The Risk-Benefit Ratio of Leech Therapy: A Single-Center Retrospective Study

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Abstract

Background: Venous congestion in transplanted or replanted tissues remains a common and challenging complication of plastic and reconstructive surgery. The local application of medicinal leeches is effective in reducing postoperative venous congestion in skin flaps and restoring normal blood flow. However, leech therapy is associated with a number of risks, including infections; in order to digest blood, leeches have a symbiotic relationship with *Aeromonas* species in their gut. *Aeromonas* infections are associated with a dramatic decrease in flap salvage rates. This is why prophylactic antibiotic treatment and external decontamination of the leeches are widely recommended.

Methods: We performed a single retrospective study of patients having undergone leech therapy between January 1st, 2010, and December 31st, 2018, at Amiens-Picardie University Hospital, France. Each patient's medical history, clinical data, laboratory results, prophylactic antibiotic use, and complications were recorded.

Results: A total of 37 patients (mean age: 47) had undergone leech therapy after reconstructive surgery. Antimicrobial prophylaxis was documented in 32 (84.6%) patients. However, there are no guidelines on the choice of prophylactic antibiotic treatment. Twenty-four of the 37 (64.8 %) patients had anemia (mean hemoglobin level: 8.5 (6-11.1) g/dL), and 13 of the 24 (54%) required a transfusion. Thirteen of the 37 patients (35.1%) had a post-operative infection mainly due to *Aeromonas* spp. (76.9%).

Leech therapy was effective in 23 of the 37 patients (62%) overall and in 2 of the 10 patients (20%) with an *Aeromonas* infection. The association between *Aeromonas* infection and flap salvage failure was highly significant ($p = 0.005$).

Conclusions: The results of the study emphasized that clinical bacteriologists and surgeons should be aware that leeches are potential sources of infection.

Background:

As one of many hundreds of leech species, *Hirudo medicinalis* has been used in medicine for more than 3500 years - starting in ancient Egypt (1). Over the centuries, medicinal leeches have been used for many indications, including migraines, arthritis, tendinitis, and (since the 1960s) postoperative venous congestion.

Venous congestion in transplanted or replanted tissues is a common and challenging complication of plastic and reconstructive surgery. Leech therapy (also known as hirudotherapy) is increasingly used to salvage compromised pedicle flaps and microvascular free-tissue transfers (1). The local application of leeches is effective in reducing postoperative venous congestion of the flap and restoring normal blood flow. In 2004, *Hirudo medicinalis* was approved as a medical device by the United States Food and Drug Administration (2). However, hirudotherapy is notably contraindicated by immunosuppression, advanced peripheral arterial disease, hemophilia, hemopathies, and sepsis (3).

Leech therapy is also associated with various risks, including significant blood loss (requiring transfusion) and infections. In order to digest blood, leeches have a symbiotic relationship with *Aeromonas* species in their gut. These bacteria appear to be the most common cause of leech-associated infections, which sometimes result in extensive soft tissue destruction and myonecrosis (3). Transmission of *Aeromonas* occurs either by direct inoculation from the leech's mouthparts or via contamination of the wound with the water in which the leeches were stored (4). Other microorganisms to have been implicated in these infectious complications include *Proteus* spp., *Morganella* spp., *Serratia* spp., *Vibrio* spp., and *Pseudomonas* spp.

Infections can occur 1 to 30 days after the application of leeches and are associated with a dramatic decrease in flap salvage rates (from 88% to 37%) (5, 6). Prophylactic treatment with antibiotics (such as third generation cephalosporins, gentamicin, fluoroquinolones and/ or cotrimoxazole) is therefore indicated during hirudotherapy (7). It has also been suggested that maintaining the leeches in clean water or decontaminating the outside of the leeches can reduce *Aeromonas* infections after leech therapy (7).

The primary objective of the present study was to determine the prevalence of adverse events (anemia and infection) among patients treated with leeches in a French tertiary hospital. The secondary objective was to evaluate the appropriateness of the prophylactic antibiotic treatment and other strategies used to prevent infection after leech therapy.

