



Clinical Implementations and Complications of Hirudotherapy in Plastic and Reconstructive Surgery and Modern Medicine

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Received: May 31, 2023

Accepted: June 10, 2023

Published Online: June 30, 2023

Journal: International Journal of Innovative Surgery

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

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Keywords: Hirudotherapy; Plastic and Reconstructive Surgery; Medicinal leech; *Hirudus medicinalis*; Bloodletting; Venous congestion; Hirudotherapy complications.

Abstract

The loss of tissue in esthetic areas such as partial or complete loss of ear, nose, and other facial and body parts can be devastating for the affected individual and can lead to severe esthetic and functional impairment, as well as psychological trauma. Reattachment of avulsed tissues, flaps in reconstructive plastic surgery, transplantation of body parts using tissue engineering allow patients who suffered complete or partial loss of external organs due to trauma, malignancy, or inherited absence, to have improved quality of life and minimize psychological trauma. Venous congestion is a frequent and challenging complication in reconstructive surgery and replantation of avulsed tissues. One of the successful therapies to prevent and/or treat venous congestion is the use of medicinal leeches, a form of "Biotherapy" also known as Hirudotherapy, with *Hirudus medicinalis* being the most common leech species used. Leeching as a method to relieve venous obstruction was used in ancient times and is currently FDA approved. It is a well-established method for treatment of venous congestion with almost no limitation to the body region. There is sound evidence for its efficacy in Plastic and Reconstructive surgery, however it is still not used as frequently. The authors are presenting an overview of the most significant characteristics and clinical implementations of Hirudotherapy in modern medicine. Furthermore, the possible complications and risks which need to be taken into consideration during treatment planning are being thoroughly discussed.

Introduction

Physiological blood circulation in distressed tissues is crucial for its reintegration after trauma or reconstructive surgery. Well-established approaches to restore physiological circulation, such as microsurgical arterial and venous repair are very well described in the literature [1]. Microsurgical replantation, especially in combination with microsurgical venous repair, is a well-known and well-established procedure in the field of

Plastic and Reconstructive surgery. It provides a higher survival rate and better esthetic outcomes compared to conventional replantation without microsurgical venous repair. However, this approach is not always available, especially in the setting of Emergency Rooms, as it requires special equipment, such as microscope and, micro-surgical instruments and very small sizes of suture material, which is oftentimes not available in the fast-paced Emergency Room Departments. Under these circum-



Cite this article: Vargas N, Manon V, Castro-Núñez J. Clinical Implementations and Complications of Hirudotherapy in Plastic and Reconstructive Surgery and Modern Medicine. *Int J Innov Surg.* 2023; 6(1): 1032.

stances, salvaging of avulsed tissues or body parts can become even more challenging in terms of repair, depending on the size of the defect, body region, severity of trauma, infection risk, and period of time the avulsed tissue has been detached from its source of blood circulation. Even after a good tissue repair, there is always risk of tissue necrosis due to avascularity and/or venous flow obstruction. While multiple factors play a role in the survival of avulsed tissue and reconstructive flaps, venous congestion is often the reason for failure. It can lead to venous thrombosis which on the other hand leads within 3 hours to severe microcirculatory lesions and within 8 to 12 hours to irreversible lesions presenting as the “no reflow phenomenon” inside the flap, and subsequently resulting in tissue necrosis [2]. Avoiding venous congestion in such cases is essential for the maintenance of the tissue vitality and survival of the affected body region. The current article emphasizes the importance of Hirudotherapy for the treatment and prevention of venous congestion. Furthermore, it explains the characteristics, indications, risks and complications of Hirudotherapy in Plastic and Reconstructive surgery and other clinical areas.

