

REVIEW

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Systematic review of medicinal leech therapy in urology

Alexander O. Battin^{1*} , Natalie Hobeika¹ and Matthew J. Zdilla¹

Abstract

Background Medicinal leech therapy, otherwise known as *hirudotherapy* or *leeching*, has been utilized for numerous pathologies over centuries. The technique resurfaced in modern medicine for its beneficial effects in microsurgical complications, particularly venous congestion. Recently, several cases have documented the utilization of medicinal leech therapy for the management of urologic disease states and surgical complications. It is important to understand the past, present, and future possibilities for hirudotherapy in urology. However, a systematic review of medical leech therapy in this context has yet to be conducted. Accordingly, and with an emphasis on salient clinical details, this study aims to systematically review the cases of hirudotherapy applied to urological conditions.

Main body of the abstract A systematic review of cases in MEDLINE/PubMed was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Of 49 search results, 11 articles detailing 13 unique cases of medicinal leech therapy used in the urological context were included. Hirudotherapy was conducted in 10 of 13 cases (76.9%) for the management of congested blood occurring in five cases post-penile replantation, two cases of postoperative scrotal hematoma, two cases of venous congestion of the glans post-neonatal bladder exstrophy repair, and one case of refractory priapism. Leeching in the remaining three cases was for the management of penoscrotal edema in patients with hormone refractory prostate carcinoma treated with radical radiation therapy. All 13 cases (100%) reported clinical improvement from hirudotherapy. Venous congestion/hematoma cases noted decreased displaced blood volume. The patient experiencing priapism reported decreased pain despite the persistence of cavernosal swelling. The three cases of penoscrotal edema reported significant decreases in swelling due to serous fluid drainage from leech puncture sites. No complications or side effects were reported in the nine adult patients. The four postoperative neonatal patients all required blood product throughout treatment.

Short conclusion The systematic review of the cases demonstrates that medicinal leech therapy is a favorable treatment option for individuals with varied urological pathologies and that hirudotherapy may improve post-surgical outcomes in the urological setting. Hirudotherapy should be considered as a viable treatment modality in specific venostatic urological conditions.

Keywords *Hirudo medicinalis*, Hirudotherapy, Leeching, Systematic review, Urology

1 Background

Medicinal leech therapy, otherwise known as *hirudotherapy* or *leeching*, has been utilized for the management of myriad pathologies (e.g., cancer, diabetes, cardiovascular disease, dermatologic disease, infectious disease) since at least its first reported use in 50 BC for “hydrotherapy” by Themison of Laodicea [1–3]. Medicinal leech therapy, once relatively uncommon in traditional medical practice, resurfaced in the nineteenth century in the realm of

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plastic and reconstructive surgery as a result of its beneficial effects regarding the management of microsurgical complications [4].

Several species of leeches have been used in leech therapy, including *Hirudo medicinalis*, *Hirudo decora*, *Hirudo nipponia*, *Hirudo orientalis*, *Hirudo verbana* [5–7]. The saliva of the leeches contains several medicinal compounds known to have anti-inflammatory, analgesic, antimicrobial, anticoagulative properties, and healing properties [1–3, 8–10]. A key biologically active compound is hyaluronidase, which promotes vascular permeability as well as histamine-like products that induce vasodilation [2, 9]. The most notable anticoagulative molecule is hirudin, which actively binds and inhibits thrombin. The inhibition of thrombin prevents platelet aggregation and coagulation [1, 3]. There are many other well-known bioactive proteins that collectively promote wound healing present in leech saliva including Eglin C, bdellins, acetylcholine, saratin, platelet-activating factor antagonist (PAFA), and thermacin [11].

The latest works in leech therapy using animal models have focused on elucidating the pathophysiology of leech therapy. One study by [11] explored the effect of leech therapy on testicular damage caused by testicular torsion/detorsion in male rats. The animal models that underwent leech therapy showed evidence of reduced oxidative damage by the changes in oxidative stress biomarkers—decreased MDA levels and increased GPx, TAC, and CAT levels—in addition to decreased apoptotic immunochemical markers [11]. In [12], the mechanism of wound healing was analyzed using excisional wounds in animal models. In the leech therapy-treated group, the inflammatory phase of wound healing was significantly decreased, which helped expedite the wound healing process. This is thought to be spearheaded by the anti-inflammatory components of leech saliva such as bdellins, eglins, and PAFA that suppress cytokine expression. The study also found evidence of increased hydroxyproline levels, known to be an indicator of collagen formation and cellular proliferation, and therefore a marker of faster wound healing [11].

