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Original

Efficacy of Holmium: Yttrium-aluminium-garnet (Ho: YAG) Laser Therapy for Arthroscopic Synovectomy of Rheumatoid Arthritis

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To clarify the efficacy of holmium: yttrium-aluminium-garnet (Ho: YAG) laser therapy for arthroscopic synovectomy of rheumatoid arthritis (RA), we treated 13 shoulders of 11 RA patients of whom 1 was stage I, 7 stage II, 2 stage III, and 1 stage IV. The duration of RA is 4.6 years on average and the follow-up period is an average of 14 months. The Ho: YAG laser was set at 10 Watt (W) to treat the bone erosion areas so as to reach the deep zones of the pannus in order to resect the synovium. We compared C-reactive protein (CRP), Disease activity score (DAS) 28 and magnetic resonance image (MRI) findings before and after surgery. We cultured primary synovial cells to assay cytokine production of interleukin (IL)-1β, IL-6 and tumor necrosis factor (TNF)-α. Morphological examination was performed after treatment with the Ho: YAG laser at 0, 1, 5, 10, 15 and 20 W. We found villous synovium proliferation with vascularity in the rotator interval and supra spinatus tendon in the shoulder joints. In the subacromial bursa, yellow fat tissue and white fibrous soft tissue were detected in almost all shoulders. After synovectomy using the Ho: YAG laser, CRP decreased from an average of 3.6 to 0.8 and DAS28 also decreased from an average of 5.4 to 3.7 at 14 months after surgery. MRI showed decreased panni with synovium and did not precede joint destruction after 14 months in 10 shoulders out of 13 (77%). At 20 W of the Ho: YAG laser treatment,the synovial cells shrank as in apoptosis and the number of cells also decreased. Laser treatment also resulted in the following significant changes: TNF-α production increased at 1, 10, 15 and 20 W (compared with 0 W) but not dose dependently; IL-1β and IL-6 increased up to 10W (compared with 0W) but decreased at 15 and 20 W (compared with 10 W). In morphological examination, after treatment with the Ho: YAG laser at 15 W, the synovial cells expanded and the number of cells decreased. Therefore, Ho: YAG laser therapy is effective for arthroscopic synovectomy, especially in treating pannus in bone erosion. We used 10 W for 5 seconds in each area where it could effectively decrease pannus formation.

Key words: arthroscopic synovectomy, rheumatoid arthritis, Ho: YAG laser

Introduction

Synovial proliferation plays a critical role in the development of rheumatoid arthritis (RA). Arthroscopic synovectomy is one of the surgical methods to remove synovium by a less invasive procedure. However, the effect of synovectomy is thought to be insufficient by itself recently. The term LASER is an acronym standing for light amplification by stimulated emission of radiation. The atomic theories leading to the discovery of lasers were established by Einstein in 1917[1]. The concept of using laser energy for medical applications dates from the early 1960s, when Theodore Maiman built the first laser and found that a ruby crystal, when stimulated by a flash lamp, emitted red laser light at a specific wavelength of 0.69 μm[2]. This laser was used in ophthalmology for photocoagulation and set the stage for the development of additional laser wavelengths for use in all types of medical applications. Lasers have been used in orthopaedics since the mid-1980s, primarily for arthroscopic procedures[3]. Surgical lasers fall between the longest and shortest wavelengths, in the infrared, visible, and ultraviolet portions of the electromagnetic spectrum.

