Analgesic Therapy of Rheumatoid Arthritis Part II: A Study of Combined Allopathic and Homeopathic Therapy

Enno Freye, M.D. and Leo Latasch

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Abstract

Nonsteroidal anti-inflammatory drugs are used in the allopathic treatment of the pain of rheumatoid arthritis, but in many cases severe adverse effects prevent their long-term use. This article discusses several therapeutic alternatives that reorganize and reactivate the immunological assistance reaction instead of suppressing the patient's immune system: Indian frankincense (olibanum), the homeopathic preparations Traumeel® S and Zeel® (used in combination with the local anesthetic ropivacaine to block pain), and high doses of vitamins C and E.

Thirty patients with long histories of rheumatic disease were closely monitored as they underwent therapy that combined several different means of administering Traumeel® S and Zeel® with ropivacaine or vitamins C and E. Patient assessments of severity of pain during movement, degree of restriction of movement, and general level of well-being were recorded before and after each treatment. Over the course of treatment, gradual improvement was noted and standard allopathic therapy was reduced or eliminated.

Although the therapy described in this article cannot completely cure rheumatoid arthritis, it offers a valuable alternative approach that is free of adverse effects. In addition, a better understanding of the mechanisms of rheumatic pain and inflammation may lead to better therapies with fewer adverse effects.

Alternative Therapies for Rheumatoid Arthritis

I. Phytotherapy

Many patients with rheumatoid arthritis request treatment with plant remedies, especially since conventional treatment fails to provide long-term relief and its adverse effects outweigh the benefits. A number of phytopharmaceuticals can be used to treat chronic pain in the musculoskeletal system. For rheumatic disorders in particular, extracts of Indian frankincense (*Boswellia serrata resin*, also known as olibanum) offer an alternative with a very low rate of adverse effects. According to scientific studies, olibanum inhibits cyclooxygenase and 5-lipooxygenase, resulting in both analgesic and anti-inflammatory effects.[1] Absence of adverse effects is the main advantage of this traditional ayurvedic medication (H15®, Olebanum RA), used primarily in long-term treatment of rheumatoid arthritis. The anti-inflammatory properties of the *Boswellia* acids in olibanum have been confirmed not only in animal experiments but also in initial clinical trials. Approximately 60%-70% of patients given *B. serrata* experienced reductions in pain, swelling, and joint stiffness.[2] At present, the effective mechanism appears to be noncompetitive inhibition of leukotriene synthesis, which plays an active role in chronic inflammation.

II. Homeopathic Combination Preparations

Homeopathic remedies are another valuable component of any rheumatoid arthritis therapy that seeks to minimize or avoid adverse effects. These medications have long-lasting effects when applied directly to the site of the inflammation via local injection. The composition of two combination preparations, Traumeel® S and Zeel® makes them especially suitable for local application (Table 1). Both of these formulas are compatible with local anesthetics and can thus be administered by injection directly into the affected joint or by other parenteral methods that deliver them to the site of the inflammation in sufficiently high levels to be effective in the acute stage of the disease (which is not the case if they are administered orally). To optimize the effect, parenteral administration is repeated twice weekly, alternating injections of Traumeel® S and Zeel®.

Traumeel® S	• Arnica, calendula, hamamelis, millefolium, belladonna, aconitum, mercurius solubilis hahnemanni, hepar sulfuris, chamomilla, symphytum, bellis perennis, echinacea angustifolia, echinacea purpurea
Zeel®	• Toxicodendon quercifolium, arnica montana, solanum dulcamara, sanguinaria canadensis, sulfur

Table 1: Ingredients of the homeopathic combination preparations Traumeel® S and Zeel® used in treating inflammatory rheumatic disorders

Zeel® and Traumeel® S are thought to work by regulating the release of free oxygen radicals that takes place during all inflammatory processes, by activating neutrophilic granulocytes, and by suppressing mediators (prostaglandins in particular) involved in inflammation.[3] More recent studies suggest that their efficacy is based on an immunological assistance reaction in which homeopathic antihomotoxic medications help the immune system revert to a lower level of reactivity and increase its tolerance of foreign bodies.[4] In effect, the body reverts to the postnatal state of tolerance of foods and certain pathogens, and the immune system intervenes only when necessary to support healing.[5]

