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КОНТРОЛЬ БОЛИ И ГИПЕРУРИКЕМИИ У БОЛЬНЫХ С ТОФУСНОЙ ПОДАГРОЙ ПОСЛЕ ОПЕРАЦИИ НА СУСТАВАХ

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Резюме

Первичная задача при лечении тофузной (узелковой) подагры – это ее лечение медикаментозными средствами. К хирургическому вмешательству прибегают дополнительно, если нужно провести косметическую корректировку деформации в суставе или убрать его инвалидизирующую дисфункцию. Однако при этом вмешательстве возникают такие осложнения, как гиперурикемия и рецидив подагрического артрита, хорошо задокументированные в литературе. *Цель:* оценить эффективность низкоинтенсивной лазерной терапии (НИЛТ) на снижение уровня соли мочевой кислоты (уратов) у пациентов с тофусной подагрой, которые перенесли хирургическое вмешательство на суставах в ревматологической больнице Чэнду (Китай), и сравнить их с показателями пациентов, которые лечились только консервативно. *Материалы и методы.* Эффективность НИЛТ как уратснижающей терапии была исследована на 63 пациентах мужского пола с тофусной подагрой, которые лечились и были прооперированы в ревматологической больнице города Чэнду. Контрольную группу составили 63 пациента с подагрой, сопоставимых по возрасту и уровню мочевой кислоты до лечения, но которым проводили только консервативное лечение. *Результаты.* Пациентам делали одноэтапную или двухэтапную операцию. Наиболее частым местом поражения были суставы стопы: пальцы ног (49,41%), голеностопный сустав (39,68%) и коленный сустав (34,92%), имевшие ограниченную подвижность. Уровни С-реактивного белка (СРБ) до лечения были повышены почти у всех пациентов (медиана 3,74 (0,2–48,75) мг/л) независимо от других сопутствующих заболеваний. Уратснижающая терапия заметно снизила уровень СРБ до 2,44 (0–33,27) мг/л в исследуемой группе и до 1,3 (0,13–31,72) мг/л в контрольной группе. После операции и уратснижающей терапии у всех пациентов отмечалось функциональное улучшение и уменьшение боли. Снижение уровня уратов в сыворотке было зарегистрировано у 96,83% пациентов основной группы и у 93,65% пациентов контрольной группы. Не было существенной разницы в уровне мочевой кислоты сыворотки у пациентов, перенесших операцию на суставах, и у пациентов, леченых только консервативно. Самый низкий средний уровень мочевой кислоты в сыворотке был у тех больных, которые дополнительно к хирургическому лечению получали лазеротерапию (280,93 ± 97,05 мкмоль/л), но из-за широкого диапазона вариаций разница с другими группами не была статистически значимой. Добавление лазеротерапии в комплексное лечение также помогло уменьшить боль почти вдвое (0,56 ± 0,56 против 1,04 ± 0,91), однако заметного противовоспалительного действия НИЛТ мы не зарегистрировали. Была установлена слабая прямая связь между уровнями мочевой кислоты и С-реактивного белка в сыворотке после лечения, но у пациентов, получавших лазерную терапию, СРБ повышался чаще, чем в контрольной группе. *Заключение:* Артроскопическая чистка сустава и другие хирургические методы лечения, как правило, никак не влияют на системную гиперурикемию и не могут рассматриваться как замена уратснижающей терапии. Однако наш опыт подтверждает, что своевременно проведенная операция способствует функциональному улучшению и уменьшению боли у больных подагрой. Низкоинтенсивная лазерная терапия не влияет на гиперурикемию и не гарантирует длительного системного противовоспалительного эффекта, но помогает дополнительно снять боль в суставах и таким образом улучшить лечебный эффект и качество жизни пациентов.

Ключевые слова: *подагра, гиперурикемия, низкоинтенсивная лазерная терапия (НИЛТ), артроскопическая чистка сустава.*

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CONTROLLING PAIN AND HYPERURICEMIA IN PATIENTS WITH TOPHACEOUS GOUT AFTER JOINTS SURGERY

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Abstract

The primary treatment of tophaceous gout is to control the disease by pharmacological therapy. Additional surgical intervention is used to correct cosmetic deformation in joints or disabling functional disorder; however, one of its reported complications is hyperuricemia and recurrent attacks of pain. *Objectives:* to access the effectiveness of Low Intensity Laser therapy as addition to urate lowering treatment in patients with tophaceous gout, who underwent joints surgery in the Chengdu Rheumatism Hospital, in comparison to those patients who received only non-surgical treatment. *Subjects and methods.* The effectiveness of Low Intensity Laser therapy (LILT) and urate lowering treatment in patients with tophaceous gout was investigated in 63 male patients of Chengdu Rheumatism hospital with tophaceous gout who underwent joints surgery. Control group was formed of 63 gout patients comparable in age and pre-treatment uric acid, who received non-surgical treatment.

