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Research Article

Hirudotherapy in Orthopedics and Traumatology: Experiences from 21 cases

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Abstract

Introduction: Hirudotherapy is an important integrative medicine application used with different indications and on a daily basis since ancient times. Herein aimed to present the clinical results of hirudotherapy in orthopedic trauma cases.

Patients and Methods: Twenty-one patients treated for extremity crush injuries accompanied by tissue loss between December 2017 and December 2020 and treated with surgery combined with hirudotherapy were included in this prospective study. The number of leeches used, demographic, clinical, and microbiological details were retrospectively analyzed to compare the postoperative clinical and functional results of the hirudotherapy.

Results: The mean age of the patients was 39.2 and the female to male ratio was 4:17. All patients underwent an average of 1.3 sessions of hirudotherapy per day. An average of 1 leech/9 cm^2 was applied. Each session lasted an average of 21 minutes. Complications of hirudotherapy (infection, wound site and/or general allergy, etc.) were not encountered in any patient. Leech phobia was not observed in any of the patients before the application and did not develop after the application during the clinical follow-up.

Conclusion: The use of hirudotherapy for crush injuries shortens the patient's stay in the hospital, prevents soft tissue loss, and improves survival in flap surgery performed for tissue defects. Despite the fact that it is not ethically appropriate to perform controlled, double-blind, prospective, patient-based hirudotherapy studies to obtain evidence-based results, the benefits of hirudotherapy in clinical practice are apparent.

Keywords: Leech; Hirudotherapy; Flap; Trauma; Open Fracture

Introduction

Hirudotherapy is a significant application of traditional and complementary medicine that has been utilized for many causes and on a daily basis since antiquity. In cases where the venous anastomoses are not able to fully reduce arterial load, such as in compartment syndrome, crush syndrome, and replantation cases, hirudotherapy is commonly used to develop tissue viability in orthopedic trauma surgery. Medical leeches' active blood sucking produces 1/10 atm negative pressure, which results in an increase in venous return and a reduction in high venous pressure[1]. In addition, some important biochemical agents in the leech's saliva (acetylcholine and histamine-like molecules, which increase blood flow; saratin, calin, apyrase, and decorsin, which inhibit platelet functions; and hirudin, gelin, factor Xa inhibitor, destabilase, new leech protein-1, whitide, and whiteman in, which have an anticoagulant effect) play a complementary role in maintaining tissue viability in addition to the mechanic reduction in venous load performed by the leech [2].

Venous congestion and secondary thrombosis are potentially fatal consequences of reconstructive orthopedic trauma procedures, which frequently involve flap surgery and/or major or minor replantation. One of the first uses of leeches for postoperative venous congestion was in the early 19th century by Dieffenbach [3]. In this respect, the first detailed international manuscript was published by Derganc., *et al.* in 1960, which describes the outcomes of a 20 case series [4]. Objective proof of the improvement in blood flow has been obtained with Doppler studies by Hayden [5]. Some randomized animal studies have proven that leech applications increase flap perfusion and are superior to other methods of treatment used to improve drainage along with normal blood supply [6-8].

Despite all of the literature on hirudotherapy, the number of clinical double-blind controlled studies is inadequate and this seems unlikely to change in the near future because there are serious limitations regarding the feasibility of randomized controlled trials. It is highly difficult to standardize the selection of indications and treatment approaches for postoperative venous congestion, which is one of the most significant restrictions. Moreover, since leech therapy is an accepted and practiced treatment method, failure to present this treatment to the patients in a control group in

a study or to conceal the treatment from the patients would be ethically indefensible. As a result, this type of study, i.e., controlled-double blind, will probably not be carried out. This is similar to the situation of operations with numerous surgical indications where treatment is considered the gold standard of care, even though the optimal treatment defined by evidence-based medical criteria is devoid of high-level evidence.

The purpose of this study was to investigate the clinical efficacy of hirudotherapy in cases of orthopedic trauma.

