojatno ne može zadržati kontinuirani dugoročni pozitivni terapijski učinak.
References

1. Gauer RL, Semidey MJ. Diagnosis and Treatment of temporomandibular disorders. Am Fam Physician. 2015 Mar 15;91(6):378-86
2. Reiter S, Goldsmith C, Emo-di-Periman A, Friedman-Rubin P, Wincour E. Masticatory muscle disorders diagnostic criteria: The American Academy of Orofacial Pain versus the research diagnostic criteria/temporomandibular disorders. J Oral Rehabil. 2012 Dec;39(12):941-7.
3. Stohler CS. Muscle-related temporomandibular disorders. J Orofac Pain. 1990;4(6):273-288.
4. Warren M, Fried JL. Temporomandibular disorders and hormones in women. Cells Tissues Organs. 2001;169:187-192.
5. Peck CC, Goulet JP, Lobbezoo F, Schiffman EL, Alstergren P, Anderson GC, et al. Expanding the taxonomy of the diagnostic criteria for temporomandibular disorders. J Oral Rehabil. 2018 Mar;45(3):258-268.
6. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. J Headache Pain. 2015;16:106.
7. Klasser GD, Greene CS. Oral appliances in the management of temporomandibular disorders. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;107(2):144-150.
8. Al-Ani Z, Gray RJ, Davies SJ, Sloan P, Glenny AM. Stabilization Splint Therapy for the Treatment of Temporomandibular Myofascial Pain: A Systematic Review. J Dent Educ. 2005 Nov;69(11):1242-50.
9. Gray RJ, Davies SJ, Quayle AA. A clinical approach to temporomandibular disorders: a clinical approach to treatment. Br Dent J. 1994 Sep 10;177(5):171-8.
10. Türp JC, Komine F, Hugger A. Efficacy of stabilization splints for the management of patients with masticatory muscle pain: a qualitative systematic review. Clin Oral Investig. 2004 Dec;8(4):179-95.
11. Friction J, Look JO, Wright E, Alencar FG, Chen H, Lang M, Ouyang W, Velly AM, et al. Systematic review and meta-analysis of randomized controlled trials evaluating intraoral orthopedic appliances for temporomandibular disorders. J Orofac Pain. 2010 Summer;24(3):237-54.
12. Michelottl A, Iodice G, Vollaro S, Steenks MH, Farella M. Evaluation of the short-term effectiveness of education versus an occlusal splint for the treatment of myofascial pain of the jaw muscles. J Am Dent Assoc. 2012 Jan;143(1):47-53.
13. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical Research Applications: Recommendations of the International RDC/TMD Consortium Network and Orofacial pain Special Interest Group. J Oral Facial Pain Headache. 2014 Winter;28(1):6-27.
14. Emshoff R, Emshoff R, Bertram S. Estimation of clinically important change for visual analog scales measuring chronic temporomandibular disorder pain. J Orofac Pain. 2010 Summer;24(3):262-9.
15. Hudek-Knežević J, Kardum I, Lesić R. Efekti percipiranog stresa i stilova sučuvanja na tjelesne simptome. Državna istraživanja. 2015;6,543-561.
16. Barros V de M, Serafianian PI, Côrtes MI, de Paula LV. The impact of orofacial pain on the quality of life of patients with temporomandibular disorder. J Orofac Pain. 2009 Winter;23(1):28-37.
17. Rener-Sitar K, Petričević N, Čelebić A, Marion L. Psychometric properties of Croatian and Slovenian short form of oral health impact profile questionnaires. Croat Med J. 2008 Aug;49(4):536-44.
18. Von Korff M, OMT, Kork FE, Dworkin SF. Grading the severity of chronic pain. Pain 1992;50:133-49.
19. Ohrbach R, Larsson P, List T. The jaw functional limitation scale: development, reliability, and validity of a 8-item and 20-item versions. J Orofac Pain. 2008 Summer;22(3):219-30.
20. Truelove E, Huggins KH, Manci L, Dworkin SF. The efficacy of traditional, low-cost and non-splint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc. 2006 Aug;137(8):1099-107; quiz 1169.
21. Alencar F Jr, Becker A. Evaluation of different occlusal splints and counselling in the management of myofascial pain dysfunction. J Oral Rehabil. 2009 Feb;36(2):79-85.
22. Solberg W, Clark G. Rug. Nocturnal electromyographic evaluation of bruxism patients undergoing short-term splint therapy. J Oral Rehabil. 1975 Jul;2(3):215-23.
23. Manns A, Miralles R, Cumsille F. J Prostheth Dent. Influence of vertical dimension on masseter muscle electromyographic activity in patients with mandibular dysfunction. J Prostheth Dent. 1985 Feb;53(2):243-7.
24. Alajbeg IZ, Gikić M, Valentić-Peruzović M. Mandibular Range of Movement and Pain Intensity in Patients with Anterior Disc Displacement without Reduction. Acta Stomatol Croat. 2015;49(2):119-127.
25. MeSH Browser [database on the Internet]. Badel T, Alajbeg I, Morroti M, Kocijan Lovko S. Temporomandibular Joint Disorder Therapy by Occlusal Splint: A Case Report. Acta stomatologica Croatica [updated 22.08.2019.] Available from: https://hrcak.srce.hr/26734.
26. Kirk WS Jr. Magnetic resonance imaging and tomographic evaluation of occlusal appliance therapy for advanced internal derangement of the temporomandibular joint. J Oral Maxillofac Surg. 1991 Jan;49(1):9-12.
27. Augusto VS, Perima KCB, Penha DSG, Dos Santos DCA, Oliveira VAS. Temporomandibular dysfunction, stress and common mental disorder in university students. Acta Ortop Bras. 2016;24(6):330–333. doi:10.1590/1413-78522016240612873.
28. Ekberg E, Nilner M. Treatment outcome of appliance therapy in temporomandibular disorder patients with myofascial pain after 6 and 12 months. Acta Odontol Scand. 2004 Dec;62(6):343-9.
29. Alajbeg IZ, Boric Brakus R, Brakus I. Comparison of amitriptyline with stabilization splint and placebo in chronic TMD patients: a pilot study. Acta Stomatol Croat. 2018 Jun;52(2):114-122.