

Medical Leeches and Hirudotherapy: Where is Nurse's Role?

Abstract

Medicinal leeches have long been used to treat some diseases since the ancient era. There are several species of leeches, and are the major species living in Turkey. Turkey is one of the leading countries exporting leeches for medicinal purposes. In the pivotal studies by Haycraft, a highly effective anticoagulant, namely hirudin, was detected in the saliva of leech in 1884. Hirudin disrupts thrombin activation by its anticoagulant characteristic and inhibits fibrinogen-fibrin conversion. Platelet aggregation is blocked, preventing leech aggregation over collagen surfaces. In contemporary medicine, medicinal products from some leech species have been used to treat cardiologic and hematologic disorders, and there is ongoing scientific research in this field. In addition to having an unfavorable ecosystem for leeches, Turkey should seize and maintain the opportunity to use leeches effectively and be the most preferred supplier worldwide. For nurses, understanding effects, adverse effects, and areas of usage for anticoagulant treatment of hirudotherapy, keeping them informed about developments in this field, and getting involved in novel studies are important to become professional in the hirudotherapy. In this review, we discuss areas of usage of hirudotherapy for anticoagulant purposes, role, and liability of nurses in this field. *Hirudo medicinalis* *Hirudo verbana*

Keywords: Hirudotherapy, Leech therapy, Nursing

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Introduction

In recent years, "Traditional and Complementary Medicine" (T&CM) has become increasingly popular in Turkey. The World Health Organization (WHO) defines traditional medicine as "the sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness".¹ In Turkey, "The Directive of Traditional and Complementary Medicine Practices" was implemented on 27.09.2014, which includes purpose, scope, and statutory basis. In the scope of the directive, many practices including acupuncture, hirudotherapy, apitherapy (treatment with honeybee products), phytotherapy (herbal medicine), hypnosis, homeopathy, chiropractic (manual therapy), cupping, larval therapy, mesotherapy (subcutaneous drug administration), prolotherapy (regenerative injection therapy), osteopathy, ozone therapy, reflexology, and music therapy have been defined.² By Directorate of Traditional and Complementary Medicine, hirudotherapy is defined as "a treatment modality based on the passage of many therapeutic active substances present in the saliva of leeches to both local and systemic circulation via administration of leech to certain areas of skin".³⁻⁵

History of Hirudotherapy

The use of leeches in the treatment of some diseases has been introduced into the medical community since the ancient era, attaining in the literature. "Hirudo" means "leech" in Latin. It is unknown when hirudotherapy was first used for therapeutic purposes; however, therapeutic use of leech was depicted in fresco dated to 1400s BC in ancient Egypt. Again, it is suggested that there were records of hirudotherapy in Babylon epigraphs in 15th century BC. It is known that hirudotherapy were used and applied by Mesopotamia, Greek, Maya, Aztec, Indian, Rome, and Arabian civilizations.⁶

The El Kanun Fi't Tib (Canon of Medicine) was written by Avicenna (980-1037) and used as a textbook in many European universities until the 18th century. In the Canon of Medicine, it was suggested that hirudotherapy could be used in the treatment of many diseases, including snakebite, gangrene, leprosy, and fungal infections, and for removal of blood from deep veins where access is not possible by cupping.⁷

In Europe and United Kingdom, hirudotherapy has been started to use in the treatment of almost all disorders in the early 19th century, threatening with the extinction of leeches.⁸ Medicinal leeches lost their significance by emergence of antibiotic treatments in the late 19th century, and even they were considered as charlatanism in many countries. By accelerated advances in medicine in early 20th century, hirudotherapy was almost excluded from medical society.⁶

There are more than 100 bioactive substances in the salivary glands of leeches. These secretions have vasodilator, bacteriostatic, analgesic, anti-inflammatory, and anticoagulant effects as well as several beneficial effects including diuresis, prevention of hypoxia in patients with

microcirculation abnormality and vascular permeability disorder, enhancing the immune system, reduction in blood pressure, and pain relief.^{9,10} Markwardt defined anti-thrombin activity of hirudin following the discovery of anticoagulant effect by Haycraft.^{9,11}