Results. Patients underwent surgery in one or two sessions, the most common lesion site being foot joints: toes (49.41%), ankle (39.68%) and knee (34.92%), with restricted mobility in the mentioned joints. Levels of CRP before the treatment were elevated in almost all patients (median 3.74 (0.2, 48.75) mg/L), regardless of the other comorbidities. Urate lowering therapy notably reduced the levels of CRP to 2.44 (0, 33.27) mg/L in study group and to 1.3 (0.13, 31.72) mg/L in controls. After surgery and following urate lowering therapy all patients noted functional improvement and reduction of pain. Decrease in serum urate levels were reported in 96.83% of patients in study group and in 93.65% of controls. There was no significant difference in serum UA between patients who underwent joint surgery and who didn't. Patients, who in addition to surgery received Low-Level Laser Therapy therapy, had a lowest mean serum UA after treatment (280.93 ± 97.05 μmol/L), but due to wide range of variation, difference to other groups wasn't statistically significant. Addition of laser therapy also helped to reduce the pain almost twice

(0.56±0.56 compared to 1.04 ± 0.91). However, we haven't registered notable anti-inflammatory influence of LILT. There was a weak direct link established between levels of serum UA and CRP after treatment, but in patients receiving laser therapy, CRP was elevated more often, compared to those who weren't prescribed with LILT or controls. *Conclusion.* Arthroscopic shaving and other surgical approaches focused on joints often doesn't affect system hyperuricemia in any way and can't be viewed as a substitute to urate lowering therapy. However, our experience confirms that timely performed surgery contribute to functional improvement and reduction of pain in gout patients. Low Intensity Laser therapy doesn't affect hyperuricemia or guarantee long-term systemic anti-inflammatory effect, but help to additionally relieve pain in joints and thus enhance treatment effect and quality of patients' life.

Key words: *gout, hyperuricemia, LILT, arthroscopic shaving.*

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INTRODUCTION

The presence of tophi was reported in approximately 12–35% of gout patients and has been associated with significant morbidity including poor quality of life and increased healthcare resource use [1]. Depending on their anatomic location, tophi have the potential to cause irreversible joint damage with bony destruction. Tophi can also entrap nerves causing compressive neuropathy, such as carpal tunnel syndrome or radiculopathy [2, 3].

Urate lowering therapy is a beneficial treatment for the majority of patients suffering from tophaceous gout, however up to an estimated 100 000 per one million cases of gout are not adequately managed with current therapies and need other options of treatment [4]. It includes cases of functional impairment with inability to perform daily work due to restricted range of motions and massive joint transformation leading to inability wear shoes or clothes. Those cases, even responsive to urate lowering therapy, might demand expeditious time-optimal solutions [5].

Publications on gout surgery are still mostly limited to isolated case reports and case series [4], with most common surgical techniques described being arthroscopic shaver and open tophectomy. The reported outcomes are generally positive, but the most common adverse outcomes include delayed wound healing [5], hyperuricemia and recurrent attack of gouty arthritis [6, 7].

Low Intensity Laser Therapy (LILT) is a new technique used for the treatment of gout. The proper application of this therapy is reported to significantly reduce the pain and swelling in joints of gout patients [8]. Additional usage of LILT is a promising aid for recovery period after joint surgery in patients with tophaceous gout.

MATERIALS AND METHODS

Medical records of 126 male patients with gout were included in the study, of them 63 patients with tophaceous gout who underwent joints surgery and control group, formed of 63 gout patients comparable in age and pretreatment uric acid, who received non-surgical treatment**.** All patients were admitted to Chengdu Rheumatism Hospital in 2019–2020 and satisfied the preliminary criteria of gout. The study was performed in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Chengdu Rheumatism Hospital. All participants provided written informed consents.

Data collection. In all patients anthropometrical parameters were measured, including waist circumference, body height and weight, body mass index (BMI). In addition, blood pressure at systolic and diastolic phases, blood levels of triglycerides, fasting serum glucose, and creatinine were measured. Serum UA was measured on the first day and after the end of treatment by standard ELISA method. Presence of fatty liver was assessed by B-ultrasonography, in some cases with additional MRI or liver biopsy. The diagnosis of renal dysfunction was based on serum creatinine and glomerular filtration rate; kidney stones was detected by X-ray and B-ultrasonography.

