

Controversy: Hirudotherapy (Leech Therapy) as an Alternative Treatment for Osteoarthritis

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ABSTRAK

Osteoarthritis (OA) merupakan penyakit sendi degeneratif tersering pada usia lanjut. Pilihan obat yang direkomendasikan oleh American Academy of Orthopaedic Surgeon (AAOS) adalah asetaminofen, OAINS, tramadol, capsaicin dan kortikosteroid intraartikular. Meskipun demikian, sejumlah efek samping akibat pemakaian jangka panjang obat tersebut cukup mengkhawatirkan. Para peneliti saat ini sedang mencari modalitas terapi yang lebih aman untuk OA. Terapi lintah (hirudoterapi) merupakan salah satu terapi yang sedang diteliti mengingat sifat analgesik dan anti-inflamasi yang dimilikinya.

Kata kunci: osteoarthritis, hirudoterapi, terapi lintah, OAINS, usia lanjut, terapi alternatif.

ABSTRACT

Osteoarthritis (OA) is the most common degenerative joint disease found in the elderly. Drug options that are recommended by the American Academy of Orthopaedic Surgeon (AAOS) are acetaminophen, NSAIDs, tramadol, capsaicin and intraarticular corticosteroids. However, there is concern for the possible side effects resulting from long term use of those medications. Researchers are searching for a safer treatment modality for OA. Leech therapy (hirudotherapy) is one of the therapies under investigation, given its purported analgesic and antiinflammatory properties.

Key words: osteoarthritis, hirudotherapy, leech therapy, NSAIDs, elderly, alternative therapy.

INTRODUCTION

Osteoarthritis (OA) is the most common degenerative joint disease found in the elderly. This disease is characterized by articular cartilage degeneration, peripheral bone hypertrophy and synovial membrane changes. Common symptoms are joint pain after activity and stiffness after periods of immobility, including sleep.¹ Therapeutic approaches to OA involve

both physiotherapy and pharmacotherapy, but the use is limited by expense and side effects.² Pharmacologic therapies recommended by the ACR (American College of Rheumatology) and the AAOS (American Academy of Orthopaedic Surgeons) include acetaminophen, oral and topical NSAIDs (Non-steroidal Anti-Inflammatory Drugs), tramadol, capsaicin and intra-articular corticosteroids.^{3,4} Additionally, they recommended

physical activity, thermal therapy and joint support devices.³ Recent research showed Hirudotherapy (leech therapy) could reduce pain from knee OA.^{2,5} It has been proposed that Hirudotherapy has better efficacy and a favorable side-effect profile compared to NSAIDs.⁶ This review aims to describe the use of Hirudotherapy as an alternative therapy for OA.

OSTEOARTHRITIS

Osteoarthritis (OA) is the most common arthritis, affecting one in five US adults. It is particularly problematic source of disability among the elderly, afflicting 49.7% of US persons >65 years old. The magnitude of this problem is expected to increase commensurate with the global increase in the elderly (>65 years) population. In the US alone, elders are projected to comprise 19% of the population by 2030, at which time 67 million cases of OA are anticipated among US adults >18 years old.^{7,8}

The objectives of OA management are pain relief and optimization of physical activity. Comprehensive OA management is multimodal, including pharmacologic and non-pharmacologic therapy.

Non-pharmacologic Therapy

Non-pharmacologic therapies recommended by the AAOS (American Academy of Orthopaedic Surgeons) are joint enhancement programs, joint sparing aerobic sports, neuromuscular education and weight loss for overweight patients (BMI ≥ 25).⁴

Pharmacologic Therapy

Drugs that are recommended by the AAOS are acetaminophen, oral and topical NSAIDs, tramadol, capsaicin and intra-articular corticosteroids for symptomatic patients.⁴

Prompted in part by the side effects of long term NSAID use, researchers are investigating leech therapy (hirudotherapy) as an alternative treatment for OA. Leech saliva has analgesic and anti-inflammatory substances which may be beneficial.^{9,10}

COMPOSITION OF LEECH SALIVA

Various components of leech saliva may have potential for clinical application, given

their anticoagulant and antimicrobial properties.¹¹ Leech saliva has activity against *E. coli*, *P. aeruginosa*, *B. cereus*, *S. Typhi* and *S. Aureus* and the fungi *C. albicans* and *C. neoformans*. Leech saliva also has analgesic and anti-inflammatory substances which may be useful for OA treatment.

Some of components of leech saliva are shown in **Table 1**.¹²

ANALGESIC PROPERTIES OF LEECH SALIVA

Several studies showed analgesia from Hirudotherapy is superior to that from natrium diclofenac.⁶ There are multiple suggested means by which leech saliva may effect analgesia. As detailed in **Table 1**, several substances in leech saliva have properties which together may contribute to analgesia, including hirudin (thrombin inhibitor), histamine-like vasodilator, kalikrein, triptase and other proteinase inhibitors, and hyaluronidase.^{9,13–17}

A second hypothesis is leech saliva could reduce pain through antinociceptive effects.⁶ One study found that hirudin can inhibit platelet derived growth factor (PDGF), a factor involved in pain induction.¹⁸

Another hypothesis proposes that joint inflammation (and consequently pain) could be reduced by the anti-inflammatory action of bdellins and eglins in leech saliva. Leech saliva also contains hirudin-, calin-, and destabilase-like substances that increase microcirculation by decreasing blood viscosity. By decreasing inflammation and increasing microcirculation, joint stiffness and restriction may decrease.⁹