Patients and Methods

Twenty-one patients who were treated at the Tertiary Level Trauma Hospital Orthopedics and Traumatology Clinic between December 2017 and December 2020 for extremities crush injuries accompanied by tissue loss and who were treated with surgery combined with hirudotherapy were included.

Prior to enrollment, all patients provided informed consent, and the study was conducted in conformity with the Helsinki Declaration's principles.

The leeches were supplied by the Hirudotherapy Department of the Turkish Republic Health Ministry's Complementary Medical Center in Kayseri and were implemented by the corresponding author of this manuscript certified orthopedic surgeon. The leeches were applied in every patient using the same protocol, provided by the Health Ministry. They were sourced from the HirudoTM Medical Leech Farm, which holds certificates from CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora) and the Turkish Republic Health Ministry. This protocol is summarized and explained step by step below.

Preparation of the application area

First the surgeon cleans the application area with sterile, heated heparinized saline to increase vasodilation and promote continued bleeding. Afterwards, any surgical or dressing residue, iodine, alcohol, ointment, etc., is removed from the application area. Although theoretically only iodine prevents leech adhesion, the presence of other chemicals often causes leech therapy to yield inefficient results. A leech tube is moistened with sterile serum water and then held in close proximity to the cleansed area, with the hole positioned above the desired location. This will prevent the leech from leaving the region by forming a barrier. In some instances, it is necessary to pierce the application site with a hypodermic needle to stimulate the animal to latch on.

Waiting and observing the leeches

The orthopedic surgeons, certified by the Health Ministry, wait until the leeches are sated with blood. This is often but not always indicated by a doubling of the size of the leech.

Ending the hirudotherapy application and handling

The leech should always be picked up gently with care and should not be forcibly removed. Plain soft forceps should be used to steer the leech's head. Once hooked, the leech will remain in place until it is completely expanded (max 20-40 min). Once satiated, the leech will detach. Throughout the application time, it is crucial to monitor the wound site to verify that the leech has not migrated or detached prematurely, which could result in the aforementioned issues.

Disposal of leeches

After use, leeches must be kept fully separate and clearly labeled. They must never be reused. Leech waste is considered clinical waste. They cannot be flushed or disposed of in a sink or toilet. Each leech should be placed in a special disposable screw-capped tube containing 10 mL of 12% ethanol. The tube should be placed into a special biohazard box to be disposed of in a biohazard facility.

Wound care after the leech application

Each bite is encouraged to bleed continuously by removing any clots that form at regular intervals, on average 2-5 times over 20 minutes. Then the wound is dressed according to its characteristics.

General considerations

Patients receiving leech therapy were required to have their total blood count monitored at least daily. We did not order any particular antibiotics during the leech therapy but all the patients to whom we applied hirudotherapy were trauma patients and they were all receiving IV antibiotherapy treatment in consultation with an infectious disease specialist.

Statistical analysis

All data were analyzed by SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL, USA). In the statistical evaluation of the data, the independent t-test was used for the determination of the mean/median differences. The Mann–Whitney U test was used for those who did not fit the normal distribution. The chi-square test was used to compare the categorical variables. The exact chi-square test was used in the boxes in the software because there were fewer than five values. Compliance with the normal distribution was assessed by Shapiro-Wilk test. Mean, standard deviation, and median (min-max) were used as descriptive statistics.

Results

Eleven of the patients in our study who were treated and follow-up prospectively had complex upper extremity injuries, whereas ten had complex lower extremity injuries. Of the upper extremity injuries, 4 required multiple minor replantations and 2 required revascularizations, while one involved compartment syndrome due to a snake bite and the rest involved tissue loss with/out fractures repaired with various flaps. All flaps used at the upper extremity were pedicle flaps (Table 1).

