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international magazine of laser dentistry

2²⁰¹⁴



| research

Diclofenac, dexamethasone or laser phototherapy?

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| industry report

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Preview on the 14th WFLD Congress in Paris



Prof. Dr Norbert Gutknecht
Editor-in-Chief

Dear colleagues,

Today, meeting all expectations participants and companies hold towards a congress has become a difficult task. Whereas in previous years, one would have attended a congress in order to expand one's knowledge with new findings, expectations towards congresses today are dominated more and more by its status as an event rather than its educational properties. Of course, both WFLD and the French organisers are open to this idea, but we also want to make sure that the congress features a programme in which the latest laser technologies and many documented case studies are presented and discussed. Of course, problems with regard to the competent integration and amortisation of laser applications in the dental practice are discussed as well.

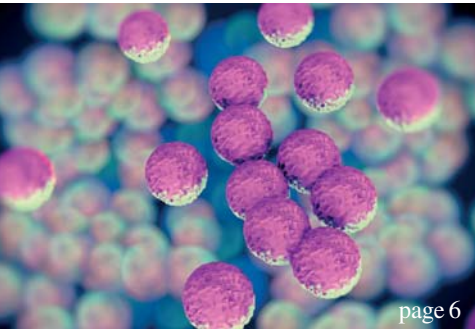
As the upcoming WFLD Congress and the Congress held by the OIWC take place at the same time and place, we came up with special topics including laser applications in implantology and periimplantitis therapy.

Last but not least: Of course, participants will meet other modern, future-oriented colleagues at the WFLD Congress in Paris. Looking forward to seeing you there!

Warm regards,

A handwritten signature in black ink, appearing to read 'N. Gutknecht', written over a light blue horizontal line.

Prof. Dr Norbert Gutknecht
Editor and CEO WFLD



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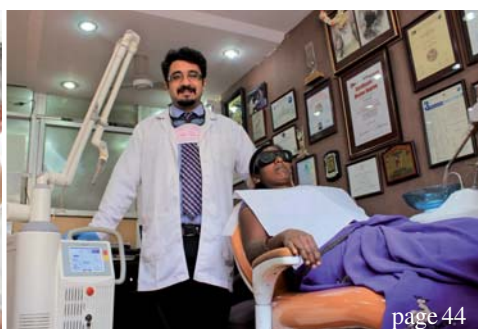
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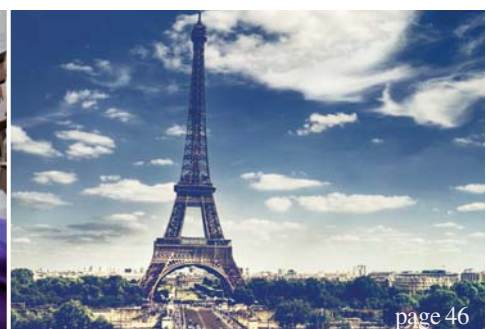
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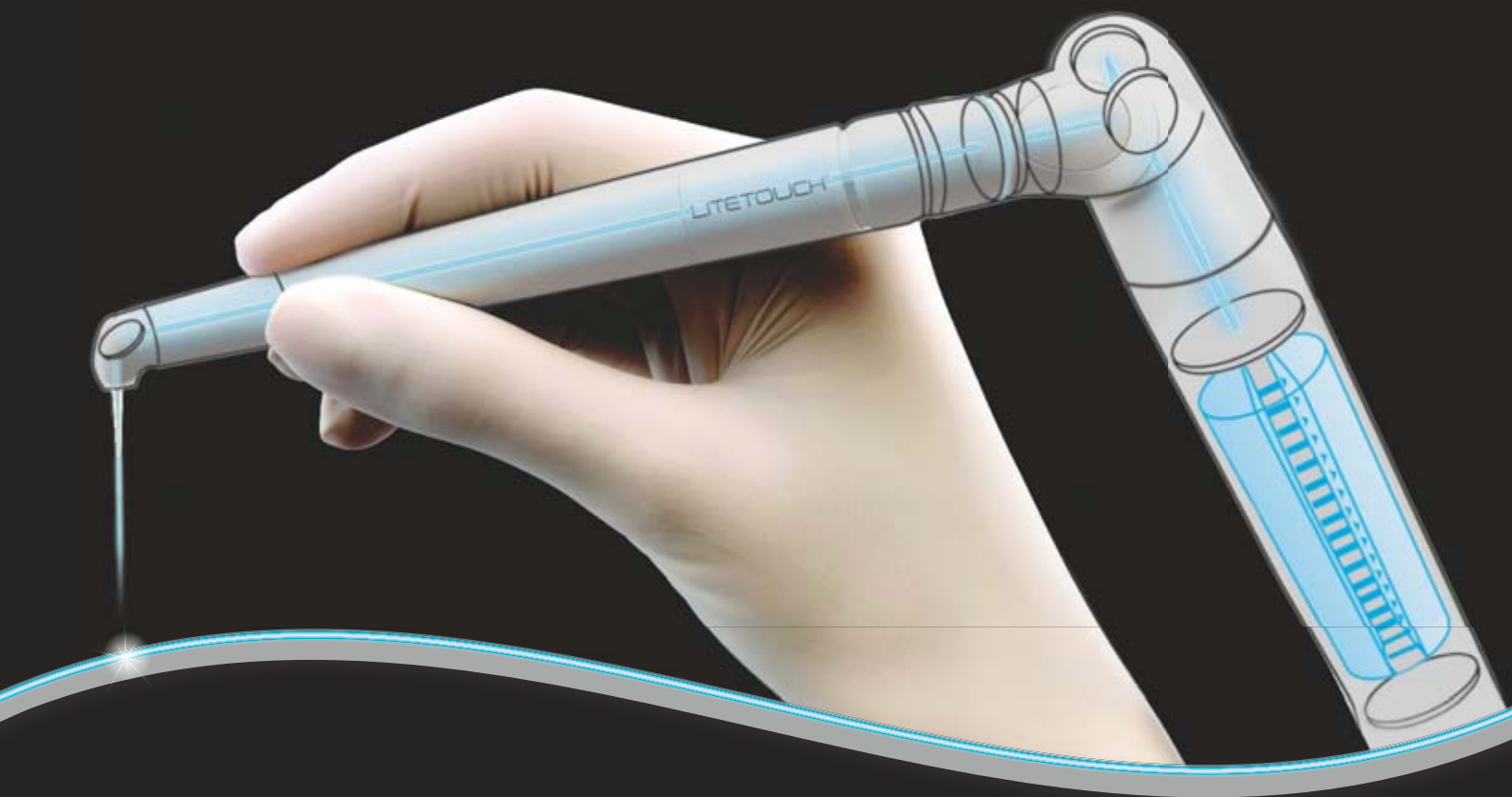
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Diclofenac, dexamethasone or laser phototherapy?