Table Patients list of Ho-YAG laser treatment of shoulder

cases	gender	age	stage	class	medicine
K.S.	M	34 y	I	II	MTX
H.O. (blt)	F	72 y	III	III	Bu
K.M.	M	77 y	II	III	MTX
S.K.	M	66 y	II	II	PLS
Y.O.	F	50 y	II	II	Bu
K.M.	F	62 y	III	III	MTX, PLS, IFN
A.I.	F	67 y	IV	III	MTX
K.K. (blt)	F	60 y	II	II	MTX, PLS
M.H.	F	66 y	II	II	MTX, ETN
N.O.	M	49 y	II	II	MTX, PLS, IFX
K.S.	F	51 y	II	II	Bu

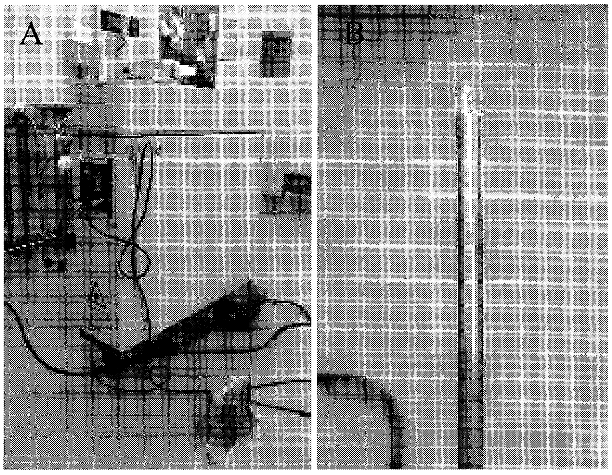

Fig. 1 Ho: YAG laser instruments
A: Ho: YAG laser from NIIC, B: Laser fiber at the tip of Ho: YAG laser.

Today, several surgical lasers are commercially available. The most frequently used medical lasers are the carbon dioxide (CO_2), argon ion, krypton ion, holmium: YAG (Ho: YAG), neodymium: YAG (Nd: YAG), doubled neodymium: YAG (KTP), helium neon (HeNe), visible dye, and excimer laser (XeF, XeCl, KrF, ArF). The Ho: YAG laser emits light at a wavelength of 2.1 μm and can be transmitted through conventional optical fibers. The Ho: YAG laser has the ability to precisely and rapidly resect, cut, coagulate, vaporize and ablate cartilaginous tissues. It causes a minimal amount of thermal necrosis while providing superior hemostatic control[4]. This laser can function in a saline medium and may be used in direct contact with the tissue, however a near contact made with a free beam is typically utilized[5]. In clinical studies, excellent results were reported after performing menisectomy using the Ho: YAG laser. Fanton and Dillinham noted less postoperative pain and swelling with a quicker return to a full range of motion when comparing laser menisectomies to conventional menisectomies[5]. Lane et al also compared the clinical efficacy of the Ho: YAG and CO_2 lasers with that of mechanical techniques in arthroscopic debridement of the knee and reported similar results without statistical significance[6]. However, there is no report about Ho: YAG laser treatment in arthroscopic surgery for RA. Here we used the Ho: YAG laser to treat bone erosion areas to assess whether it is effective for treatment of arthroscopic synovectomy in the shoulders of RA patients.

Patients and Methods

We performed shoulder arthroscopic synovectomy on 13 shoulder joints in 11 patients of RA, including 1 in stage I, 7 in stage II, 2 in stage III, and 1 in stage IV. The disease duration of RA is an average of 4.6 (range, 2.5-13) years and the follow-up period is an average of 14 months. We compared C-reactive protein (CRP), disease activity score (DAS 28) and MRI findings before and after surgery. Those patients who were taking disease-modifying antirheumatic drugs (DMARDs) including methotrexate (MTX) numbered 7, bucillamine 3, steroids 4, infliximab 2 and etanercept 1 (Table) . We used a 4.0-mm arthroscope, VAPR (VAPR; Mitek, Norwood, MA) and a shaver for synovectomy. The Ho: YAG laser was set at 10W to the bone erosion areas so as to reach the deep zones of the pannus in order to resect the synovium (Fig. 1).