Medicinal leech anatomical characteristics and mode of action

The medicinal leech, *Hirudo medicinalis* (Figure 1) is a hermaphrodite and hematophagous annelid, about 12 cm long when actively feeding, whereas at rest its body can contract to about one-third of its size. It is bilaterally tapered, and each end has a sucker, with the larger posterior one being the attachment sucker. The anterior and smaller in size sucker contains three retractable jaws with around 300 miniature teeth. The Y-shaped incision created by the jaws allows the substances in the leech saliva to enter the host and facilitate attachment and feeding. The anterior, also known as “oral” sucker creates a tight seal around the incision. Blood is actively suctioned into small chambers, from where it is further propelled in peristalsis-like movements into the intestine, where it is ultimately digested (Fig. 2). The application of medicinal leeches presents an ancient method to release pressure built in tissues, due to inappropriate blood flow and venous congestion. Leeches mechanically reduce the accumulated blood volume through continuous bleeding. The combination of three mechanisms of action - active suction while feeding, secretion of vasoactive substances and passive oozing result in alleviation of clinical symptoms, which makes the use of leeches a valuable adjunct therapy for variety of medical conditions. Sometimes medicinal leeches are used as only and final treatment option when all other approaches fail [3]. Additionally to the active suctioning properties, their saliva contains bioactive substances released in the host that include anticoagulants, vasodilators, inhibitors of platelet aggregation, thrombin regulators, extracellular matrix degradation enzymes, proteinase inhibitors, as well as analgesic, anti-microbial and anti-inflammatory substances [4-7]. The most important and well-studied active substance in leech saliva is Hirudin - a potent thrombin-specific inhibitor (Fig. 3.), which according to some studies is considered to have more therapeutic benefits and more potent than Heparin [8,9].

Clinical implementations of Hirudotherapy in ancient and modern medicine

Medicinal leeches have been used for centuries for blood-letting, also known as phlebotomy, as one of several remedies used to restore the balance of the four humours - blood, phlegm, choler, melancholy [10]. Due to the variety of valuable bioactive substances and long history of effective-

ness, leeches can be used in the treatment of many medical conditions, such as phlebitis and other thromboembolic diseases, high blood pressure and other cardiovascular diseases, diabetes, hemorrhoids, arthritis, tendinitis, old hematomas, migraines, tooth ache and other pain syndromes, nose bleeds, mental illness, insomnia, strokes, gout, sialadenitis, obesity, proliferative vitreous retinopathy, autoimmune diseases, priapism, meningococcal purpura fulminans, tumors, and even cancer [11-18]. There is evidence in the literature suggesting medicinal leech therapy in Dermatology and Cosmetology for variety of skin conditions [19,20]. In Plastic and Reconstructive surgery their application has been essential for the reestablishing of physiological blood circulation while preventing venous congestion and improving local hemodynamic conditions [21]. Leeches are used for salvaging of free and pedicled flaps, re-plantation of digits, noses, lips, ears, penises, facial lacerations, as well as fragile tissues such as the earlobe [23-25]. The use of medicinal leeches is multifaceted, Table 1.

Risks and complications of Hirudotherapy

These include mild symptoms such as pruritus, erythema, bite scars, allergies, localized cellulitis, as well as adverse events such as prolonged bleeding and blood loss, bacterial infections mostly with *Pseudomonas hirudinis* and *Aeromonas hydrophila* species, in rare cases with *Protozoa*, anaphylaxis, septic shock, as well as transmission of viral blood-borne infections such as HIV and hepatitis [26-31]. Furthermore a few studies report rare complications such as tunneling, migration, meningitis, and psychosis [22,32,33]. In their review article Pourrahimi et al. summarize the possible complications of Hirudotherapy as follows - 51% infections, 21% allergies, 15% prolonged bleeding, 8% migration, 5% other - tunneling, meningitis [34]. Table 2. Summarizes the most common clinical complications of Hirudotherapy.

Contraindications

In their book *Medicinal Leech Therapy* P. Flecken and A. Michalsen describe thoroughly the most important clinical considerations. The authors discuss in a systematic and detailed manner the clinical implementations, as well as possible risks and complications in the application of medicinal leeches [35]. Even though there are not many absolute contraindications, there are conditions which need to be considered a high risk for possible complications, such as severe infections, bleeding disorders, immunosuppression, tissue necrosis, malignancies, and mental illness. Table 3. presents a summary of potential contraindications according to Flecken and Michalsen. The listed conditions should raise awareness and high precaution while treating patients with Hirudotherapy for salvaging of flaps in Plastic and Reconstructive Surgery or any other clinical presentation which requires bloodletting.