Part II

Author_Jan Tunér, Sweden

[PICTURE: ©ROBERT KNESCHKE]

_Introduction

In part I, the author informed about studies which investigated the effects of diclofenac and LPT. In the second part, they continue their investigation into the vast literature and studies on this topic and give their conclusion.

In the May 2013 edition of *Photomedicine and Laser Surgery*, the editorial written by Prof. Tina Karu is titled "Is it time to consider photobiomodulation as a drug equivalent?" Well, is it? Let us have a look and see what the literature has to say about two very popular drugs. Although the previously-mentioned studies indicate that LPT is as effective, or more effective as diclofenac, a potentiation of the effect of diclofenac by adding LPT is suggested in the following study:

The aim of the study by Markovic¹¹ was twofold: (1) to evaluate the postoperative analgesic efficacy, comparing long-acting and intermediate-acting local anaesthetics; and (2) to compare the use of laser irradiation and the non-steroid anti-inflammatory drug diclofenac, which are claimed to be among the most successful aids in postoperative pain control. A twofold study of 102 patients of both sexes undergoing surgical extraction of LTM

was conducted. In the first part of the study, twelve patients with bilaterally impacted lower molars were treated in a double-blind crossover fashion; local anaesthesia was achieved with 0.5% bupivacaine plain or 2% lidocaine with 1:80,000 epinephrine. In the second part of the study, 90 patients undergoing lower molar surgical extraction with local anaesthesia received postoperative laser irradiation (30 patients) and a preoperative single dose of 100 mg diclofenac (30 patients), or only regular postoperative recommendations (30 patients). The results of the first part of the study showed a strikingly better postoperative analgesic effect of bupivacaine than lidocaine/epinephrine (eleven out of twelve; four out of twelve, respectively, patients without postoperative pain). In the second part of the study, LPT irradiation significantly reduced postoperative pain intensity in patients premedicated with diclofenac, compared with the controls. Provided that basic principles of surgical practice have been achieved, the use of long-acting local anaesthetics and LPT irradiation enables the best postoperative analgesic effect and the most comfortable postoperative course after the surgical extraction of lower molars.

Dexamethasone is a corticosteroid, thus not an NSAID, but the issue of replacing pharmaceuticals



with long-term negative effects to a treatment with no side effect is urgent here as well.