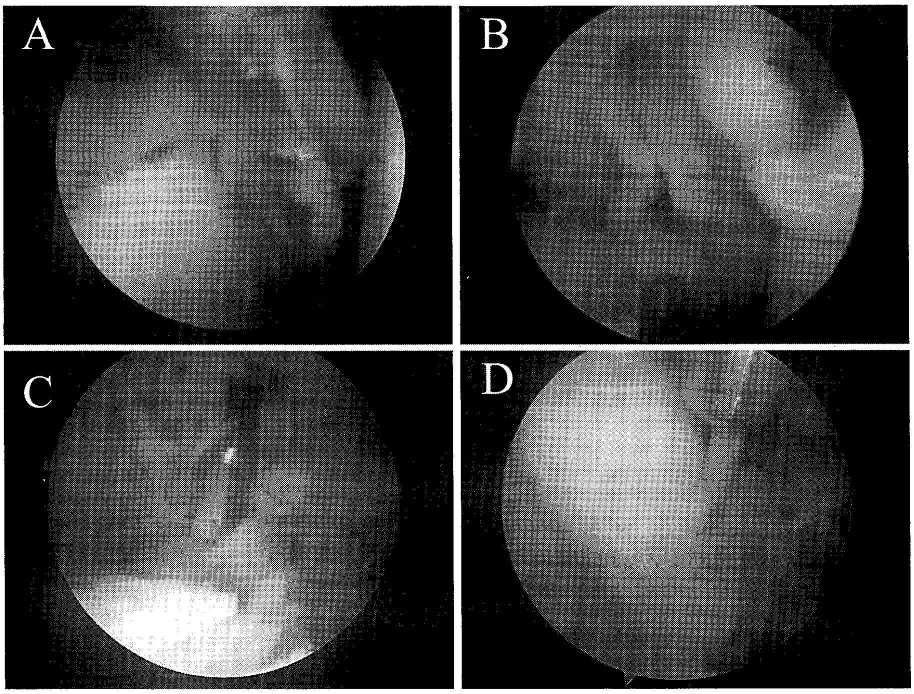

Fig. 2 Arthroscopic finding of a shoulder joint
A: Gleno-humeral joint. B: Synovial proliferation at rotator interval. C: Ho: YAG laser treatment at pannus around bone erosion. D: Ho: YAG laser treatment around limbs of glenoid for synovectomy.

We got informed consent from patients to perform this study.

1. Arthroscopic procedure by using the Ho: YAG laser

After placing the patient in the beach-chair position under general anesthesia, the shoulder was manipulated to assess the range of motion in flexion, external rotation at 0 degrees abduction, external rotation at 90 degrees abduction, and internal rotation at 90 degrees abduction. After introducing the 4-mm arthroscope through a standard posterior portal and performing initial diagnostic arthroscopy, we created an anterior portal just superior to the subscapularis tendon using the outside-in technique in order to facilitate maneuvers by instruments such as the shaver and a radiofrequency instrument. After arthroscopically observing the joint, we moved the scope into the subacromial space via a lateral and antero-lateral portal, shaved the synovium in the subacromial bursa, and carefully observed the rotator cuff. Then, we placed the scope into the gleno-humeral joint to precede the capsular release. We removed the synovium just next to the labrum using the radiofrequency instrument and shaver before using the Ho: YAG laser. Around the labrum on the pannus, we treated the bone erosion and synovial proliferation areas with the Ho: YAG laser at 10 W for 5 seconds after arthroscopic synovectomy (Fig. 2).

2. Postoperative protocol

Passive, assisted-active exercises and a stooping exercise were commenced for forward flexion and external rotation one day after surgery. After 1 week of passive exercise, the patients began active exercise to strengthen the rotator cuff and scapular stabilizers. Three months after the operation, the patients were back on normal work schedules without any limitations to daily activity.