These bioactive molecules are able to enter into the body after a leech latches onto skin and utilizes its proboscis, which mimics a hypodermic needle, to penetrate and absorb blood from their host [13]. Leeches typically withdraw 2–20 mL of blood within 10–30 min; then, once engorged, leeches spontaneously detach from the skin [14].

Recently, several cases have documented the utilization of medicinal leech therapy for the management of urologic disease or the complications associated with urologic surgeries; however, a systematic review of medicinal leech therapy in the context of urology has not been

conducted. Accordingly, this study aims to systematically review cases regarding the application of medicinal leech therapy in the context of urology with special consideration for clinically relevant details.

2 Materials and methods

The review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines [15].

2.1 Eligibility criteria

All published case reports regarding medicinal leech therapy applied to urology available on MEDLINE were included in this review. Reports published in languages other than English without translation and those not consistent with leech therapy in urology were excluded. Furthermore, publications without full text available were excluded.

2.2 Information sources and search strategy

The MEDLINE database search was performed by the authors March 8, 2023 via the PubMed search engine. The advanced search script used was “((((hirudo*[Title/Abstract]) OR (leech*[Title/Abstract])) AND (peni*[Title/Abstract])) OR (((hirudo*[Title/Abstract]) OR (leech*[Title/Abstract])) AND (peno*[Title/Abstract]))) OR (((hirudo*[Title/Abstract]) OR (leech*[Title/Abstract])) AND (scrot*[Title/Abstract])))”

2.3 Study selection

Authors independently screened the titles and abstracts of each article to assess eligibility criteria. Full-text was accessed for all manuscripts to accurately assess the eligibility of prospective studies. Eligibility of each publication was confirmed by the authors after preliminary screening was completed.

2.4 Data collection process, data items, and data analysis

Patient demographic data, clinical presentation, diagnosis, treatment course including medicinal leech therapy, and treatment outcome were collected from each article. All units of measurement were presented in SI units. Article quality was assessed through the CARE (Case REports) guidelines [16–18]. Each article was graded by the CARE guidelines and given one point for every checklist item met. A maximum of 30 points was possible for each article.

3 Results

3.1 Selection of cases and case quality

The database search revealed 49 results. There were no duplicates and all articles were selected to search for full-text availability. Out of the 49 articles screened, 38

were omitted according to exclusion criteria. The search results had 33 articles omitted because they were not reports of cases. The other five articles were omitted because they were not related to medicinal leech therapy in the context of urology. Accordingly, 11 articles were included for detailed review (Fig. 1). Among these articles, one contained three separate cases resulting in a total of 13 documented patients who were treated with leech therapy for a urological condition (Table 1) [1, 5, 9, 19–26]. The average CARE score of quality assessment among the cases was 21.3 ± 2.8 (Mean \pm Standard Deviation). The minimum score was 16 and the maximum was 25 out of 30.

3.2 Patient demographics

All patients who underwent published medicinal leech therapy for a urological condition were male. The average

age of the patients was 36.4 ± 30.9 years (Mean \pm SD). The youngest and oldest patients were a neonate of 18 h and an octogenarian of 81 years, respectively. All reports included geographic location. Of the 13 cases, five occurred in the United States (38.5%), four in the United Kingdom (30.8%), one in Canada, one in Belgium, one in Germany, and one in Iran (7.6% for each reporting an individual case) (Table 1).