III. Orthomolecular Therapy of Rheumatoid Arthritis

In addition to treatment with plant-based homeopathic preparations, our patients were given antioxidants (1000 mg of vitamin C and 800 mg of vitamin E intramuscularly) to strengthen and "reprogram" the immune system.[6,7] The assumption that adequate amounts of vitamin E must be present to optimize immune response is confirmed by the observation that in outwardly healthy patients, cell-mediated immunity is enhanced by supplementation with high doses of vitamin E.[8-10]

Experimental Therapy Combining Vitamins and Plant-based Homeopathic Remedies

To date, our investigation has included 30 patients who received alternative therapy for rheumatoid arthritis. The average age of these patients was 56.6 years (SD, 13.4 years) with an average duration of illness of 10.1 years (SD, 11.7 years). The number of female patients (n = 21) was significantly greater than the number of males (n = 9) (Figure 1).

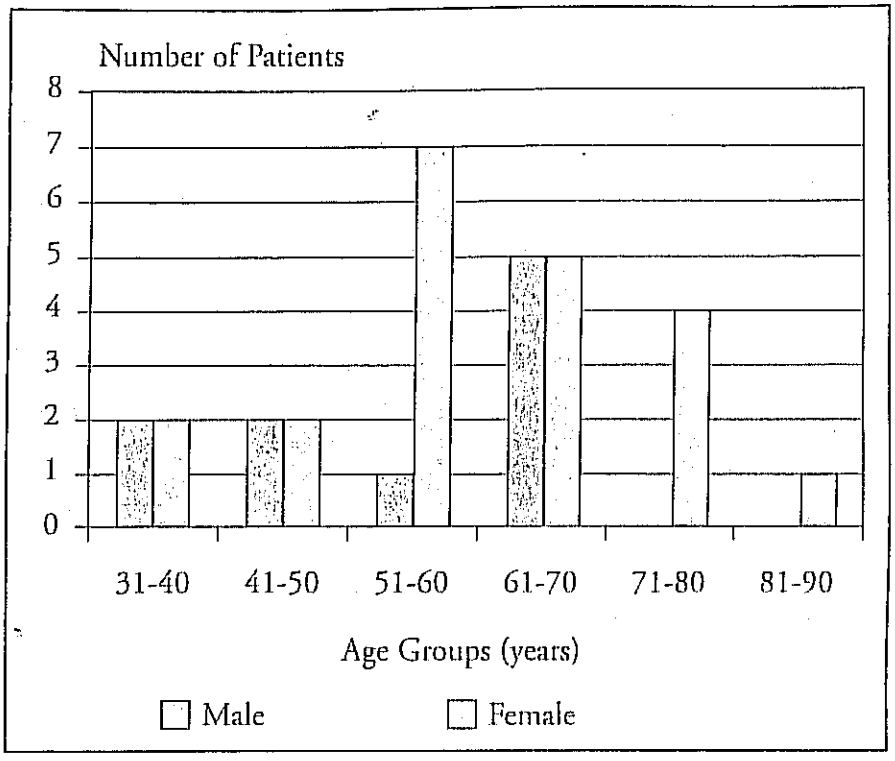

Figure 1: Age and gender distribution of the patients treated for rheumatoid arthritis (N = 30)

These patients, who presented with classic symptoms of rheumatoid arthritis, rheumatic pain, and inflammation, were given a combined therapy of vitamin C, vitamin E, and plant-based homeopathic medications. (This protocol, proven to be a viable alternative to standard therapy for rheumatoid arthritis, was selected for its low rate of adverse effects. For example, it entails no risk of gastrointestinal hemorrhaging or renal adverse effects. Nerve-block injections were administered concurrently to relieve acute pain and to prevent sensitization and the development of chronic pain syndrome). Our goal was not only to promote short-term pain reduction during the acute phase but also long-term improvement in the patients' general level of well-being. In addition, we attempted to gradually reduce or even eliminate the patients' baseline dosages of cortisone, gold, and/or methotrexate.