3. Measurement of outcome

All patients were assessed by CRP and DAS 28 preoperatively and a final evaluation was performed at an average of 14 (range, 8-25) months postoperatively. The preoperative and postoperative ranges of motion, including forward elevation (flexion), external rotation, and the highest reach of the thumb behind the back, were assessed at the fi-

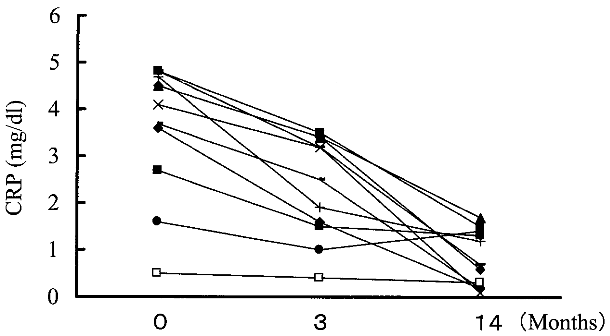

Fig. 3 CRP change after Ho: YAG laser therapy for shoulder

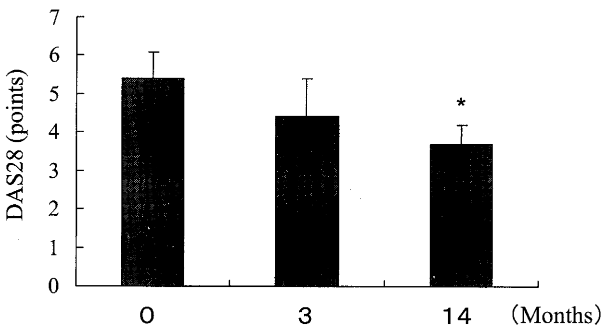

Fig. 4 DAS28 change after Ho: YAG laser therapy for shoulder

nal evaluation.

4. Synovial cell culture and cytokine assay

We primarily cultured synovium cells after arthroscopic synovectomy in 10% FSC DMEM with informed consent. 1×10^4 cells were seeded in 24-well cultured tissue plates over night, then they were treated with the Ho: YAG laser at 0, 4, 10 and 20 W. After culturing for 24 hours, we assayed the production of IL-1β, IL-6 and tumor necrosis factor-alpha (TNF-α) by using ELISA in a cultured supernatant. ELISA kits were used for high-sensitivity TNF-α (range: 0.31-10 pg/ml, Amersham Biosciences; code RPN2788), IL-1β (range: 10-400 pg/ml, Amersham Biosciences, code RPN2751), and IL-6 (range: 10-400 pg/ml, Amersham Biosciences, code RPN2754). Morphological examination of the cells was done after treatment with the Ho: YAG laser at 0, 1, 5, 10, 15 and 20 W by Nikon digital light (DS-2MBWc).

5. Statistical analysis

The changes in CRP and DAS28 were compared using Wilcoxon's signed-rank test. The Mann–Whitney U test was used for continuous variables of cytokine assay by ELISA compared with control. P-value <0.05 was considered significant.

Results

We found villous synovial proliferation with vascularity in the rotator interval and supra spinatus tendon in the shoulder joints (Fig. 2A, B). In the subacromial bursa, yellow fat tissue and white fibrous soft tissue were detected in almost all shoulders. Synovial proliferation was found in bone erosion areas around the glenoid limbs and was treated with the Ho: YAG laser for 5 seconds at 10W for each area (Fig. 2C, D). Ten to 15 areas of synovial proliferation were treated totally in each shoulder joint. Cartilage fibrillation was removed by the shaver to get a smooth surface. After synovectomy using the Ho: YAG laser, CRP decreased from an average of 3.6 to 0.8 and DAS28 also decreased from an average of 5.4 ± 0.7 to 4.4 ± 1.0 at 3 months and to 3.7 ± 0.5 at 14 months after surgery (Fig. 3, 4). Visual analogue scale (VAS) changed from an average of 75.4 ± 0.9 mm before surgery to 44.4 ± 0.8 mm at 3 months and to 23.7 ± 0.5 mm at 14 months after surgery. Therefore, the clinical results were satisfactory with good scores of DAS28 after Ho: YAG laser treatment. In X-ray examination, bone atrophy was improved from 11 shoulders out of 13 (85%) at humeral head and neck lesion (Fig. 5A, B). MRI showed decreased pannus formation with synovial proliferation in 10 shoulders out of 13 (77%). Furthermore, MRI showed no preceding joint destruction at 14 months after Ho: YAG laser treatment in 13 cases (Fig. 5C, D).