3.3 Leech therapy indications

Medicinal leech therapy was utilized in 10 of the 13 (75%) cases for the treatment of congested blood (Table 1). These included five cases (38.5%) of venous congestion status post-penile replantation, two cases (15.4%) of scrotal hematoma presenting as postoperative complication, two cases (15.4%) of venous congestion of the glans following neonatal bladder exstrophy repair, and one case

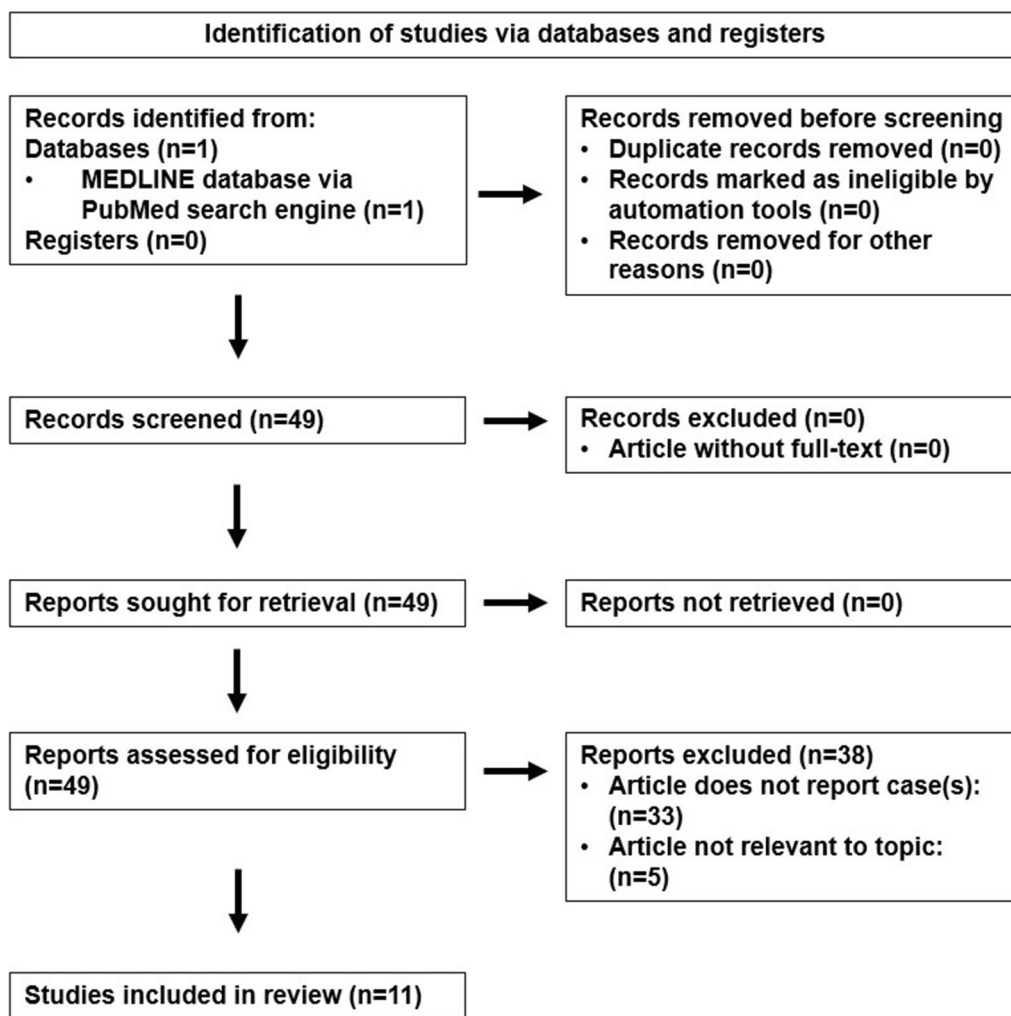


Fig. 1 2020 PRISMA flow diagram of the systematic review

Table 1 Results of systematic review detailing salient manuscript, patient, and leech information