Discussion

Hirudotherapy as such is very effective and relatively cost efficient. There are many commercial leech-sources currently on the market. According to the one of the most popular leech-suppliers LEECHES U.S.A. LTD., <http://leechesusa.com/>, pricing varies between 16.15 and 18.15 dollars per leech, depending on the number of leeches ordered. Because of their easy maintenance, which includes only a “leech mobile home” and a special medium storing solution, leeches are considered affordable and uncomplicated to use, store and transport. From the clinical perspective, leeches have a sound history for use in va-

riety of conditions [36]. There is sound evidence for the use of medicinal leeches in Plastic and Reconstructive surgery for the salvage of avulsed tissue [37,38]. Herlin et al. report in their systematic review a success rate of leech therapy of 83.7% in the salvage of flaps [39]. Michalsen et al. demonstrate the use of Hirudotherapy for symptomatic treatment of knee osteoarthritis, in which the application of leeches led to rapid relief of knee pain in all treated patients, being most effective within 24 hours of treatment [40]. Similar clinical improvement was observed in 50% of patients suffering from sialadenitis and sialadenosis, in contrast to the patients presenting with Sjogren's syndrome in which Hirudotherapy was not effective [41], which suggests that patients with autoimmune diseases might not benefit from the application of medicinal leeches. More clinical and experimental research is needed to establish their role in the treatment and alleviation of autoimmune diseases. The literature refers to medicinal leeches as a predictable and reliable Biotherapy for a variety of conditions in the face, mouth, body, extremities and even in urologic disease states and surgical

complications [42]. Considering the few relative contraindications as well as the possibilities to manage complications such as simple tools to hold back leech migration [33] and use of antibiotic leech-feeding as antibiotic prophylaxis for the prevention of infective complications [43], Hirudotherapy can be used in facial regions with reliable efficacy.

Conclusion

Medicinal leeches also known as Hirudotherapy are a very well tolerated treatment option, with little contraindications, manageable risks and complications, and almost no limitation for the application in terms of body region. The authors emphasize the efficacy and simplicity of Hirudotherapy and suggest it as an essential modality for the treatment or prevention of venous congestion. The current article has the purpose to awaken awareness and encourage clinicians for more frequent application of Hirudotherapy. The authors suggest its use as a part of a routine flap and avulsed tissue protocol in Plastic and Reconstructive Surgery.

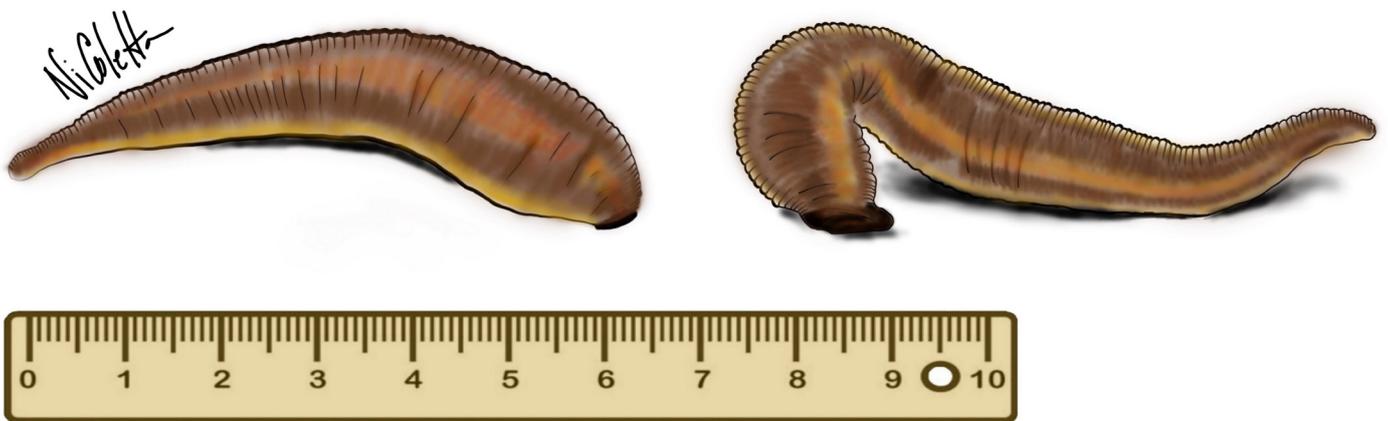


Figure 1L: *Hirudo medicinalis*, "unfed" state - Nikoletta Vargas DMD. MS. PhD.