In morphological examination of cultured synovial cells, after treatment with the Ho: YAG laser at 15 W, the synovial cells expanded and the number of cells decreased. At 20 W of Ho: YAG laser treatment, the synovial cells shrank as in apoptosis and the number of cells decreased more (Fig. 6). Laser treatment also resulted in the following significant changes: TNF-α production increased at 1, 10, 15 and 20 W (compared with 0 W) but not dose dependently; IL-1β and IL-6 increased up to 10 W (compared with 0 W) but decreased at 15 and 20 W (compared with 10 W) (Fig. 7).

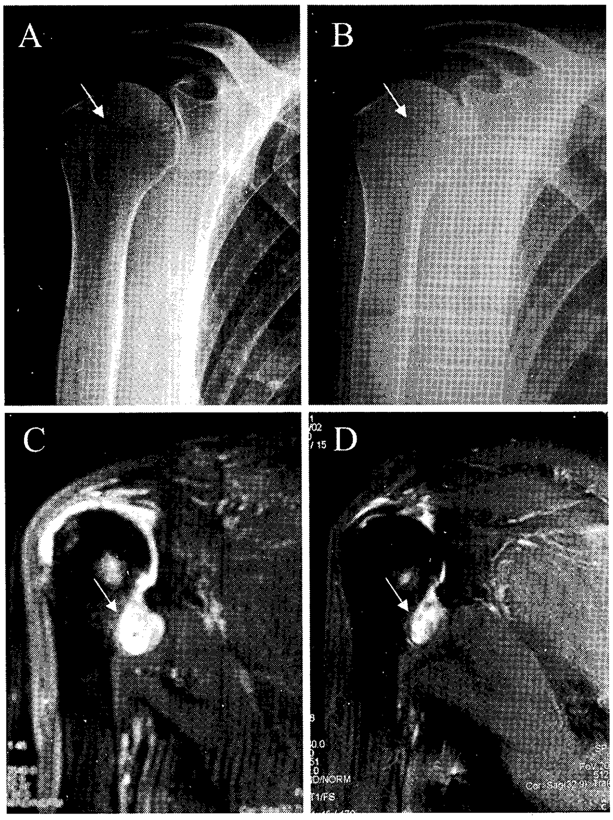

Fig. 5 X-ray examination before (A) and after (B) the Ho: YAG laser treatment. MRI before (C) and after (D) the Ho: YAG laser treatment.

Discussion

The Ho: YAG laser is effective for arthroscopic synovectomy, especially in treating the pannus in bone erosion. The amount of Ho: YAG laser energy needed for synovectomy is still not clear. We used 10 W for 5 seconds in each area where it could effectively decrease pannus formation. Inoue et al reported that cytokine production increases in synovial fibroblasts with the Nd: YAG laser[7]. We will carry out further investigations at basic experimental levels to confirm Ho: YAG laser efficacy in regard to analyzing cytokine production in the synovium. After our treatment, IL-1β and IL-6 increased up to 10 W and decreased gradually from the synovial cells. Therefore, 10 W of Ho: YAG is the turning point to determine stimulation or inhibition of synovial proliferation.

It is reported that early synovectomy results in pain relief and improvement of function, whereas late synovectomy must be regarded as a palliative procedure in order to postpone total knee arthroplasty[8]. Arthroscopic synovectomy provides the advantages of less morbidity and functional impairment. Improvement of the surgical instruments (shaver, radiofrequency instrument) used in arthroscopy has facilitated access to joint compartments, which are difficult to reach using open synovectomy[9)~11)]. Moreover, post surgical fibrosis reduces the range of function, or neuromuscular impairment might be considerably lessened[12].