Manuscript details		Patient details				Treatment				Outcomes		Leech details		
Author(s), year, PMID	CARE score	Age Years or as noted	Sex	Country	Indications reason for therapy	Prior treatment history	Leech Therapy details	Hematology	Medications	Favorable outcome?	Infection following therapy?	Additional information	Species	Post-treatment leech details
Mousa et al. 20227, 35263644	25	1 month	M	Canada	Penile replantation	Heparin soaked gauze over penile replant	Leeches were placed on penile glans a total of 4 times and allowed to feed until engorged POD 4–5	Following therapy patient developed hypovolemic shock with hgb 6.7g/dL requiring IV crystalloid resuscitation and blood products	Tetanus immunoglobulin, fluconazole, cefazolin, ciprofloxacin	Yes	No	POD 9 ischemia of foreskin developed, however glans well perfused	<i>Hirudo medicinalis</i>	Not discussed
Asgari et al. 2017 ¹⁷ , 28845411	19	26	M	Iran	Priapism	No other treatment before or after leech therapy, No penile prosthesis insertion due to financial restraints	2 leeches on each side of penile shaft until engorged, 1 hour break and repeated	Initial CBC and BMP, Anticoagulation panel followed during therapy	IV Ceftriaxone 1.5 grams, antihistamines 7 days	Yes	No	Priapism presented at 80 h. Cavernosal swelling decreased but present post-therapy day 2, resolved at 1 month	<i>Hirudo medicinalis</i>	Not discussed
Wagenheim et al. 2015 ⁹ , 26433079	23	2 week	M	USA	Glans penis congestion after bladder extrophy repair	No other treatment before or after for indication	1 leech to glans every hour with willing detachment, therapy stopped after venous congestion improved after 24 h of treatment	Hgb and Hct monitored q6 h, blood transfusions given if Hct <30%, 4 cc/kg given PRBC 15	Ceftazidime	Yes	No	Not discussed	<i>Hirudo medicinalis</i>	Placed in alcohol after and never reused

Table 1 (continued)

Manuscript details		Patient details				Leech details								
Author(s), year, PMID	CARE score	Age Years or as noted	Sex	Country	Indications reason for therapy	Prior treatment history	Treatment leech Therapy details	Hematology	Medications	Favorable outcome?	Infection following therapy?	Additional information	Species	Post-treatment leech details
Banihani et al. 2014 ¹⁸ , 24928459	21	1 week	M	USA	Penile replantation	1/4 baby aspirin given daily in solution through NG to prevent platelet sludging but leech therapy first line for venous congestion	1–2 leeches applied then willingly detached every 15 min–1 hr continuously through POD 3 and used for relief prn of glans/corporal engorgement for 1 week, 2 x sutures placed to leech sites bleeding refractory to pressure	Several blood, FFP and platelet transfusions given throughout treatment to maintain INR < or equal to 1.5, Platelets 50k–100k	Cefazolin 50mg/kg/day and bacitracin ointment TID, then cefepime 50 mg/kg/day, then PO amoxicillin BID	Yes	No	The first case of penile replantation for complete penile amputation with arterial microvascular anastomosis and the use of postoperative leech therapy for venous congestion.	Not discussed	Placed in alcohol after and never reused

Table 1 (continued)

Manuscript details		Patient details				Leech details								
Author(s), year, PMID	CARE score	Age Years or as noted	Sex	Country	Indications reason for therapy	Prior treatment history	Treatment leech Therapy details	Hematology	Medications	Favorable outcome?	Infection following therapy?	Additional information	Species	Post-treatment leech details
Roche et al. 2012 ¹⁹ , 22399258	22	28	M	Belgium	Penile replantation	Prophylactic low molecular weight heparin given before post-operative but prior to therapy	Leech therapy started post-operative day 1 every 6–8 h for 4 days	Not discussed	Not discussed	Yes	No	3 days after leech therapy, moderate wound mal-union necrosis presented on ventral side of penis; POD 21- urethral fistula [suprapubic catheter Tx for 4 weeks]; normal functioning/sensation by 18 months	Not discussed	Not discussed
Mineo et al. 2004 ²⁰ , 15134999	23	32	M	USA	Penile replantation	no prior treatment	6 treatments of 3 leeches over 20 h, spontaneous neous detachment q3–4 h	Hematocrit monitored stable throughout	Cefazolin and bacitracin ointment	Yes	No	Edema resolved at day 10, necrosis req some debridement, non-micro-surgical	<i>Hirudo medicinalis</i>	Not discussed