There was an increase in the number of scientific research attempts following the definition of anticoagulant and anti-thrombin effects of substances available in the saliva of the leech. Some substances present in the saliva of leeches were introduced into the market for the treatment of cardiologic and hematologic disorders by pharmaceutical companies. The major example is Hementin (Biopharm USA) which is a very potent anticoagulant and manufactured via genetic engineering.¹² Besides, additional substances such as (Transgene, France), Eglin (CIBA/Geigy-Switzerland), Geleen (Euro Biopharm, Netherlands), Ghilanten (Merrell Dow Research Inst. USA), and Orgelase (Biopharm, United Kingdom) were also introduced into the market by relevant companies.¹³

Turkey is the single country that harvests 5000 kg leeches on an average annually, corresponding to two-third of medicinal leech trade and exports with a tariff worldwide.¹⁰

The leeches were included to scope of “Washington Endangered Species Act, Appendix II” and are taken under international protection by The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).¹⁴ In the context of protection, the export tariff for *Hirudo medicinalis* was reduced to 2000 kg in 2011 from 10,000 kg in 1996 in Turkey. Again, the export tariff for *Hirudo verbane* was reduced to 3000 kg.¹⁵

Characteristics of Medicinal Leeches

Although there are more than 650 species, only a few species of leeches are used for medical purposes. The *H. medicinalis* is the most used species (Figure 1). It has a flat appearance with segments.¹⁶ The maximum length of a mature leech may reach up to 120 mm. The leeches can increase their length by 30-35 mm when they achieve maximum contraction. Their width is generally 8-10 mm, which can be widened to 15-18 mm in case of maximal blood suction.¹⁷

The leeches use sucking discs localized at the head and tail when attaching to another organism or object. The leeches have more than 100 teeth, small orifices between teeth, and 3 distinct mandibles. The leeches leave a Y-type scar at the attachment site. When the leeches start feeding, they release chemicals that leads vasodilatation, increased blood viscosity, and pain control in the organism being sucked. They hold on to the host for up to 20-120 minutes and suck 5-20 mL blood, although it varies according to the capacity of the leech. They spontaneously unhook and drop off the host.¹⁸



Figure 1. Appearance of a mature leech during treatment.

The major leech species are¹⁹:

- *Acanthobdellida*: *Acanthobdella peledina* belongs to this genus.
- *Rhynchobdellida*: *Glossiphonia complanata*, *Piscicola geometra*, *Protoclepsistesselata* and *Theromyzon spp.* belong to this genus.
- *Gnathobdellida*: *Hirudo medicinalis*, *Haemopsis sanguisuga*, *Limnatis nilotica* ve *Macrobdella decora* belong to this genus.

Mechanism of Action of Leech Saliva

The leech saliva contains hirudin, calin, kallikrein inhibitor, hyaluronidase, histamine, and collagenase, as well as many substances with weak anesthetic and analgesic effects.²⁰ Hirudin, one of the substances in the leech saliva, is used to prevent pulmonary inflammation and thrombophlebitis following surgical interventions to prevent clotting. Calin is another substance that prevents coagulation, and it ensures maintenance of bleeding over 12 hours (on an average) after the leech is unhooked and dropped-off. In addition, a histamine-like substance leads to blood leakage from the wound site by ensuring vasodilatation. Again, hyaluronidase accounts for the preparation of the wound site for the absorption of substances that ensure healing.²¹

Indications for Hirudotherapy

Today, the leeches are used in many regions (Russia, USA, Australia, Canada, etc.) for medicinal purposes. The use of leeches shows variations as an adjunct to medical treatment in many areas such as hematoma, thrombosis, arthritis, myasthenia gravis, atherosclerosis and diabetic vascular complications²¹ (Table 1).

The primary objectives of hirudotherapy include²²:

- Clearance of morbid condition in the diseased area.
- Effective suction of hematoma in deeper tissues.
- Pain relief.
- Relieving venous congestion.