In orthopedic surgery the CO_2-laser has been used arthroscopically for chondral debridement and meniscal lesions, and for more than 10 years, for the treatment of joint diseases in hemophilia[13]. The disadvantages of CO_2-lasers are mainly due to its fiber optic incompatibility and the high incidence of emphysema. CO_2-laser application has increased with the development of the bubble technique in a fluid medium. Recent experiments compared the biological reaction of meniscal tissue and articular cartilage after using the contact Nd: YAG-laser, scalpel, and electrocauterant lesion[14)15)]. The results showed that Nd: YAG-laser lesions set in saline led to less depth of damage than those set in open air. Defects created by laser radiation resulted in small margins of necrosis with a vigourous healing response of meniscal tissue, whereas necrosis caused by electrocautery was more extensive and increased with time.

In clinical studies on arthroscopic menisectomies the contact Nd: YAG-laser provided good access even to the posterior parts of the meniscus. Postoperatively, there was no significant effusion or pain within the first year of follow-up[15]. Reports on the arthroscopical application of Nd: YAG-laser radiation immediately after mechanical abrasion in synovitis has shown remarkably good results in 15 clinical cases with reduced morbidity, no or minor functional impairment, short rehabilitation periods, and significantly fewer effusions than preoperatively over a 6-month follow-up period[16]. Recently Ho: YAG-lasers were introduced in various experimental and clinical medical applications, e.g., cervical and lumbar discectomy and ophthalmology[17)~20)]. The effects of eximer-, Ho: YAG-, Nd: YAG-, CO_2-laser, and electrosurgical devices on meniscal tissue

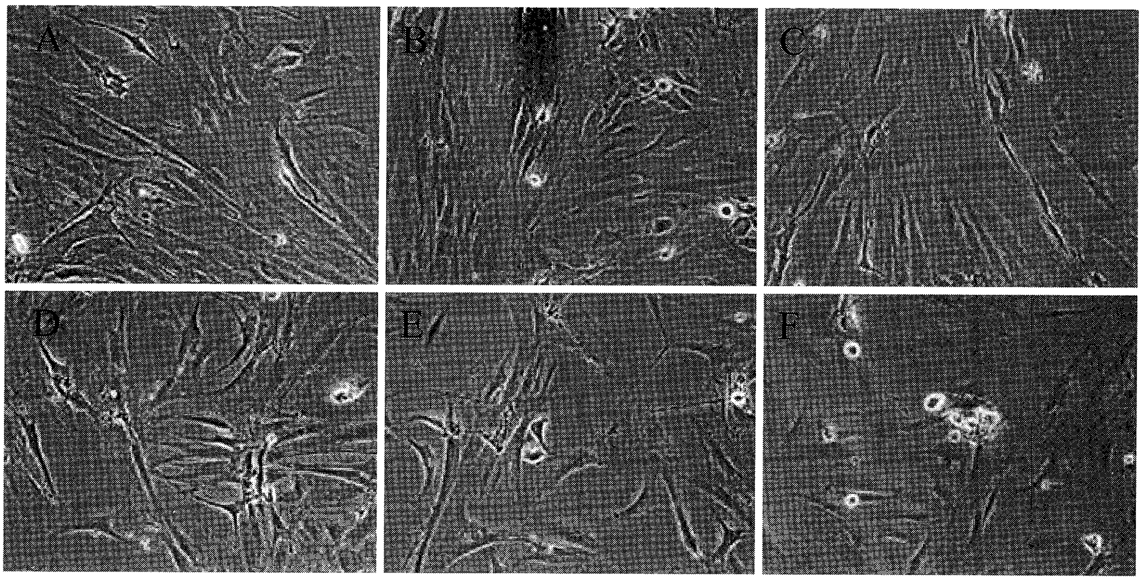

Fig. 6 Morphological examination of synovial cells after treatment with the Ho: YAG laser
A: 0 W, B: 1 W, C: 5 W, D: 10 W, E: 15 W, F: 20 W of Ho: YAG laser.