Materials And Methods:

We performed a single-center retrospective study of patients having undergone leech therapy between January 1st, 2010, and December 31st, 2018, at Amiens-Picardie University Medical Center (Amiens, France). We recorded the study population's demographic characteristics, specimen sources and bacteriological data, the date and type of surgical procedure, the date of onset of infection, the clinical characteristics of the infection, the laboratory results, the duration of leech therapy, prophylactic antibiotic treatment (if applied), underlying conditions, and the clinical outcome of leech therapy.

In our hospital, the central pharmacy manages the purchase, maintenance and distribution of leeches. We obtained data from the pharmacy on the numbers of leeches delivered, the clinical units, the treated patients' names, and the number of leeches used per patient. We also retrospectively surveyed the conditions under which the leeches were maintained, delivered, and (if applicable) cleaned/disinfected. All leeches were purchased from the same supplier (Ricarimpex, Eysines, France).

In our descriptive analysis, categorical variables were expressed as the number (percentage), and continuous variables were expressed as the mean ± standard deviation or the median (range), depending on the data distribution. The threshold for statistical significance was set to $p<0.05$. All analyses were performed using R software (version 3.6.0, R Foundation for Statistical Computing, Vienna, Austria).

In line with the French legislation on retrospective studies of routine clinical practice, the study protocol was approved by a hospital committee with competency for studies not requiring approval by an

institutional review board (AMLEE; Amiens, PI2020_843_0136), and was registered at ClinicalTrials.gov (NCT04676581).

Results:

Between January 1st, 2010, and December 31st, 2018, a total of 37 patients underwent leech therapy. The use of leech therapy increased markedly over during this period. Eight patients were treated with leeches between January 2010 and December 2015, whereas 29 were treated between January 2016 and December 2018 (p=0.0001).

The mean age of the study population was 47 (range: 12–84), and there was male predominance (22 men and 15 women). On average 37 leeches (range: 5–126) were used per patient. The mean duration of leech therapy was 4 days (range: 1–12 days).

All patients had undergone reconstructive surgery mainly digital replantation (n=12), a deep inferior epigastric artery free flap for breast reconstruction (n=6), replantation of an arm flap (n=5), resection of a sarcoma (n=2), scrotal necrotizing dermohypodermitis (n=2), a thoracic scar band (n=1), an elbow scar band (n=1), chronic tibial osteitis (n=1), multiple open fractures (n=1), and replantation of a tendon (n=1).

The orthopedic surgery department, the plastic and reconstructive surgery department, and the maxillofacial surgery department used 38%, 32% and 27% of the leeches, respectively (Table 1).

Table 1
– Leech prescriptions between 2010 and 2018 at Amiens-Picardie University Medical Center

	Number of patients	Number of leeches used per patient (mean (range))	Mean number of leeches per patient per day	Treatment duration, in days (mean (range))	Number of patients with prophylactic antibiotics (n (%))	Number of infected patients ((n (%)))
Plastic and reconstructive surgery department	12	40 (10-105)	8.16	4.9 (2-7)	10 (83.3%)	6 (50%)
Maxillofacial surgery department	10	36.2 (10-34)	11.67	3.1 (1-5)	8 (80%)	2 (20%)
Orthopedic surgery department	14	25 (8-126)	7.42	5.87 (2-12)	13 (92.8%)	4 (28.6%)
Intensive care department	1	35	8.75	4	1 (100%)	1 (100%)
Total	37	37 (8-126)	9.25	4 (1-12)	32 (86.4%)	13

During the study period, we did not decontaminate the leeches but prophylactic antibiotics were usually administered. Indeed, 32 of the 37 patients (86.4%) were prophylactically treated with antibiotics. In 2010-2015, amoxicillin plus clavulanic acid was typically used (in 62.5% of the patients). In 2016-2018, a cotrimoxazole-fluoroquinolone combination (31%) and cotrimoxazole (27.5%) were mainly used.

Twenty-four of the 37 (64.86%) patients had anemia (mean hemoglobin level: 8.5 (6-11.1) g/dL), and 13 of the 24 (54%) required a transfusion.