The 30 patients, who sought more effective or alternative treatment due to persistent pain or excessive adverse effects of current medication and a resulting decline in quality of life, were thoroughly informed about the study before receiving treatment of at least five weeks' duration (two treatments per week) according to the following protocol:

1. Targeted administration of Traumeel® S or Zeel® (one ampule) combined with 2-5 mL (2-10 mg) of the local anesthetic ropivacaine (Naropin®).
2. Administration of 1000 mg of vitamin C and 800 mg of vitamin E administered concurrently with one ampule of Traumeel® S or Zeel® (in alternation).
3. For broad-based pain, nerve block injections of 2-5 mL, or 2-10 mg, of ropivacaine combined alternately with one ampule of Traumeel® S or Zeel®
4. Injection of one ampule of Traumeel® S or Zeel® into existing rheumatic nodules.

Before and after each treatment, patients were questioned about pain during movement, degree of restriction

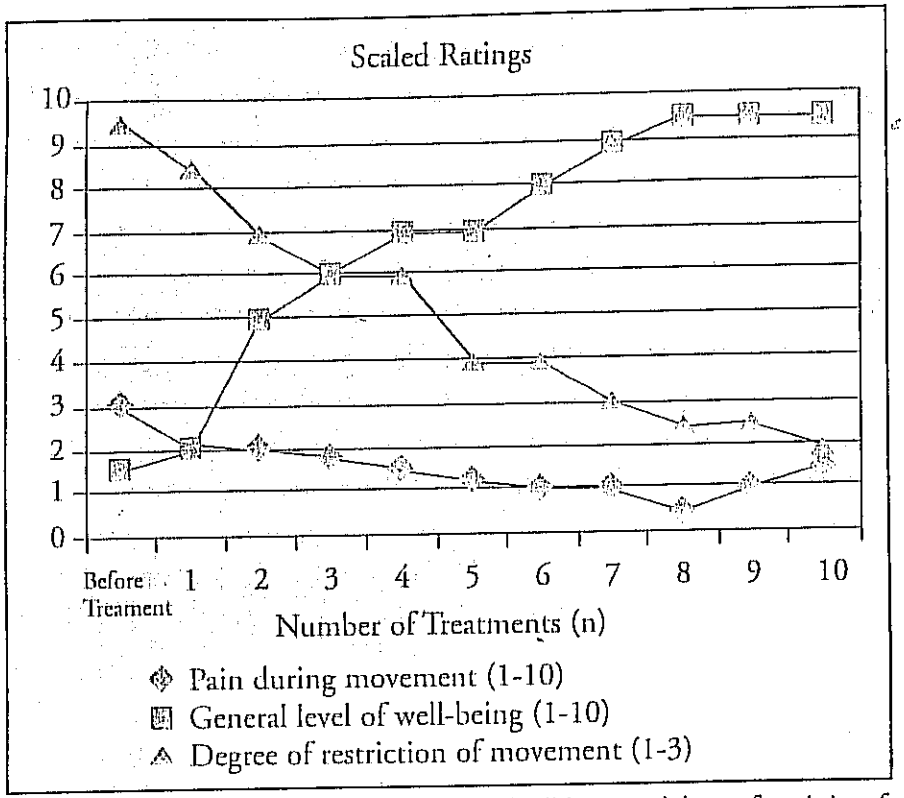

Figure 2: Averaged values for pain, general level of well-being, and degree of restriction of movement in patients with Rheumatoid Arthritis (N = 30) during therapy with plant-based homeopathic preparations, high doses of Vitamins C and E, and nerve-block injections

of movement, and general level of well-being. The first two criteria were rated on a visual analog scale of 0 to 10 (0 = no pain or good subjective condition; 10 = extreme pain or very poor subjective condition). Restriction of movement was rated on a scale of 1 to 3 (1 = slight, 2 = moderate, 3 = severe).

As the treatments continued, decreases in pain were noted along with slow but steady improvements in the patients' level of well-being and degree of restriction of movement (Figure 2).

Discussion

For use in this study, we selected ropivacaine, one of the new generation of local anesthetics, because it offers a broader range of therapeutic applications and has longer lasting effects than other well-known local anesthetics such as lidocaine and bupivacaine.

The patients had been suffering from rheumatoid arthritis for an average of 10 years and were therefore highly motivated. The primary purpose of therapy was to relieve acute pain to prevent the development of chronic pain syndrome ("pain memory").[2] Long-term objectives were to decrease pain-triggering inflammation and to improve the patients' general level of well-being. A secondary objective (to be achieved over a period of weeks or months) was to reduce or eliminate the patients' baseline dosages of cortisone, methotrexate, or gold. Despite the rapid improvement in general well-being that was observed in individual cases, the patients' dosages of standard allopathic medications, especially cortisone, were reduced only gradually to prevent acute flare-ups of the disease.