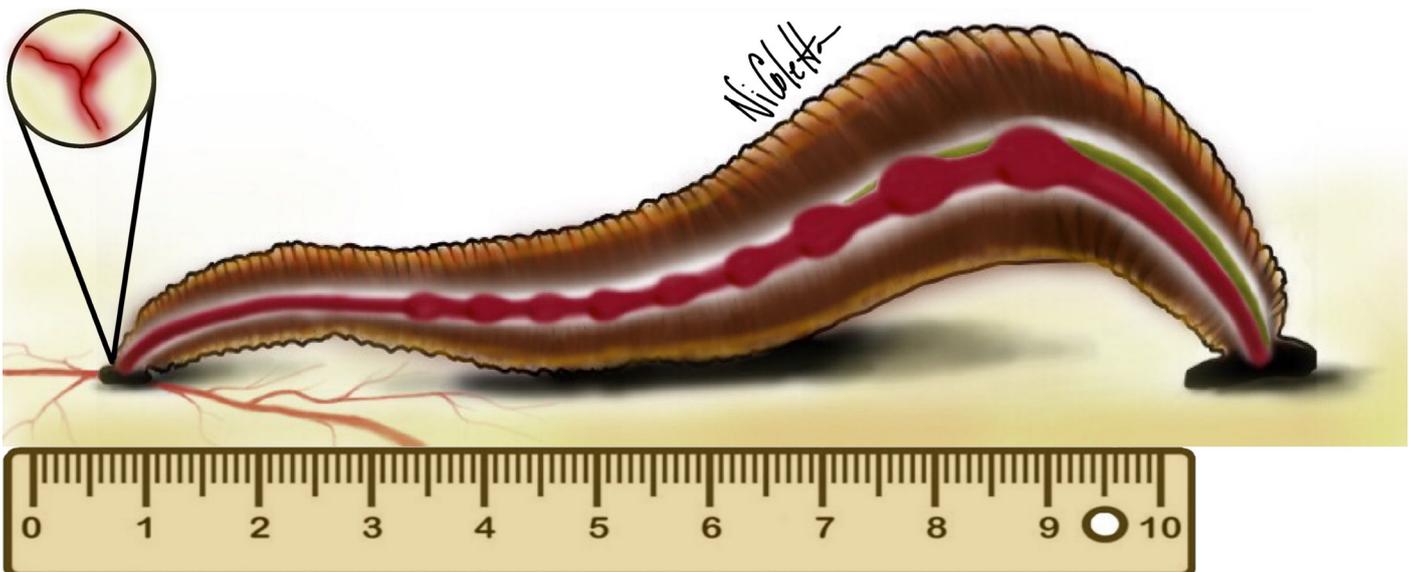


Figure 2: *Hirudo medicinalis*, "attached". Blood is actively suctioned into small chambers (red), from where it is further propelled in peristalsis-like movements into the intestine (green), where it is ultimately digested. - Nikoletta Vargas DMD. MS. PhD.

Table 1: Clinical Implementations of Hirudotherapy.

Clinical Implementations	Study	Year published
Acne vulgaris [44]	Samaranayake et al.	2018
Arthrosis, symptomatic [45]	Michalsen et al.	2008
Baker's Cyst [46]	Iqbal et al.	2019
Cancer [47]	Merzouk et al.	2012
Cardiovascular diseases [48]	Konyrtaeva et al.	2015
Deep Vein Thrombosis [49]	Khan et al.	2018
Dermatitis [50]	Özkaya et al.	2023
Diabetic neuropathy [51]	Farshad et al.	2022
Diabetic foot [52]	Rehman et al.	2020
Digital replantation [53]	Pickrell et al.	2020
Ear diseases [54]	Seleznev et al.	1992
Ear reconstruction [55]	Facchin et al.	2018
Earlobe salvage [25]	Vargas et al.	2023
Epilepsy [56]	Sun t al.	2007
Facial laceration, complex [57]	Cohn et al.	2021
Flap salvage [37]	Herlin et al,	2017
Gingivitis, Periodontitis, Tooth pain [57]	Thakur et al.	2016
Gout, acute [58]	Panda et al.	2012
<i>Hematomas</i>		
Forearm hematoma [59]	Schenker et al.	2006
Massive lingual hematoma [60]	Grossman et al.	1998
Periorbital hematoma [61]	Menage et al.	1991
Scrotal hematoma [62]	Isgar et al.	1989
Sublingual hematoma [63]	Lee et al.	1996
Hemorrhoids [64]	Menteş et al.	2019
Ischemia [65]	Durrant et al.	2006
Meningococcal purpura fulminans [16]	Dippenaar et al.	2006
Microsurgery [66]	Green et al.	2010
Migraine [67]	Bakhshi et al.	2015
Nose replantation [68]	Larsson et al.	2016
Osteoarthritis [69]	Andereya et al.	2008
Pain syndromes [15]	Koeppe et al	2014
Penile replantation [23]	Mineo et al.	2004
Priapism [14]	Asgari et al	2017
Proliferative vitreous retinopathy [17]	Huang et al.	2021
Psoriasis [70]	Hemanta et al.	2020
Sepsis [71]	Davis et al.	2000
Sialadenitis, Sialadenosis [41]	Abal'masov et al.	2003
Stroke [72]	Wang et al.	1995
Tendinitis [73]	Bäcker et al.	2011
Thromboembolic diseases (arterial and venous) [74]	Büller et al.	1993
Urologic disease states and surgical complications [42]	Battin et al.	2023
Varicose vein [75]	Iqbal et al.	2022
Vitiligo [76]	Panigrahi et al.	2012