LILT. Joints were exposed to laser light source L.H.H. Medicallaser (fig. 1), whose characteristics are as follows: wavelength centered at λ = 810 nm (peak 1600 mw), pulse width of τ = 13 ns, repetition frequency of fR = 210 kHz. The exposure time was 20min, once a day, 7 days as a course of treatment. 810-nanometer light wave was adopted to reach the biological stimulation effect through the beam of semiconductor laser, in order to reduce or eliminate pain, improve local blood circulation, tissue repair, and quickly diminish inflammation, thus promoting wound healing.

Statistical analysis. Baseline characteristics of participants were evaluated by descriptive statistics and results were presented in the form of mean ± standard deviation. Comparisons in the means of continuous variables with a normal distribution were performed by using Student's t-test. Comparisons in medians of continuous variables with a skewed distribution were performed by using a Wilcoxon rank-sum test. All reported probability values (P-values) were based on two-sided tests and P value <0.05 was considered statistically significant. Statistical analysis was conducted using IBM IPSS statistics software (version 23, IBM Co., Armonk, NY, USA).

RESULTS

Total of 126 patients with gout were included in this study. All patients were of male gender. Study patients who underwent surgery and those of control group were comparable by age (mean age was 47.24 ± 11.81 years and 47.57 ± 14.49 years respectively) and serum UA before treatment (503.35 ± 124.35 μmol/L and 505.48 ± 129.29 μmol/L respectively). Almost half of all patients who underwent surgery had been diagnosed with fatty

Fig. 1. Laser light source L.H.H. Medicallaser used in the treatment of gout: general view (a), characteristics (b), work mode (c)

liver (42.86%), 28.57% with hyperlipidemia, and 12.69% had diabetes mellitus.

Routine laboratory tests were performed, including ESR and CRP, but the range of variation amongst the data was too wide. Levels of CRP before the treatment were elevated in almost all patients (median 3.74 (0.2, 48.75) mg/L), regardless of the other comorbidities. Urate lowering therapy notably reduced the levels of CRP to 2.44 (0, 33.27) mg/L in study group and to 1.3 (0.13, 31.72) mg/L in controls. Other general characteristics of study patients are described in table 1.

Patients underwent surgery in one or two sessions, the most common lesion site being foot joints: toes (49.41%), ankle (39.68%) and knee (34.92%), with restricted mobility in the mentioned joints. Among common complaints were inability to perform daily routines due to enlarged joints (inability to wear shoes), joints' dysfunction and pain. Extracted mass size ranged from 1.0 to 7.0 cm in diameter. After surgery and following urate lowering therapy all patients noted functional improvement and reduction of pain. Decrease in serum urate levels were reported in 96.83% of patients in study group and in 93.65% of controls.

Technique of arthroscopic shaving was used to access smaller tophi and softer lesions. For the excision of large tophi, complex surgical approach was needed, combining open tophectomy and aspiration of tophaceous masses. In addition to urate lowering therapy, all patients were treated by the principles of Traditional Chinese Medicine (TCM). Half of the patients who underwent surgery (n = 35) also received additional LILT (fig. 2), and 3 patients – additional platelet rich plasma therapy.

Table 1

General characteristics of gout patients

Factor	Surgery patients (n = 63)	Controls (n = 63)
Age (M ± m), years	47.24 ± 11.81	47.57 ± 14.49
Serum UA before treatment (M ± m), μmol/L	503.35 ± 124.35	505.48 ± 129.29
CRP before treatment [median (min, max)], mg/L	3.74 (0.2, 48.75)	4.97 (0.19, 39.7)
CRP after treatment [median (min, max)], mg/L	2.44 (0, 33.27)	1.3 (0.13, 31.72)
Accompanying diseases and conditions	Prevalence rate, %	
Hypertension	22.22	25.39
Diabetes mellitus	12.69	7.94
Fatty liver	42.86	33.33
Hyperlipidemia	28.57	25.39
Hepatic dysfunction	12.69	14.29
Renal dysfunction	9.52	22.22
Kidney stones	28.57	25.39

As a result, there was no significant difference in serum UA between patients who underwent joint surgery and who didn't (table 2). Patients, who in addition to surgery received laser therapy, had a lowest mean serum UA after treatment (280.93 ± 97.05 μmol/L), but due to wide range of variation, difference to other groups wasn't statistically significant ($p > 0.05$).