Hirudotherapy for Flap Formation

It has been reported that the medicinal leeches were successfully used in plastic and reconstructive surgery. The hirudotherapy provides significant contributions to decrease venous congestion and structuring at the vascular level. In animal studies, it was shown that hirudotherapy replaced new arterial blood by congestive venous blood and enhanced tissue viability.^{23,24}

The hirudotherapy used in flap repair can be applied a few times daily at the initial phase after surgery. It might be continued until flap recovery and resolution of venous congestion.^{25,26} The success rate is not always 100% for hirudotherapy applied in flap repair. In particular, a 100% success rate cannot be achieved in individuals with low hemoglobin levels requiring more packed red cell transfusion.²⁷

In plastic and reconstructive surgery, another area of use is the compensation of venous congestion that can occur after replantation of organs such as finger, toe, and nose. The hirudotherapy increases perfusion resulting in hyperemia. The hirudin, found in leech saliva, up-regulates mRNA levels to increase vascular endothelial growth factor and vascularization response of flap.²⁸

Hirudotherapy for Pain Management

The hirudotherapy can be used in the management of pain induced by several reasons. There are studies reporting successful use of cancer-related severe pain.^{29,30}

It has been reported that there are many bioactive substances with anti-inflammatory and anesthetic effects in leech saliva.³⁰ A recent

Table 1. Areas of Use for Leeches²³

<ul style="list-style-type: none"> • Inflammatory reactions. • Passive congestion. • Plastic and reconstructive surgery. • Cardiovascular disorders. • Hypertension. • Varicose veins. • Hemorrhoid. • Arthrosis, osteoarthritis, peri-arthritis, and rheumatoid arthritis • Thrombophlebitis, thrombosis, and embolism. • External otitis and chronic otitis. • Ocular diseases such as cataract, glaucoma, traumatic injury, and inflammation. • Gum disorders such as gingivitis, parodontitis, and gingival edema. • Painful vertebra disorders. • Hepatitis, cholecystitis, pancreatitis, gastric ulcer. • Skin disorders such as dermatitis, psoriasis, and chronic ulcers. • Respiratory diseases such as asthma and acute rhinopharyngitis. • Male and female infertility, endometriosis and mastitis.

study reported encouraging results for hirudotherapy used in pain management in individuals with osteoarthritis. In a meta-analysis including 237 patients with osteoarthritis, authors found strong evidence for rapid and short-term management of pain by hirudotherapy. In addition, it was shown that there was rapid recovery of physical functions after hirudotherapy and rapid and long-term recovery in stiffness.³¹

In a case report using hirudotherapy in pain management, favorable outcomes were reported in patients with Vatarakta (gout). The leeches were applied for 20-25 minutes to areas of pain and tenderness reported by the patient (four sessions per week over 4 weeks). The patients reported complete pain relief after 4 sessions, and no relapse or complication was reported during 6-weeks of follow-up.³²

Hirudotherapy for Vascular Disorders

In vascular disorders, hirudotherapy was started to use in the treatment as it improves regional blood flow and relieve pain in connective tissue.³³ In 1997, in Russia, preparations with the anti-thrombotic and anticoagulant effect that contains leech saliva were introduced into the market, and they have been prescribed as thrombolytic and anti-platelet drugs.⁶

In cardiovascular disorders, the efficacy of leech is due to the effects of hirudin, a thrombin inhibitor. The hirudin is the single agent approved by the FDA for medicinal purposes, which is found in the *H. medicinalis* species of the leeches. The hirudin has a potent inhibitor effect on both free and bounded thrombin. In the literature, there are studies showing that hirudin is more effective in the prevention of ischemic events in patients with deep vein thrombosis and unstable angina pectoris.²¹

The hirudin can directly block thrombin without the need for cofactor such as anti-thrombin 3. Thus, it is preferred to prevent intravenous

coagulation in patients with anti-thrombin 3 deficiency. Also, it can be used safely in the presence of abnormal platelets and heparin-induced thrombocytopenia since it has no immune effect over red cells that may be harmful to patient.³⁴ In addition, unlike heparin, hirudin has a promising prophylactic effect in patients at high risk for cardiovascular events. It has been reported that the hirudin diminished deep vein thrombosis, pulmonary embolism, and diffuse venous thrombosis.^{12,35}

Besides *H. medicinalis*, there are more than one leech species in which substances with thrombin inhibitory effects are isolated. Bufrudin (with a similar chemical structure to hirudin) is isolated from *H. Manillensis*. Again, haemadinin, which is known as bounding thrombin inhibitor and can be identified in whole body extracts, is obtained from *Haemadipsa Sylvestris*. are *H. Nipponia* ve *Theromyzontes sulatum* other leech species with anti-thrombin effect.²¹

Contraindications for Hirudotherapy

- Coagulopathies (Hemophilia).
- Severe anemia.
- Arterial insufficiency.
- Hematological malignancies.
- Hypotension.
- Septic conditions.
- Known allergic reactions against substances (hirudin, hyaluronidase, etc.) in the leech saliva.
- Lack of patient approval.