Thirteen of the 37 patients (35.1%) had a post-operative infection. The isolation of an organism from the surgical site during leech therapy was considered to be a surgical site infection. On average, the infections appeared 15 days (range: 5-30) after leech therapy. Twelve of these 13 patients (92.3%) had received prophylactic antibiotics (mainly amoxicillin plus clavulanic acid, in 58.3% of cases, or a cotrimoxazole-fluoroquinolone combination (in 13.3%)).

Twenty-two cultures (59%) of suspected post-operative wound infections were performed. These cultures yielded 40 isolates, including *A. hydrophila* (n=6), *A. veronii* (n=2), *Aeromonas* spp. (n=2), and *A. sobria* (n=1). Additional microorganisms include *Proteus vulgaris* (n=6), *Morganella morganii* (n=4), *Escherichia coli* (n= 3), *Staphylococcus aureus* (n=2), *Enterococcus faecalis* (n=3), *Pseudomonas aeruginosa* (n=2), *P. mirabilis* (n=2), *Providencia* spp. (n=2), *Citrobacter freundii* (n= 1), *Enterobact*er spp. (n= 1), and *Serratia marcescens* (n=1).

Aeromonas spp. was isolated from 10 of the 13 infected patients (76.9%), and the three other infected patients (23%) variously carried *P. vulgaris, P. mirabilis, M. morganii*, and *E. faecalis*.

More than one species were found in 9 of the 10 patients (90%) with an *Aeromonas* infection. One patient carried two *Aeromonas* species (*A. hydrophila* and *A. veronii*). The other bacteria carried in addition to *Aeromonas* spp. were *P. vulgaris* (n=5), *M. morganii* (n=3), *S. aureus* (n=2), *P. aeruginosa* (n=2), and *E. faecalis* (n=2).

All eleven *Aeromonas* strains (100%) were resistant to amoxicillin plus clavulanic acid, whereas four (36.4%) were resistant to fluoroquinolones, three (27.3%) were resistant to cotrimoxazole, and two (18.2%) were resistant to cefotaxime. One of the *A. hydrophila* strains was multidrug-resistant, with resistance to extended spectrum beta-lactamase, cotrimoxazole, and fluoroquinolones.

For the other bacteria, five of the six *P. vulgaris* strains (83%) were resistant to fluoroquinolone, and four (67%) were both resistant to cotrimoxazole and fluoroquinolone. Two of the four *M. morganii* strains (50%) were resistant to cotromoxazole but all four strains (100%) were susceptible to fluoroquinolone. The single *P. rettgeri* strain was resistant to both cotrimoxazole and fluoroquinolone.

All other tested bacteria strains were susceptible to fluoroquinolone and cotrimoxazole.

The leech therapy was effective in 23 of the 37 patients (62%) overall and in 2 of the 10 patients (20%) with an *Aeromonas* spp. infection. *Aeromonas* infections were occurred more frequently in 2010-2015

than in 2016-2018 (87.7% *vs* 10.3%, respectively).

We used data from medical records to divide the patients into three groups: noninfected patients (n=24), patients with an *Aeromonas* infection (n=10), and patients with another bacterial infection (n=3). We found that the risk of anemia was similar in the three groups (p=0.48). However, the relationship between *Aeromonas* infection and a flap salvage failure was highly significant (p=0.005) (Table 2).

Table 2
– Characteristics of the three patient groups

	No infected patients group (n=24)	***Aeromonas* infected patients group (n=10)**	**Other infected patients group (n=3)**	***p*-value**
Age (years), mean ± standard deviation	49.56 ± 4.09	44.1 ± 4.722	46 ± 4.395	0.65
Duration of leech therapy (days)	4.28 ± 1.66	5.5 ± 0.671	4.6 ± 0.678	0.42
Prescription of prophylactic antibiotic treatment (n (%))	22 (91.6%)	8 (80%)	2 (66.66%)	0.38
Anemia (n (%))	14 (58.3%)	8 (80%)	2 (66.66%)	0.48
Transfusion required (n (%))	7 (29%)	5 (50%)	1 (33.33%)	0,51
Successful leech therapy (n (%))	19 (79.1%)	2 (20%)	2 (66.66%)	**0.005**
Length of hospital stay (days), mean ± standard deviation	13.25 ± 3.42	14.8 ± 3.235	10.3 ± 2.17	0.13
Immunocompromised patients (n (%))	10 (41.7%)	4 (40%)	1 (33.33%)	0.96