Table 2: Risks and complications of Hirudotherapy.

Risks and complications	Study	Year published
Abscess, anal [64]	Menteş et al.	2019
Allergies [77]	Conley et al.	2023
Bleeding, prolonged [28]	Zengin et al.	2012
Blood loss, severe [78]	Güven et al.	2016
Cellulitis, due to Ciprofloxacin resistant <i>Aeromonas hydrophila</i> [79]	Giltner et al.	2013
Central black eschar [80]	Rasi et al.	2014
Diffuse cutaneous pseudo lymphoma [81]	Altamura et al.	2014
Erythema [82]	Pietrzak et al.	2012
Infections, bacterial [27]	Verriere et al.	2016
Infections, protozoa [83]	Corrêa et al.	2016
<i>Infections, viral</i>		
Hepatitis [84]	Wilken et al.	1993
HIV [29]	Mehlhorn et al.	1993
Keratitis [50]	Özkaya et al.	2023
Kounis syndrome [85]	Çakmak et al.	2018
Lichen Planus [86]	Daye et al.	2021
Meningitis [87]	Ouderkirk et al.	2004
Migration [33]	Conroy et al.	2006
Pruritus [88]	Seiverling et al.	2014
Pyoderma Gangrenosum [89]	Sadeghi et al.	2016
Sepsis, lethal [90]	Sproll et al.	2022
Tunneling [32]	Flurry et al.	2011

Table 3: Considerable contraindications for Hirudotherapy according to Flecken and Michalsen [35].

Contraindications
Allergy, severe
Anemia
Anticoagulants use (e.g. Acenocoumarol, Marcumar, Warfarin, Heparin and Heparinoids)
Bleeding disorder
Deep vein thrombosis
Dermatomycoses
Diabetic foot
Infection, severe
Immunosuppression, severe
Internal diseases, severe
Keloids
Mental illness
Pemphigus
Pregnancy
Skin malignancies
Tissue necrosis
Ulceration (e.g. decubitus)
Unconscious patients
Upper gastrointestinal tract post – hemorrhage condition
Wound healing complications

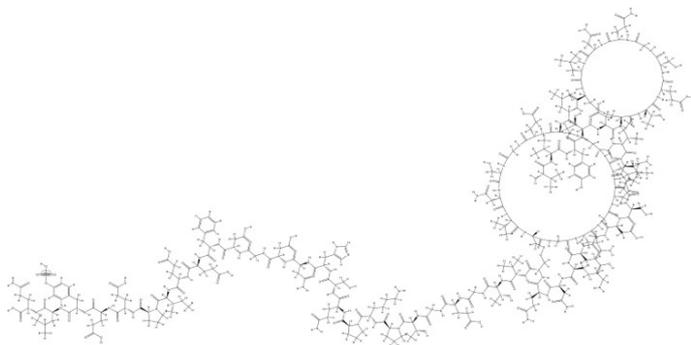


Figure 3: Hirudin, chemical formula, source - Chemicalbook.com

Financial Disclosure

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Conflicts of interest

The authors are disclosing any conflicts of interest.

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