S. No	Age & Gender	Additional Morbidity	Diagnosis	History	State of Trauma	Treatment	Reconstructive Solution	Clinical Infection	Survival of Flap or Replantation (%)	Start of leech therapy (hours)	Length of leech therapy (day-average minutes per session)	Blood Transfusion Requirement after surgery-unites	Leech Session (average per day)
1	34M	None	Minor Replantation	Chopping knife	Suitable for replantation and/or revascularization indication	Replantation of right-hand index finger	Replantation or revascularization	None	100	6*	6-14	None	2
2	47M	None	Crush Injury with fracture and tissue loss	Traffic Accident	Right supracondylar T-Y humerus Gustillo-Anderson type 3B open fracture with antecubital 7 x 4 x 5 cm tissue defect	Open Reduction and Plate Fixation & retrograde flow radial forearm flap	Pedicle Flap	None	100	12	3-24	1	1
3	16M	None	Re-vascularization	Chopping knife	Suitable for replantation and/or revascularization indication	Revascularization of left-hand index and middle finger	Replantation or revascularization	¥	100	4*	8-12	None	2
4	42M	None	Compartment Syndrome	Snake bite	Intensive care follow-up	Left hand and forearm multi-fasciotomies	Open wound care and primary closure	None	100	14	6-18	1	2
5	44M	HypoT	Open Fracture with tissue loss	Traffic Accident	Right tibia 1/3 distal Gustillo-Anderson type 3C open fracture with lateral malleolus 4 x 5 x 4 cm tissue defect	Closed Reduction External Fixation with propeller flap	Pedicle Flap	None	≥80	24	10-15	2	0.5
6	45F	None	Crush Injury with tissue loss	Traffic Accident	Right hand dorsum 8 x 6 x 2 cm abrasion type tissue necrosis	Ext. Tendons reconstruction & radial forearm flap	Pedicle Flap	¥	100	16	5-25	1	1.5
7	38M	None	Minor Replantation	Circular electrical saw	Suitable for replantation and/or revascularization indication	Replantation of right-hand thumb and index finger	Replantation or revascularization	None	100	8*	12-17	1	1.5
8	34M	None	Fracture with Compartment Syndrome	Traffic Accident	Calcaneus open fracture with loss of tissue over heel 4 x 3 x 5 cm and Lisfranc (mid-foot) joint dislocation with multiple metatarsi proximal fractures	Open reduction to Lisfranc joint and internal fixation with K-wires, fasciotomy on foot, plate fixation to calcaneus fracture and sural retrograde flow flap to tissue defect on heel.	Pedicle Flap	None	≥80	13	14-21	2	1

9	39M	None	Crush Injury with fracture	Traffic Accident	Right hand thump pulpal defect 1,2 x 2 x 1 cm	Distal phalanx close reduction and internal K-wire fixation with First dorsal metacarpal artery flap	Pedicle Flap	None	100	4	4-14	None	1
10	30M	None	Open Fracture with tissue loss	Traffic Accident	Right tibia shaft Gustillo-Anderson type 3B open fracture with anterior 4 x 5 x 4 cm tissue defect	Open Reduction and External Multiaxial Fixation with Anterior Lateral Thigh Flap to cover the open bone.	Free flap	None	100	15	8-18	4	1.5
11	32M	None	Minor Replantation	Circular electrical saw	Suitable for replantation and/or revascularization indication	Replantation of right-hand thumb and index finger	Replantation or revascularization	None	100	10*	14-21	1	1.5
12	36M	None	Open Fracture with tissue loss	Traffic Accident	Left elbow olecranon Gustillo-Anderson type 2 open fracture with the loss of joint coverage 6 x 4 x 6 cm tissue loss	Closed Reduction and External Fixation with latissimus dorsi musculocutaneous flap	Pedicle Flap	None	100	16	8-25	3	1.5
13	44M	None	Crush Injury with fracture and tissue loss	Traffic Accident	Right tibia shaft Gustillo-Anderson type 3B open fracture with anterior 5 x 5 x 4 cm tissue defect	Open Reduction and External Multiaxial Fixation with Anterior Lateral Thigh Flap to cover the open bone.	Free flap	None	100	15	8-18	4	1.5
14	52M	None	Crush Injury with tissue loss	Motorcycle Accident	Left shoulder musculus deltoideus anterior area total loss with open joint due to drifting on road	Pectoralis major musculocutaneous flap	Pedicle Flap	¥¥	≥80	24	12-18	2	2
15**	48M	None	Minor Replantation	Chopping knife	Suitable for replantation and/or revascularization indication	Replantation of left-hand index finger	Replantation and / or revascularization	None	0 (amputated)	5*	8-15	None	1.5