Discussion:

Venous congestion is a critical, frequent complication of flap preimplantation; in the absence of treatment, it leads to transplant failure (2). Leeches are indicated in reimplantation and in the salvage of free flaps and pedicled flaps (3). Hirudotherapy's mechanism of action is based on the composition of the leech's saliva, with a combination of anticoagulant enzymes (such as hirudin), factor Xa inhibitors, platelet inhibitors (calin-saratin), and vasodilators (e.g. acetylcholine) (8).

In our hospital, leeches were most commonly used in the orthopedic surgery department, the plastic and reconstructive surgery department, and the maxillofacial surgery department. This was expected because

leech therapy is recommended for the salvage of compromised pedicled flaps and in microvascular free tissue transfers. The mean duration of leech therapy and the mean number of leeches per patient were similar to those reported in the literature (3).

The great majority of the patients (32 out of 37 (86.4%)) received prophylactic antibiotics at the time of the leech therapy. However, there are no guidelines on the choice of appropriate prophylactic antibiotics; 12 of the 32 (37.5%) patients received an inappropriate prescription of amoxicillin plus clavulanic acid, while seven of them (58.3%) had an infection (mainly due to *Aeromonas*). Eleven of the 32 (34.4%) patients received a cotrimoxazole-fluoroquinolone combination, and one patient (9%) carried an extensively drug-resistant, extended-spectrum β-lactamase-producing *A. hydrophila* strain. The fact that this same strain was isolated from the water in which the leeches were stored strongly suggests that the patient had been infected by *A. hydrophila*- contaminated leeches (9). Thirteen of the 37 patients (35.1%) had a post-operative infection - mainly due to *Aeromonas* spp. (76.9%). *Aeromonas* infection was mainly associated with *P. vulgaris* (50%), and *M. morganii* (30%); the latter bacteria were also resistant to cotrimoxazole, fluoroquinolone or both (62.5%, 50%, and 37.5%, respectively).

In the literature on leech therapy, the tissue salvage rate ranges from 70–80% (10). However, between 7% and 20% of patients developed an infection and the flap salvage rate in cases of a clinically significant infection is low (30% or less) (5, 6). The proportion of patients with an infection was higher in our study (35.1%) than in the literature. Indeed, the leeches were not decontaminated before use. However, the success rate was 79%, and it decreases to 20% in *Aeromonas* spp. infected patients. External decontamination of the leeches (treatment with 0.02% chlorhexidine solution for 10-15 seconds, followed by two rinses with mineral water) prior to their therapeutic use also appears to be necessary (10, 11). This decontamination does not alter the leeches' sucking power, and its effects last for about at least two hours.

Along with infections, the risks of leech therapy include blood loss and a requirement for transfusion if the hemoglobin level falls below 8 g/dL (12). In this study, 64.8% of our patients had anemia, and more than half (54.2%) of the latter required blood transfusion, while is not a routine procedure. The blood count should thus be monitored on a daily basis, as suggested previously (3).

Anaphylaxis and local allergic reactions to leech salivary gland products have also been described (2, 5). Furthermore, leech therapy can cause emotional reactions in some patients, who may therefore need to prepare psychologically and/or take an anxiolytic (12). In our study, none of the 37 patients developed an allergic reaction or had to be treated with an anxiolytic during leech therapy.

Patients with immunosuppression or those taking immunosuppressive medications should not undergo leech therapy because of the risk of overwhelming bacterial sepsis (13). However, 14 of the 37 patients (37.8%) in the present study were immunocompromised but nevertheless underwent leech therapy; fortunately, no serious complications were reported. Hence, the risk-benefit ratio of leech therapy should always be considered prior to initiation.