CONTRAINDICATIONS, SAFETY AND COMPLICATIONS OF HIRUDOTHERAPY

Contraindications to Hirudotherapy include blood coagulation disorders, severe anemia, allergy to leech saliva, pregnancy and frailty. A patient's bleeding and clotting times must be established as normal prior to initiating hirudotherapy.^{19–23}

Infection is the most common complication of Hirudotherapy, affecting 2–36% of patients.²⁴ Common bacteria encountered are *Aeromonas spp.*, *Pseudomonas spp.* and *Vibrio spp.* We recommend preventive treatment with oral antibiotic prophylaxis.²⁵

Other reported complications are a range of local hypersensitivity reactions, described as mild itching, blister formation, ulcerative necrotic lesion, and/or local tissue destruction.^{6,10} Some patients also reported prolong bleeding or persistent skin lesions from incomplete healing at the leech attachment site.²⁴

HIRUDOTHERAPY FOR OSTEOARTHRITIS: CURRENT EVIDENCE

A systematic review and meta-analysis regarding the use of Hirudotherapy for knee OA done by Lauche R, et al.² from three randomized control trials (RCT) and one non-randomized clinical control trial (CCT), showed moderate to strong evidence for the reduction of pain, functional impairment and joint stiffness after hirudotherapy of 237 patients with knee OA.²

An RCT by Michalsen A, et al.⁹ showed significant reductions in pain and stiffness, as well as improved joint function.⁹ Among 51 patients with knee OA, 24 received 4-6 sessions of leech therapy, while 27 patients were given topical diclofenac for 28 days. This research showed on day-7 of treatment pain in leech therapy group was decreased from average score 53.5 +/- 13.7 (+/-SD) unto 19.3 +/- 12.2 (+/-SD), while pain reduction from topical diclofenac

use decreased from 51.5 +/- 16.8 (+/-SD) unto 42.4 +/- 19.7 (+/-SD) [95% CI, -32.8 to -15.1]; $P < 0.001$). However, further follow-up revealed no significant pain difference between leech therapy and topical diclofenac arm.⁹ This result should be interpreted with cautious, given some methodical weaknesses encountered: small number of patients, non-blinded study, subjective outcome measurement, possible placebo effect, and non-standard treatment comparison. No serious adverse event reported from this research.

Andereya, et al.¹⁰ tried to correct the methodological weaknesses of the previous study with a new RCT of 113 patients with severe knee OA. Patients were randomized unto 3 groups: Group I (n=38) received a single session of leech therapy. Group II (n=35) had two hirudotherapy sessions, separated by four weeks. The treatment of control group (n=40) was simulated with an "artificial leech". Results were documented with the Knee injury and Osteoarthritis Outcome Score, Western Ontario and McMaster osteoarthritis index and the Visual Analog Score for pain. Improvement in each of these measures was found in all three groups. These improvements were statistically significant for treatment groups I and II during follow-up. Group II (treated twice with leeches)

Table 1. Component in leech Saliva¹²

Components	Functions
Hirudin	Inhibits blood coagulation by binding to thrombin
Calin	Inhibits blood coagulation by blocking the binding of von Willebrand factor to collagen. Inhibits collagen-mediated platelet aggregation
Destabilase	Monomerizing activity. Dissolves fibrin. Thrombolytic effects
Hirustasin	Inhibits kallikrein, trypsin, chymotrypsin, neutrophilic cathepsin G
Bdellins	Anti-inflammatory. Inhibits trypsin, plasmin, acrosin
Hyaluronidase	Increases interstitial viscosity. Antibiotic
Tryptase Inhibitor	Inhibits proteolytic enzymes of host mast cells
Eglins	Anti-inflammatory. Inhibit the activity of alpha-chymotrypsin, chymase, subtilisin, elastase, cathepsin G
Factor Xa inhibitor	Inhibits the activity of coagulation factor Xa by forming equimolar complexes
Complement inhibitors	May replace natural complement inhibitors if they are deficient
Carboxypeptidase A inhibitors	Increases the inflow of blood at the bite site
Histaminelike substances	Vasodilator. Increases the inflow of blood at the bite site
Acetylcholine	Vasodilator
Anesthetics substances	Anesthetic

demonstrated the greatest degree of improvement, with both long term reduction of joint stiffness and improved function in the activities of daily living. Repeated use of leeches appeared to make the improvement of symptoms more durable. The most frequent side effect described in this study was local irritation, which had receded by the follow-up evaluation at 4 weeks. Given other studies' lack of positive findings, one questions to what degree the benefits noted in this trial stem from the activity of leech saliva versus the placebo effect or other uncontrolled bias from expectations placed on an unusual treatment.¹⁰

HIRUDOTHERAPY IN INDONESIA

Until recently, no official agency exists in Indonesia to supply standardized medicinal leeches although Indonesia has a big population of leeches. Hirudotherapy has not been routinely used in hospitals, and to our knowledge only by alternative medicine therapists.

CONCLUSION

Osteoarthritis (OA) is one of the most common causes of joint discomfort and disability. Since its prevalence increases with age, the global rise in the geriatric population portends an increased burden of this disease on individuals and the health care system. Hirudotherapy may offer another therapeutic option to reduce the pain and debility caused by OA. However, additional studies with robust methodology and adequate sample size are needed to better evaluate whether hirudotherapy should be among standard clinical practice for OA treatment.

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