Table 1 (continued)

Manuscript details		Patient details				Leech details							
Author(s), year, PMID score	CARE score	Demographics	Indications	Treatment	Outcomes	Additional information	Species	Post-treatment leech details					
Age	Sex	Country	reason for therapy	leech Therapy details	Favorable outcome?	Infection following therapy?							
Years or as noted				Hematology	Medications								
			Prior treatment history										
Philip et al. 2003 ²¹ , 12656920	18	M	UK	Penoscrotal edema	no prior treatment	Area cleaned with soap and water, placed and normally released after engorge-ment (15–40 min), puncture sites continued to drain the next 6–10 h. Repeated daily for 6, 11, and 15 days	Hgb monitored stable throughout no dec >5%	Not discussed	Yes	No	Primary benefit was drainage from puncture	<i>Hirudo medicinalis</i>	Not discussed
Goessl et al. 1997 ²² , 9224347	20	56	M	Germany	Scrotal hematoma	No prior treatment w/puncture or surgery due to diffuse tissue layer spread of hematoma	12 days; 70 total leeches, 5–7 daily	No significant decrease in Hgb throughout treatment	Not discussed	Yes	No	1.5L scrotal hematoma	Not discussed

Table 1 (continued)

Manuscript details		Patient details				Leech details								
Author(s), year, PMID score	CARE score	Age Years or as noted	Sex	Country	Indications reason for therapy	Prior treatment history	Treatment leech Therapy details	Hematology	Medications	Favorable outcome?	Infection following therapy?	Additional information	Species	Post-treatment leech details
Pantuck et al. 1996 ¹ , 8973688	23	37	M	USA	Penile replantation	Post-operative aspirin but leech therapy first line for venous congestion	1–2 leeches added daily to distal third until sated (20–45 min) no signs of venous congestion at 5 days and treatment stopped	4 g/dL drop in Hgb but no transfusion required	IV antibiotics unspecified	Yes	No	Swelling improved, required debridement	<i>Hirudo medicinalis</i>	Discarded in 70% alcohol as medical waste
Lafolla, 1995 ⁵ , 7595772	24	18 h	M	USA	Glans penis congestion after bladder extrophy repair with penile lengthening and pelvic osteotomy	Prior to leech therapy, venous engorgement by bilateral incisions after dilute heparin to glans was unsuccessful	Leech therapy started post-operative day 2, 6 leeches over 5-h period, stored in physiologic saline, attachment facilitated by nick with 22-gauge needle. ooze of blood from sites occurred up to 24 h after therapy	Hematocrit 40% before and 26% after procedure. 10ml/kg pRBC given during procedure and again 10 mL/kg pRBC given after 20ml/kg was given over 48 h after procedure, raising Hct to 38%. Normal coag studies prior, after PTT was 85 sec and corrected with post-op 10ml/kg FFP	Cefazolin and gentamicin given for 72 h after procedure	Yes	No	Failed initial tx bilateral incisions after injection of dilute heparin solution into glans penis; given total of 40 mg/kg packed RBCs to control Hg levels; given 10 mg/kg FFP due to increased PTT	<i>Hirudo medicinalis</i>	Engorged leeches were killed with immersion in isopropyl alcohol and discarded as biohazard waste

Table 1 (continued)

Manuscript details	Patient details				Leech details									
	Author(s), year, PMID	CARE score	Demographics	Indications	Treatment	Outcomes	Additional information	Species	Post-treatment leech details					
		Age Years or as noted	Sex	Country	Reason for therapy	Prior treatment history	leech Therapy details	Hematology	Medications	Infection following therapy?	Favorable outcome?			
Isgar and Turner, 1989 ²³ 2611633	16	81	M	UK	Scrotal hematoma s/p bilateral hydroceles/ epididymal cysts	Intraoperative 200 ml blood evacuated from scrotum, tissue remained tense	Applied to scrotum until engorged with blood (approx. 20 min). Process was repeated 6 days daily with 6 leeches per day	Not discussed	Not discussed	No	Yes	Not discussed	Not discussed	Leeches were placed in 6% solution for 2min, where blood was regurgitated, and placed in individual tanks containing rainwater.