However, leech therapy is contraindicated in pregnant women and breastfeeding women since they are at risk for infection and bleeding. The leech therapy should not be applied to individuals on anticoagulant and immunosuppressive treatment.

Complications of Hirudotherapy

Although leech therapy is an innovative and safe approach, many complications have been reported for leech therapy. The common complications during therapy include³⁶:

- Prolonged bleeding.
- Allergic reactions and bacterial infections.
- Itching and subsequent burning sensation and vesicle formation or ulcerative necrosis because of toxic effect induced by leech saliva.
- Disseminated infection.

Liabilities of Nurses in Hirudotherapy

Before leech therapy, the nurses should thoroughly know indications and contraindication, the importance of patient selection, and issues taken into consideration during hirudotherapy and should manage potential side effects; in addition, they should keep in mind that they have a key role to promote timely intervention by maintaining strong communication within the team.

Patient Assessment and Counseling

Comprehensive information about treatment (effects, side effects, risk factors and process) should be provided to the patient before treatment in a verbal and written manner; a written informed consent must be obtained after ensuring that the patient appreciated the information provided.

Again, a detailed patient assessment should be performed before treatment. The nurses should know the differences between arterial insufficiency and venous occlusion. The nurses should have the knowledge that there is faded, cold, and swollen with prolonged or no capillary refill (> 2 seconds) in case of arterial insufficient. They should keep in mind that

skin is purple, stretched, tight, and warm with sudden, rapid capillary refill (<1 second) in case of venous occlusion.³⁷ The nurse should question patients whether they use any vitamin, herbal supplementation, or drug. It should be kept in mind that high doses of vitamin E supplementation can cause coagulopathy by prolonging prothrombin time and suppress the immune response. Since nutritional supplements such as Dong Quai (*Angelica sinensis*), garlic, ginger, ginkgo biloba, and ginseng, and drugs such as acetyl salicylic acid, heparin, warfarin, and non-steroid anti-inflammatory agents cause increased risk for bleeding, these agents should be questioned in detail.³⁸ The patient should be instructed not to consume coffee/tea, carbonated drink, and chocolate, if possible, during leech therapy since they increased the risk for vasoconstriction. Again, it should be emphasized that smoking is an absolute contraindication as carbon monoxide and nicotine have potent vasoconstrictive effects.³⁹ The hirudotherapy should not be employed in individuals with immunosuppression or those with hemophilia and arterial insufficiency, and the patients with such diseases must be informed.⁴⁰ Patient education is important in leech therapy. The patient may feel discomfort or disgust in case of contact with leech. The only way for the patient to adopt the benefits of treatment is by being sufficiently informed. Thus, before treatment, information such as number of leeches to be used, areas where leeches will be applied, and frequency of treatment should be provided to the patient. Aspirin, heparin, or low-molecular-weight dextrane may be prescribed to the patient by the doctor in charge to improve the efficacy of treatment and to reduce the risk for thrombosis; again, drugs containing chlorpromazine can be given to achieve specific vasodilatation in small vessels.^{37,40} Comprehensive information about leech therapy (effects, side effects, risk factors, and process) should be provided to the patient before treatment in a verbal and written manner; a written informed consent must be obtained after ensuring that the patient appreciated the information provided.

Special Considerations in Application of Hirudotherapy

The temperature should not exceed 25°C in the area where leech therapy is applied. Temperature offers convenience for application by improving blood circulation.⁴¹ Before placement of leech, the area should be washed with soap and water and rinsed with distilled water.³⁹ Whitaker et al.⁸ recommend the use of a heparinized, warm saline solution for disinfection of the application area.⁴² Some clinicians may use smooth forceps, but it is more appropriate to handle with a glove since forceps may harm the leech. A gauze in the freehand may be helpful to detach the leech in case of attachment to the glove. The head of the leech can be more readily directed in the area of application by using gauze.³⁹