A rabbit model of endophthalmitis was established by Ma¹² to evaluate the anti-inflammatory effect of LPT as an adjunct to treatment for *Staphylococcus epidermidis endophthalmitis*. Rabbits were randomly divided into three groups to receive intravitreal injections into their left eye: group A received 0.5 mg vancomycin (100 µl), group B received 0.5 mg vancomycin + 0.2 mg dexamethasone (100 µl), and group C received 0.5 mg vancomycin (100 µl) and laser irradiation (10 mW, 632 nm) focused on the pupil. Slit lamp examination and B-mode ultrasonography were conducted to evaluate the symptoms of endophthalmitis. Polymorphonuclear cells and tumour necrosis factor alpha (TNF-α) in aqueous fluid were measured at 0 h, and one, two, three, seven and 15 days. A histology test was conducted at 15 days. B-mode ultrasonography and histology revealed that groups B and C had less inflammation than group A at 15 days. Groups B and C had fewer polymorphonuclear cells and lower levels of TNF-α in aqueous fluid than group A at two, three and seven days. There was no significant difference between groups B and C. There was no significant difference between groups A, B and C at 15 days. As an adjunct to vancomycin therapy to

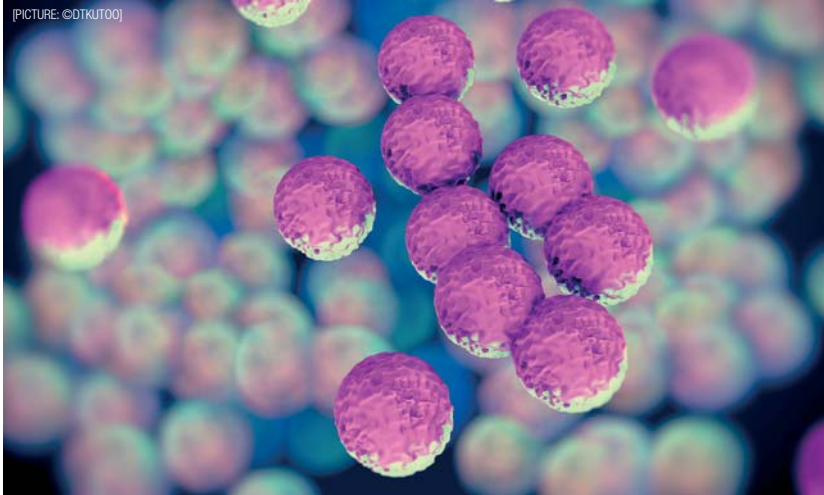
treat *S. epidermidis endophthalmitis*, LPT has an anti-inflammatory effect similar to that of dexamethasone.

Castano¹³ tested LPT on rats that had zymosan injected into their knee joints to induce inflammatory arthritis. The author compared illumination regimens consisting of a high and low fluence (3 and 30 J/cm²), delivered at high and low irradiance (5 and 50 mW/cm²) using 810 nm daily for five days, with the positive control of conventional corticosteroid (dexamethasone) therapy. Illumination with a 810 nm laser was highly effective (almost as good as dexamethasone) at reducing swelling, and a longer illumination time (10 or 100 minutes compared to 1 minute) was more important in determining effectiveness than either the total fluence delivered or the irradiance. LPT induced reduction of joint swelling correlated with reduction in the inflammatory marker serum prostaglandin E2 (PGE2).

Reis¹⁴ investigated the role of extracellular matrix elements and cells during the wound healing phases following the use of LPT and anti-inflammatory drugs. Thirty-two rats were submitted to a wound inflicted by a 6-mm-diameter punch. The animals were divided into four groups: sham treated, those treated with the LPT (4 J/cm², 9 mW, 670 nm), those treated with dexamethasone (2 mg/kg), and those treated with both LPT and dexamethasone. After three and five days, the cutaneous wounds were assessed by histopathology using polarised light and ultrastructural assessments by transmission electron microscopy. Changes seen in polymorphonuclear inflammatory cells, oedema, mononuclear cells, and collagen fibre deposition were semi-quantitatively evaluated. The laser-treated group demonstrated increased collagen content and better arrangement of the extracellular matrix. Fibroblasts in these tissues increased in number and were more synthetically active. In the dexamethasone group, the collagen was shown to be non-homogenous and disorganised, with a scarcity of fibroblasts. In the group treated with both types of therapy, fibroblasts were more common and they exhibited vigorous rough endoplasmic reticulum, but they had less collagen production compared to those seen in the laser group. Thus, LPT alone accelerated post-surgical tissue repair and reduced oedema and the polymorphonuclear infiltrate, even in the presence of dexamethasone.