(7.6%) for refractory priapism. The remaining three cases (23.1%) treated penoscrotal edema in patients with hormone refractory prostate carcinoma treated with radical radiation therapy.

Medicinal leech therapy was the first and only treatment reported for urological indication in 10 of the 13 urological cases (76.9%) (Table 1). One case reported a scrotal hematoma refractory to intraoperative evacuation during a bilateral hydrocele procedure. The other case documented an attempt to relieve glans venous congestion status post-bladder exstrophy and epispadias repair by bilateral incision after dilute heparin injection to the site. The two cases that resorted to leech therapy reported clinical improvement of blood congestion.

3.4 Infection prophylaxis

Of the 13 cases, seven (53.8%) reported the use of an antibiotic for each patient prior to medicinal leech therapy. The most common prophylaxis antibiotic was in cephalosporin class (cefazolin, ceftriaxone, or ceftazidime) and was used in at least six of the seven cases. Regarding the case in which a cephalosporin was not reported, the patient was treated with an intravenous antibiotic that was not disclosed. Of the cases that reported antibiotic prophylaxis, cefazolin was used four times (57.1%), ceftazidime was used once (14.3%), and ceftriaxone was used once (14.3%). In addition to the cephalosporins, some cases augmented antibiotic therapy with gentamicin, cefepime, ciprofloxacin, or amoxicillin.

3.5 Medicinal leech therapy treatment course and outcome

Each of the 13 cases varied in leeching with regard to the area of engorgement, age of the individual, and severity of condition (Table 1). The number of leeches used varied from 1 to 3 at a time. The total duration of leech therapy varied from 5 h for an infant, twice, with willing detachment, to 15 days for an adult. Leeches were reported to feed for 15 min to an hour before willingly detaching.

All 13 cases (100%) reported some clinical improvement from leech therapy and no post-procedural infection. For venous congestion and hematoma cases, the therapeutic benefit was that of decreased volume of displaced blood. Regarding the case that documented leech therapy for the management of priapism, the patient reported decreased pain despite the persistence of cavernosal swelling. The three cases that utilized leech therapy for penoscrotal edema reported significant decreases in swelling, noting the primary benefits were serous fluid drainage from leech puncture sites. No complications or side effects were reported from medicinal leech therapy in the nine adult patients. The four postoperative

neonatal patients all required some form of blood product throughout treatment.

4 Discussion

Medicinal leech therapy is widely accepted in plastics and reconstructive surgery as an effective interim method for decreasing venous congestion which would otherwise promote deleterious effects upon tissues [27, 28]. Effective medicinal leech therapy for venous congestion is marked by the return of the targeted tissue to a fleshy, pink skin color from a dusky congested purple color [29]. This review identified that medicinal leech therapy has had such efficacy, in the urological context, in cases of penile replantations and exstrophy/epispadias repairs, while the other urological indications likely involved different therapeutic mechanisms (Table 1). The results of this review suggest that medicinal leech therapy is valuable in urology.

The intestinal flora of medicinal leeches contains microorganisms such as species of *Acinetobacter*, *Vibrio fluvialis*, and *Aeromonas hydrophila* that can cause a wide variability of infections, some antibiotic-resistant, ranging from superficial infections to bacteremia with resultant septicemia [30, 31]. Antibiotic prophylaxis is used before leeching to decrease the risk of infection [3]. Quinolones and third-generation cephalosporins are commonly used as prophylactic antibiotics, in addition to aminoglycosides, tetracyclines, and sulfamethoxazole-trimethoprim [5, 9, 32]. Although initially used as the antibiotic of choice, quinolones, specifically ciprofloxacin, are falling out of favor due to the emergence of resistant strains of *Aeromonas* [32, 33]. Double antibiotic therapy, rather than monotherapy, has been shown to decrease chances of infection [34]. Furthermore, in addition to allergic reactions that might be attributed to antibiotics, allergic reactions, ranging from minor local reactions to anaphylaxis, may be attributed to leeches [35].