In almost all cases, the combined therapy described here resulted in clear reduction in pain and improvement in mobility and general well-being. We successfully reduced the dosages of drugs the patients had been taking previously, immediately eliminating all medications (nonsteroidal anti-inflammatory drugs, methotrexate, and/or acetaminophen) associated with severe adverse effects. Cortisone dosages were reduced over a period of weeks to a low dosage of 2-4 mg/d or even eliminated in some cases. (Depending on the original dosage, discontinuing cortisone may require months because the body needs time to boost endogenous cortisone synthesis.)

We must emphasize that the therapy described here cannot cure rheumatoid arthritis. The disease remains active, although to a lesser extent, even though its symptoms are reduced. Until the actual trigger of rheumatic processes is discovered, the goal of therapy is simply to reduce symptoms. For this reason, patients appreciate forms of treatment with minimal adverse effects. Appropriate medication not only reduces pain but also improves mobility. While the therapy described here accomplishes symptom reduction in the short term, only continued investigation over longer periods will show whether it can be maintained for the long term.

The Role of Peripheral Opioid Receptors in Rheumatic Pain: Prospects for Future Therapies

Although nociceptors, the terminal structures of peripheral sensory nerves, are sensitive to prostaglandins and other mediators, they are not specially evolved receptor organs, but simply nerve endings that are stimulated even by pressure. In chronic irritation such as that of rheumatoid arthritis, however, these nerve endings function as opiate receptors. A test system involving chronic inflammation in rat paws has shown that such peripheral opiate receptors are also involved in pain transmission.[12,13] In the experimental animals, pain triggered by

- In chronic inflammation, opiate receptors form on peripheral nerves.
- T and B lymphocytes and monocytes are the source of the endogenous ligands that bind to the opiate receptors.
- The endogenous ligands enkephalin and dynorphin are formed from proenkephalin and prodynorphin, respectively.
- In inflamed tissue, dynorphin increases more than any other endogenous ligand.

Table 2: The interaction of endogenous opioid-like substances with newly formed peripheral opiate linkage sites in a test model of inflammation

the specific antagonist naloxone was suppressed by opioids. The development of new, specific opioid linkage sites is mediated by peripheral opiate receptors, as demonstrated by immunohistochemical activity in inflammation in the animal model. The discovery of these newly formed linkage sites and the specific ligand involved, a dynorphin type, may prove significant in developing new medications.[14] During inflammation, immune cells release opioid-like peptides that bind to the peripheral receptors of sensory nerves in the synovial membranes, thus inhibiting pain due to inflammation. An obvious next step is to apply these findings to patients with rheumatoid arthritis.

New peripheral opioid linkage sites develop in chronic inflammations as well as in rheumatic diseases, supplying the prerequisite for the development of opiate-like receptors. Such opiate receptors have been found on inflamed tissue, immune cells (lymphocytes, mast cells, monocytes), and peripheral sensory nerves, which also initiate the formation of endogenous opioid peptides (Table 2). The analgesic effect can be explained by the fact that inflamed cells always release peptides (such as interleukin 8) with opioid-like effects. The prerequisite to a peripheral opioid effect, however, is always prior inflammation, which is substantially involved in the development of peripheral opiate linkage sites. Analgesic effects are then triggered via such linkage sites. Whether they are also triggered by local inhibition of prostaglandin synthesis is unknown.

Initial results of animal experiments have proved that asimadoline (EMD 61753) and U50.488H have anti-inflammatory effects.[15-17] The κ-subclass of opiate receptors plays a central role in pain due to inflammation, as is evident not only from the increased concentration of dynorphin in cell layers below the inflammation but also from the fact that in the animal model of inflammation, the cells that developed, even in the spinal cord, were primarily afferent, pain-transmitting neurons. Such changes strongly suggest that sensitization of the central nervous system plays a role in the development of chronic pain in joint inflammation. Because formation of κ-linkage sites and their endogenous ligands increases as a result of inflammation due to rheumatoid arthritis, it may be possible to develop selective, peripherally active drugs that not only control pain but also effectively treat inflammation.

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For the authors:

c/o Enno Freye, M.D.
Pain Therapy Center
Graf-Adolf-Straße 16
D-40212 Düsseldorf
Germany