In a study by Jajarm¹⁵ thirty patients with erosive-atrophic OLP were randomly allocated into two groups. The experimental group consisted of patients treated with the 630 nm laser. The control group consisted of patients who used dexamethasone mouth wash. The response rate was defined

[PICTURE: ©DTKUT00]



based on changes in the appearance score and pain score (VAS) of the lesions before and after each treatment. Appearance score, pain score, and lesion severity was reduced in both groups. No significant differences were found between the treatment groups regarding the response rate and relapse. The study demonstrated that LPT was as effective as topical corticosteroid therapy without any adverse effects and it may be considered as an alternative treatment for erosive-atrophic OLP in the future.

The aim of a study by Aimbire¹⁶ was to investigate if LPT can modulate the formation of haemorrhagic lesions induced by immune complex, since there is a lack of information on LPT effects in haemorrhagic injuries of high perfusion organs, and the relative efficacy of LPT compared to anti-inflammatory drugs. A controlled animal study was undertaken with 49 rats, randomly divided into seven groups. Bovine serum albumin i.v. was injected through the trachea to induce an immune complex lung injury. The study compared the effect of irradiation by a 650 nm laser with doses of 2.6 J/cm² to celecoxib, dexamethasone, and control groups for haemorrhagic index (HI) and myeloperoxidase activity (MPO) at 24 h after injury. The HI for the control group was 4.0. Celecoxib, laser, and dexamethasone all induced significantly lower HI than in the control animals at 2.5, 1.8 and 1.5, respectively. Dexamethasone, but not celecoxib, induced a slightly, but significantly lower HI than laser. MPO activity was significantly decreased at 1.6 in groups receiving celecoxib at 0.87, dexamethasone at 0.50, and laser at 0.7 when compared to the control group, but there were no significant differences between any of the active treatments. In conclusion, LPT at a dose of 2.6 J/cm² induces a reduction of HI levels and MPO activity in haemorrhagic injury, which is not significantly different from that obtained by celecoxib. Dexamethasone is slightly more effective than LPT in reducing HI, but not MPO activity.

In an effort to clarify the molecular based mechanism of the anti-inflammatory effects of laser irradiation, Abiko¹⁷ used a rheumatoid arthritis (RA) rat model with human rheumatoid synoviocytes (MH-7) challenged with IL-1, treated with laser or dexamethasone (DEX), monitored by gene expressions and analysed by the signal pathway database. RA rats were generated by the immunisation of type-II collagen, after which foot paws and knee joints became significantly swollen. The animals were laser treated and the swelling rates measured. MH-7 was challenged with IL-1 β and gene expression levels monitored, using the Affymetrix Gene Chip system, and the signal pathway database analysed using the Ingenuity Pathway Analysis (IPA) tool. LPT significantly reduced swellings in the rats' foot paws and knee joints and made it possible for them to walk on their hind legs. LPT altered many gene expressions of cytokines, chemokines, growth factors and signal transduction factors in IL- β induced MH-7. IPA revealed that LPT as well as DEX kept the MH7A at a normal state to suppress mRNA levels of IL-8, IL-1 β , CXCL1, NF κ B1 and FGF13, which were enhanced by IL-1 β treatment. However, certain gene expression of inflammatory factors were reduced by LPT, but were enhanced by DEX. LPT reduced inflammatory factors through altering signal pathways by gene expression levels. Interestingly, LPT altered useful targeted gene expressions, whereas DEX randomly altered many gene expressions, including the unwanted genes for anti-inflammation. Dexamethasone is a steroid known for having a long range of serious side effects. Thus, genome-based gene expression monitored by the Gene Chip system together with a signal pathway based database provide unprecedented access to elucidate the mechanism of the biostimulatory effects of LPT.

It has been suggested that LPT acts on pulmonary inflammation. Thus, Mafrade Lima¹⁸ investigated in a work if LPT (650 nm, 2.5 mW, 31.2 mW/cm², 1.3 J/cm², spot size of 0.08 cm² and irradiation time of 42 s) can attenuate oedema, neutrophil recruitment and inflammatory mediators in acute lung inflammation. Thirty-five male Wistar rats (n = 7 per group) were distributed in the following experimental groups: control, laser, LPS, LPS+laser and dexamethasone+LPS. Airway inflammation was measured 4 h post-LPS challenge. Pulmonary microvascular leakage was used for measuring pulmonary oedema. Bronchoalveolar lavage fluid (BALF) cellularity and myeloperoxidase (MPO) were used for measuring neutrophil recruitment and activation. RT-PCR was performed in lung tissue to assess mRNA expression of tumour necrosis factor-alpha (TNF-alpha), interleukin-1 β (IL-1 β), interleukin (IL-10), cytokine-induced neutrophil chemoattractant



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