Recommendations for antibiotic prophylaxis include administering antibiotics at least 60 min before leech application, continuing antibiotics during treatment, and discontinuing antibiotics 24 h after completion of leech therapy [36, 37]. If eschar or open wounds are present, antibiotic therapy may be discontinued once the wounds are closed [36, 38].

In addition to the direct prophylactic treatment of patients, the prophylactic treatment of leeches, including external decontamination and internal sterilization of the leech digestive tract has also been performed in order to decrease the risk of infections among patients [29, 33, 34]. Aydin et al. [39] noted that the use of hydrochloric acid showed suppression of oral leech flora; though, there was a significant decrease in the sucking duration of leeches. Litwinowicz and Blaszkowska studied leeches that were

artificially fed ciprofloxacin and cefotaxime, with results showing undetectable levels of *Aeromonas* species in the gut and preservation of leech functionality [32]. Despite the potential utility of the prophylactic treatment of leeches, no cases assessed in this study reported any antibiotic pre-treatment or external sterilization performed on leeches as a prophylactic measure. Regardless of antibiotic prophylaxis among patients and/or leeches, it has been advised that immunosuppressed individuals should avoid leech therapy due to the increased risk of infection [40].

Another complication of medicinal leech therapy is acute blood loss anemia. Resultant anemia may require blood transfusions. Accordingly, it is important to monitor hemoglobin levels and replace blood components as needed during leech therapy to prevent hypovolemia or excessive blood loss. Before initiating therapy, anticoagulants must be held and patients should be screened for hemophilia and severe anemia, as these are contraindications to leech therapy [40]. As revealed in this review, adults did not have significant changes in hemoglobin concentration while neonates required numerous blood products throughout medicinal leech therapy.

While some of the urological cases were reconstructive in nature, others were not and, accordingly, may have different mechanisms of therapeutic benefit. Specifically, the case series using leeches for the management of penoscrotal edema noted that the punctures produced by the leeches were the effective components of the therapy. Future research should compare leech punctures to instrumentation punctures to assess relative effectiveness.

The case that documented the utilization of leech therapy for priapism did not offer conventional benefit aside from analgesia. For ischemic priapism, it is recommended to first aspirate the corpora cavernosa with or without irrigation, and to inject phenylephrine to the site [41]. It is important to note that first-line therapy was not delivered prior to the application of medicinal leech therapy and that the priapism did not resolve. One possible reason for the ineffectiveness of leech therapy in the case of priapism is the inability to puncture the thick tunica albuginea layer responsible for venous-occlusion in erection. Although the case reported unsuccessful penile detumescence, the patient reported decreased pain. Although the exact mechanism is unknown, leech therapy has been observed to provide analgesia [42].

This study provides a reproducible systematic review of the literature regarding medicinal leech therapy in the context of urology. However, the analysis is limited by the paucity of publications. The information and generalizability of the systematic review is capped to the 13 published cases. By collecting the available literature and

comparing indication, methodology, and outcomes, clinicians can utilize the information for future application in practice when indicated.

5 Conclusion

This study provides a reproducible review of the literature regarding medicinal leech therapy in the context of urology. The review of the cases, though limited in number, suggests that medicinal leech therapy is a favorable treatment option for individuals with varied urological pathologies and that leeching may improve post-surgical outcomes in the urological setting. Venous congestion was adequately relieved in the reconstructive cases such as penile replantation and exstrophy/epispadias. Further research is recommended to determine the benefits of medicinal leech therapy in scrotal hematoma, penoscrotal edema, and priapism. Though cases are limited, the results of this study suggest that medicinal leech therapy in the urological setting is a viable treatment option and should be utilized when appropriate.

Abbreviations

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
CARE	CAsE REports

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Author contributions

The author AB was responsible for the database search collection, data analysis, and interpretation of the results of this investigation. The author NH was responsible for systematic result analysis and interpretation of the data. The author MZ is responsible for the research concept, study design, and interpretation of the data. All authors have read and approved the manuscript.

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Availability of data and materials

The data utilized in this study were retrieved from open access sources Pubmed/Medline.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors have no competing interests, conflicts of interest, or relevant financial disclosures. All authors have met criteria for authorship and ethical adherence.

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