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16	25 M	None	Compartment Syndrome	Ext CM	Acute compartment syndrome	Right hand and forearm multi-fasciotomies	Open wound care and primary closure	None	-	6	10-16	2	1
17	54F	HT,	Compartment Syndrome with tissue loss	Ext CM	Acute compartment syndrome with acute renal failure	Left hand and forearm multi-fasciotomies	Open wound care and primary closure	None	-	6	10-16	2	1
18	34M	None	Re-vascularization	Chopping knife	Suitable for replantation and/or revascularization indication	Revascularization of left-hand index and middle finger	Replantation and / or revascularization	None	100	5*	6-23	None	1
19	58M	HT, DM	Fracture with Compartment Syndrome	Motorcycle Accident	Right tibia shaft Gustillo-Anderson type 3B open fracture with anterior 4 x 5 x 4 cm tissue defect	Open Reduction and External Multiaxial Fixation with Anterior Lateral Thigh Flap to cover the open bone.	Free flap	None	100	15	8-18	4	1.5
20	32M	None	Crush Injury with Compartment Syndrome	Motorcycle Accident	Left tibia crush under the heavy material with acute compartment syndrome	Left tibia and foot multi-fasciotomies	Open wound care and primary closure	¥¥	-	6	10-16	1	1
21	39M	None	Open Fracture with tissue loss	Motorcycle Accident	Right tibia shaft Gustillo-Anderson type 3C open fracture with anterior 5 x 6 x 4 cm tissue defect	Open Reduction and External Multiaxial Fixation with Anterior Lateral Thigh Flap to cover the open bone.	Free flap	None	100	15	8-18	4	1.5

Table 1: Patients' Characteristics.

*: In all replantation and revascularization cases; first leech application was performed right after the surgery finished in operation room.

**: In case 15, replantation was not successful and final decision was amputation to the index finger.

Abbreviations: F: Female; M: Male; p/y: Pack/Year; DM: Diabetes Mellitus; HypoT: Hypo Thyroiditis; HT: Hypertension;
Exv CM: Extravasation of Radiological Contrast Material; ¥: Pseudomonas spp Treated with IV Antibiotics; ¥¥: S. Aureus Treated with IV Antibiotics

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All of the lower extremity injuries were crush injuries accompanied by fracture and secondary compartment syndrome with crush injuries accompanied by tissue defects. The most affected anatomical region was the tibia, mainly due to open fractures.

The mean age of the patients was 39.2 and the female to male ratio was 4:17. Each patient underwent 1.3 sessions of hirudotherapy on average per day. An average of 1 leech/9 cm^2 was applied in each session. Blood transfusions were necessary in 16 patients (76%) (mean 3.2 units, range 0-4 units). Each session lasted 21 ± 4.2 minutes.

Secondary finger loss was encountered in one minor replantation, case 15, due to venous congestion. In 4 cases minor infections were detected but they were successfully treated with intravenous antibiotics. A nosocomial pathogen was detected in all four patients' wound cultures that was sensitive to second generation cephalosporins. Full recovery was achieved in all cases of infection with appropriate antibiotic treatment. In one Gustilo-Anderson type 3B open fracture patient, tibial pseudarthrosis was seen during the follow-up period. Revision surgery for the pseudarthrosis was performed. When examined retrospectively, it was seen that union had been achieved. No secondary complications of hirudotherapy (infection, wound site and/or general allergy, etc.) were encountered in any patient followed up in our study. Leech phobia was not observed in any patient before the application and it did not develop after the application during the clinical follow-up.