Patients, who underwent surgery, more often had complains about pain both before surgery and after the ending of treatment. Therapeutic effect of LILT was noted by the managing physician: including reducing inflammation and relieving pain, improvement in local blood circulation and faster tissue repair. Addition of laser therapy helped to reduce the pain almost twice (0.56 ± 0.56 compared to 1.04 ± 0.91).

However, we haven't registered notable anti-inflammatory influence of LILT. There was a weak direct link established between levels of serum UA and CRP after treatment, but in patients receiving laser therapy, CRP was elevated more often, compared to those who weren't prescribed with LILT or controls.

DISCUSSION

The lack of controlled clinical studies justifies the need to determine when, or if, a specific patient should be referred to surgery for tophaceous gout. Published literature on the indications for the surgical treatment of gout is quite limited and mostly recommend that surgery be reserved for patients with severe, debilitating tophaceous gout, impending or current complications or for those who have failed maximal medical therapy [9]. In our hospital 2 most common indications for surgery were severe functional impairment of the joint (and following inability to perform daily work due to restricted range of motions) and massive joint transformation (inability to wear shoes/clothes).

All patients, who underwent surgery under this study, reported functional improvement and reduction of pain, and the risk of complications was very low. In addition to urate lowering therapy and Traditional Chinese medicine (local topical application), some of the patients (n=35) were prescribed with LILT.

In an experimental arthritis models [10,11] LILT preserved the content of glycosaminoglycans, reduced the

Fig. 2. In-treatment photo of post-operative gout patient (big gout stone of the first metatarsophalangeal joint removed by open tophectomy with aspiration of tophaceous masses)

Table 2

Treatment results in gout patients (Surgery VS controls)

		TCM (n = 25)	TCM + LILT (n = 35)	Controls (n = 63)
Serum UA (M ± m), μmol/L	Before treatment	497.88 ± 117.21	500.63 ± 133.9	497.7 ± 128.36
	After treatment	335.92 ± 64.41	280.93 ± 97.05	322.53 ± 89.83
Pain in VAS score (M ± m)	Before treatment	4.56 ± 1.01	4.34 ± 1.59	4.68 ± 1.29
	After treatment	1.04 ± 0.91	0.56 ± 0.56	0.65 ± 0.81
CRP [median (min, max)], mg/L	Before treatment	5.83 (0.35, 35.69)	3.47 (0.2, 48.75)	4.97 (0.19, 39.7)
	After treatment	0.61 (0, 2.27)	7.06 (0.99, 33.27)	1.3 (0.13, 31.72)

cellular changes and the inflammatory process. Induced reduction of joint swelling correlated with reduction in the inflammatory markers, including serum prostaglandin E2 [11]. Laser therapy has an anti-inflammatory effect in arthropathy induced in rats injected with urates, determined by fibrinogen levels and by histological involution [12].

Decomposition of uric acid crystals by ultra-short laser pulses was described in 2020 by Rodriguez-Silva et al [13]. As a result of photochemical interaction between light and UA crystals, variations in molecular structure were observed by author. In addition to decrease in their concentration within the joints or tissues, UA crystals were more soluble and more likely to be eliminated through the urine, therefore, providing at the same time analgesic and anti-inflammatory action in the affected area.

In our study, while LILT helped to reduce the pain in joints, no pronounced anti-inflammatory affects were noted. There was a weak direct link established between levels of serum UA and CRP after treatment, mostly explained by urate lowering therapy affecting both biomarkers [14], but in patients receiving laser therapy, CRP was elevated more often, compared to those who weren't prescribed with LILT or controls. It may be partly explained by the fact, that an increase in CRP due to the post-effects of surgery was doubled by accumulation of adenosine triphosphate and reactive oxygen species [11] due to applied laser therapy.

Despite that fact that laser therapy is often viewed in literature as a natural alternative to pharmaceutical treatment [8], we haven't observed significant decrease in serum UA in gout patients prescribed with LILT. Those patients had a lowest mean serum UA after treatment (280.93 ± 97.05 μmol/L), but due to wide range of variation, difference to other groups wasn't statistically significant ($p > 0.05$).

CONCLUSION

Arthroscopic shaving and other surgical approaches focused on joints often doesn't affect system hyperuricemia in any way and can't be viewed as a substitute to urate lowering therapy. However, our experience confirms that timely performed surgery contribute to functional improvement and reduction of pain in gout patients. Low Intensity Laser therapy doesn't affect hyperuricemia or guarantee long-term systemic anti-inflammatory effect, but help to additionally relieve pain in joints and thus enhance treatment effect and quality of patients' life.

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Conflict of interest statement

None of the authors have any conflict of interest regarding this manuscript.

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