During leech therapy, leech migration should be checked every 15 minutes throughout the application. When a displacement of the leech is recognized, the leech should not be forced to unhook since the teeth may remain in the area of application, resulting in risk for infection. Instead, the head and trunk of the leech should be detached from the area of application by spilling alcohol, saltwater, or vinegar on a gauze or a swab.⁴³ The excessive amounts which cannot be tolerated by leech can cause damage in the leech or tissue bite by leech, resulting in increased risk for infection.⁸

The leeches may migrate from one area to another during application, which is termed as “leech migration” in the literature. Thus, it may be helpful to place gauzes in a circular manner around the area of application to prevent leech migration.³⁹

The field temperature should be checked every 3 hours to maintain a temperature over 30°C. The field temperature below 30°C may be a symptom of arterial or venous circulation problems. Thus, areas other than the application site should be supported by gauzes or blankets, and heat loss should be prevented.³⁹

The application area should be checked for symptoms and findings as well as skin color every 4 hours, and pulse must be checked in adjacent areas.⁴⁴ The nurses should follow patients in collaboration with the clinicians by monitoring hemoglobin, hematocrit, bleeding time, and bleeding-clotting time ordered by the clinician.³⁹

Special Consideration after Completion of Hirudotherapy

The leeches with fulfilled capacity can drop off from the host without intervention. The mean feeding time ranges from 20 to 120 minutes for leeches.⁴⁵ A leech sucks approximately 5-20 mL of blood in each application. The maximum benefit from leech therapy is achieved in the phase where blood loss occurs via leakage from bite site.¹⁰

The leeches should be disposed by placing 70% alcohol solution. In general, leeches are placed into capped, plastic urine sample containers containing 20 mL of alcohol solution. The leeches die within 10 minutes in alcohol solution. The waste should be treated as a hazardous biological waste and should be disposed into a hazardous waste container. The leeches are disposed to prevent transmission of bloodborne infections.⁴⁵

If the same leech will be used for the same patient, an interval of 1 to 2 weeks is required for application since leeches do not need feeding over 1 to 2 weeks after being fed. The efficacy of leech therapy and discontinuation criteria should be checked. The following criteria indicate effective leech therapy; thus, treatment can be discontinued²:

- Angiogenesis and sufficient venous drainage in the tissue.
- Skin color returning to more normal from purplish discoloration/
- Capillary refill time < 1 seconds.

Estimated blood loss must be noted. The application area should be cleansed before and after the application. The blood values should be closely monitored. In addition, signs and symptoms of infection should also be monitored in the application area. The expectations of the patient and the need for additional education should be assessed.³⁹

Nursing Management for Complications

Bleeding

The nurses should be competent regarding complications that may develop following hirudotherapy. Bleeding is the most common complication after hirudotherapy. In general, compression or topical thrombin administration is sufficient to achieve hemostasis.⁸ Excessive blood loss may require blood transfusion; thus, the patients should be informed about this potential complication.³⁷ Allergic reactions, including anaphylaxis, may also occur. Allergy must be monitored closely and documented accordingly. The patients and their relatives should be informed regarding the likelihood of allergy. Small scars may develop at the application site after treatment.

Infection

The major complication is an infection in hirudotherapy. The digestive system of leech harbors a Gram-negative bacillus, namely *Aeromonas hydrophilia*, which degrades blood swollen by leech. Although the majority of hirudotherapy-related infections are caused by *A. hydrophilia*,

infections caused by *Serratia marcescens*, *A. sobria* ve *Vibrio fluvialis* have also been reported.^{8,46}

The signs and symptoms of infections can be seen 2-11 days after onset of treatment, and the infection may occur as abscess or cellulitis and may progress to sepsis.^{47,49} In a study by Sartor et al. (2002), it was reported that infections occurred in 4.1% of patients.⁴⁷

Conclusion

Turkey is a prosperous country regarding the presence of medicinal leeches. The active substances in medicinal leeches are more cost-effective with a more favorable side effect profile when compared to drugs. It is important to use leeches as an adjunct in medicine and to improve the awareness of nurses in this issue. In the literature, there is a paucity of studies on hirudotherapy in the nursing field. Thus, it is of value to conduct scientific investigations by nurses. We think and recommend that there is a need to plan education by identifying the gap of knowledge about liabilities of nurses before, during, and after leech therapy and assess results of these educations.

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