were compared in an experimental setting. Due to its penetration depth, the Ho: YAG-laser produced zones of necrosis that extended over less than a quarter of the depth of those caused by the contact Nd: YAG-laser. After Ho: YAG-laser radiation, the adjacent pale zones, which were not obviously necrotic, measured only two-thirds of those following Nd: YAG-radiation[21]. After meniscal and cartilage tissue ablation using the Ho: YAG-laser, the residual tissue damage was found to be relatively constant with varying radiant exposure[22]. No significant differences between the Ho: YAG laser and mechanical debridement were found in regard to the complication rate, incidence of postoperative effusions, or time to regain function, but the Ho: YAG-laser proved advantageous in reaching areas of difficult access, thus allowing for shorter operative periods[23].

Synovectomies with the Ho: YAG laser could be an alternative to existing therapeutic techniques in the treatment of rheumatoid arthritis and other synovial proliferate disorders such as synovial chondromatosis or pigmented villonodular synovitis (PVNS)[24]. In an experimental study, Lind et al compared laser synovectomy using the Ho: YAG laser to mechanical synovectomy in the knees of 48 rabbits after inducing chronic arthritis immunologically[25]. In the laser group, edema, acute inflammation, and coagulation necrosis occurred immediately; however, after 1 week, the synovial layer showed slight fibrosis similar to that seen in the control group. One month later, the laser-synovectomized surface appeared to be smooth; in contrast, the mechanical abrasion group had pronounced hemorrhage, necrosis and fibrosis in all capsular layers. At 3 months, the synovial layer of knees in the mechanical abrasion group appeared coarse and villous. The results in the laser group were superior.

In this study, morphological examination of synovial cells revealed that an over dosage of Ho: YAG-laser radiation induced synovial cell death, which may be apoptosis. Therefore over 10 W doses may be useful to decrease synovial proliferation clinically. In cytokine assays, TNF-α did not decreased dose dependently. The reason may be that it is difficult to compare a small range of TNF-α in a supernatant of a cell culture or the synovial number of cells may be too large to compare in this assay. However IL-1β and IL-6 decreased from the synovial after an overdosage. Therefore, inflammation cytokines increased with a low dose of laser radiation and decreased with a high dose with a decrease in cell number. This presumably indicated