The results of the present retrospective study emphasize that clinical bacteriologists and surgeons who use leech therapy should be aware that leeches are a potential source of infection (mainly *Aeromonas* spp.). It has been suggested that maintaining the leeches in clean water or decontaminating the outside of the leeches can reduce *Aeromonas* infections after leech therapy, and our results also confirm the importance of choosing an appropriate prophylactic antibiotic regimen; as previously suggested (14), the regimen should be based on leech cultures and resistance patterns.

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Availability of supporting data

Please contact corresponding author for data requests.

Authors' contributions

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Competing interests

The authors declare that they have no competing interests.

References

1. Cornejo A, Shammas RL, Poveromo LP, Lee H-J, Hollenbeck ST. Institutional Outcomes of Leech Therapy for Venous Congestion in 87 Patients. J. Reconstr Microsurg. 2017; 33(9):612–8.
2. Abdullah S, Dar L, Wani A, Tewari A. Hirudotherapy Leech therapy: Applications and Indications in Surgery. Arch. Clin. Exp. Surg. ACES. 2012; 1:172–80.

3. Herlin C, Bertheuil N, Bekara F, Boissiere F, Sinna R, Chaput B. Leech therapy in flap salvage: Systematic review and practical recommendations. Ann Chir Plast Esthét. 2017; 62(2): e1–13.
4. Ott BM, Dacks AM, Ryan KJ, Rio RVM. A Tale of Transmission: *Aeromonas veronii* Activity within Leech-Exuded Mucus. Appl Environ Microbiol. 2016; 82(9):2644–55.
5. Hackenberger PN, Janis JE. A Comprehensive Review of Medicinal Leeches in Plastic and Reconstructive Surgery. Plast Reconstr Surg Glob Open. 2019; 7(12): e2555
6. Whitaker IS, Oboumarzouk O, Rozen WM, Naderi N, Balasubramanian SP, Azzopardi EA, Kon M. The efficacy of medicinal leeches in plastic and reconstructive surgery: a systematic review of 277 reported clinical cases. Microsurgery. 2012,32:240–250.
7. Grau D, Masson R, Villiet M, Lamy B, and French Hospitals Group. Leech management before application on patient: a nationwide survey of practices in French university hospitals. Antimicrobial Resistance and Infection Control. 2018, 7:19.
8. Sig AK, Guney M, Uskudar Guclu A, Ozmen E. Medicinal leech therapy-an overall pe spective. Integr Med Res. 2017;6(4):337–343.
9. Floug Q, Sinna R, Fillatre A, Plésiat P, Hamdad F. A case of leech-associated infection involving an extended-spectrum β-lactamase-producing and extensively drug-resistant *Aeromonas hydrophila*. Clin Microbiol Infect. 2019 Mar; 25(3) :394–5.
10. Perrier Q, Parmentier R, Bros A, Pavese P, Hitier M, Caspar Y, Grevy A, Gibert P, Brudieu E, Foroni L, Bedouch P. Réflexion pluri-professionnelle pour la promotion du bon usage des sangsues en établissement de santé. Le pharmacien hospitalier et clinician. 2018, 53:1-5.
11. Bauters TG, Buyle FM, Verschraegen G, Vermis K, Vogelaers D, Claeys G, Robays H. Infection risk related to the use of medicinal leeches. Pharmacy World and Science PWS. 2007, vol. 29 (3):122–125.
12. Mumcuoglu KY. Recommendations for the Use of Leeches in Reconstructive Plastic Surgery. Evidence-Based Complementary and Alternative Medicine. 2014; 205929.
13. Porshinsky BS, Saha S, Grossman MD, Beery Ii PR, Stawicki SP. Clinical uses of the medicinal leech: a practical review. J Postgrad Med. 2011; 57(1):65–71.
14. Kruer RM, Barton CA, Roberti G, Gilbert B, McMillian WD. Antimicrobial Prophylaxis during *Hirudo medicinalis* Therapy: A Multicenter Study. J Reconstr Microsurg. 2015;31(3):205–9. doi: 10.1055/s-0034-1395395.