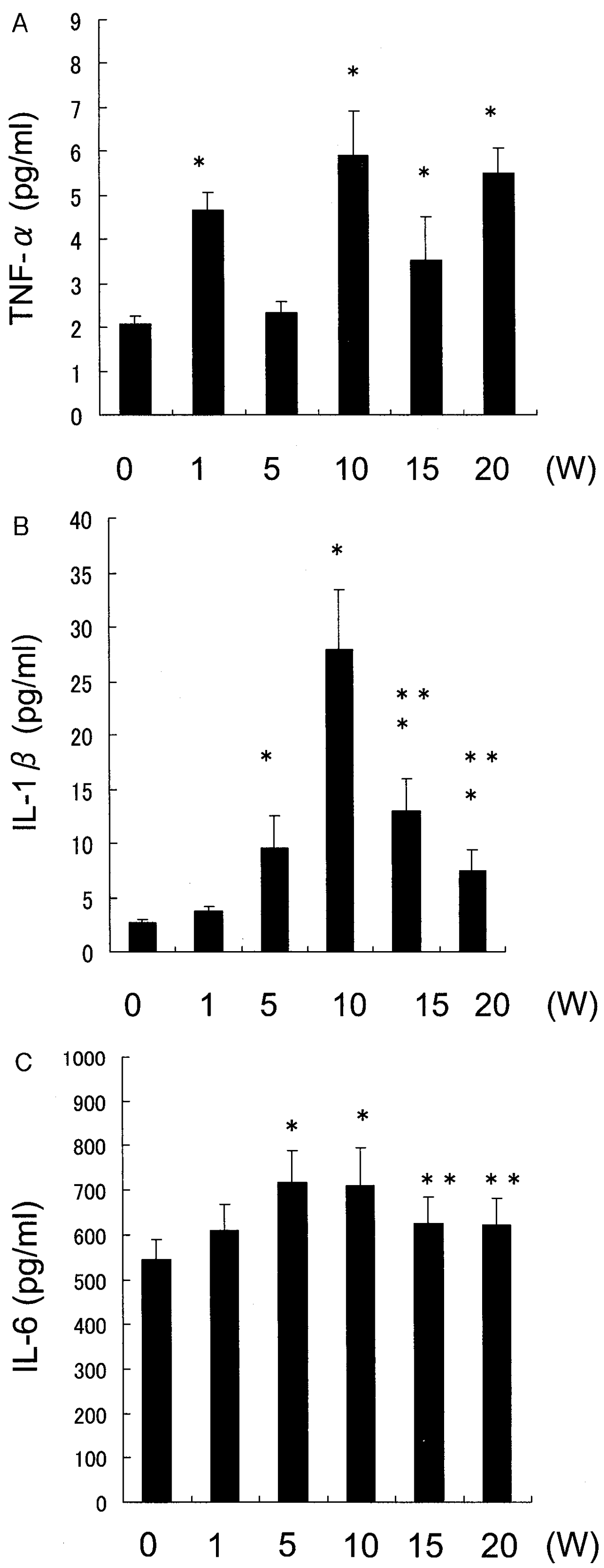

Fig. 7 Cytokine assay by ELISA of supernatant of synovial cells after treatment with the Ho: YAG laser A: TNF-α, B: IL-1β, C: IL-6. * = significant difference compared with 0 W ($p < 0.05$). ** = significant difference compared with 10 W ($p < 0.05$).

that the production of cytokine from each synovial cell increased by laser therapy. Clinically, our data revealed that the Ho: YAG laser is effective in improving bone erosion (by X-ray examination and MRI findings). These results indicated that the Ho: YAG laser might be one of the useful methods to assist arthroscopic synovectomy in RA.

Acknowledgements

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関節リウマチに対する関節鏡視下滑膜切除術における Ho：YAG レーザー治療の効果

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近年，関節リウマチ（RA）の治療においてレーザー治療が行われているが，その効果については明らかではない．RA 患者 11 例 13 肩（stage I　1 例，stage II　7 例 stage III　2 例，stage IV　1 例）に対して関節鏡視下滑膜切除術に Ho：YAG レーザーを使用し，臨床的評価および MRI による評価を行った．RA の平均罹患期間は 4.6 年で経過観察期間は平均 14 ヵ月であった．さらに関節滑膜を初代培養し Ho：YAG レーザーによる影響を細胞の形態学的およびサイトカイン産生を IL-1β，IL-6 および TNF-α について ELISA を用いて調べた．その結果，臨床的評価 DAS28 は術前平均 5.4 から術後平均 3.7 へ低下し，CRP は術前 3.6 から術後 0.8 に低下した．MRI では 13 肩中 10 肩（77%）に滑膜増生の減少を認めた．滑膜細胞の形態は 20W の Ho：YAG レーザーにおいてアポトーシス様縮小を認めた．TNF-α は 20W まで増加を認めた，IL-1β と IL-6 は 15W 以上において低下を認めた．以上より 20W 以上の Ho：YAG レーザーにおいて滑膜細胞障害性が認められた．Ho：YAG レーザーは今後 RA 治療において滑膜細胞増殖を抑制させる手段として発展する可能性がある．