Discussion

Hirudotherapy is widely used in reconstructive surgery and replantation cases to prevent venous congestion. The two most common indications for hirudotherapy are cutaneous pedicle and/or free musculocutaneous flaps, described by Derganc., *et al.* [4], and replantation, clearly defined by Foucher., *et al.* [9]. Since then how hirudotherapy should be used and in which patients with before which conditions in reconstructive surgery and microsurgery have become much clearer. When the indication is obvious, use of leeches should always be considered as an effective solution for venous congestion when flaps or replantation have been used. Graham., *et al*. reported that when replantation was performed in 125 cases there was only a 27% salvage rate in replanted digits exhibiting venous congestion postoperatively [10]. In that study, leeches were not used. When utilizing leeches frequently, Foucher., *et al.* found an overall salvage rate of 55-60% [9]. Although it is impossible to verify conclusively, a number of these failed replantations would not have occurred if leeches had been used.

Despite their undeniable therapeutic efficacy, leeches are not the solution to all postoperative issues. This is especially true for the treatment of clogged free-tissue transfers. Our experience with the use of leeches on free anterior thigh flaps is comprehensive and extensive. In free flaps with a venous drainage problem, the therapy of first choice should be re-exploration of the anastomosis, and the treatment of second choice, if practicable, should be leech application. In our free flap instances, the initial hirudotherapy sessions are performed immediately following the anastomosis in the operating room.

Experimental evidence reveals that venous supercharging employing additional routes of venous drainage can have a statistically significant advantage, with a correlation between the number of venous outflow routes and the survival of free flaps and the reduction of venous congestion occurrence [6,7]. Based on our clinical experience, hirudotherapy should be at the top of the list of these additional routes of venous drainage. The use of a secondary vein in the drainage of a free flap can significantly reduce the incidence of venous congestion without having a significant effect on the incidence of complete flap failure and overall takebacks, according to a second retrospective review of 564 consecutive free flaps performed at a single institution [11]. In another big case series, it was established that the use of a secondary vein does not appreciably lengthen the duration of an operation [12]. If as promised in that large clinical experience of free flaps, supercharge does not increase the operative time, it is probably responsible for some of the cases requiring re-exploration of the anastomosis, because when the number of anastomoses increases it is obvious that the surgical team has developed some hesitations after the first observation of venous congestion even if it has occurred due to the patient's lying in a wrong position in bed.

Although blood transfusions were required in our cases and were necessary for all four free flap patients, none of the replantation cases required them. Clearly, the necessity for transfusion will depend on the comorbidities of the patients and the type of the surgical procedure. However, the use of leeches increases the danger of bleeding significantly. In the majority of instances, excessive bleeding can be effectively managed with direct pressure and topical thrombin. During leech therapy, it is reasonable to monitor hemoglobin daily, especially in children [13]. Previous research has demonstrated that any combination of anticoagulant treatment and leech use significantly increases the requirement for blood transfusion [14].

Leech therapy was started in the first 4-12 hours in all our clinical cases. The relationship between the commencement of leech therapy and outcome needs to be discussed because conducting a study that can reveal the results of this comparison will not be possible in the future and was not possible in the past due to ethical concerns. It has been hypothesized that leech therapy should be initiated at the first sign of outflow obstruction [12], however, to the best of our knowledge, there is no conclusive evidence that a reasonable delay in application has an effect on the outcome.

In general, the volume/number of leeches used per unit of reconstructive surgery, the time of initiation, the duration of administration, and the number of leeches used in the patient and/or flap area reflect a tremendous variety of ideas and practices but there is little in the literature in this regard. Based on our experience, it is not possible to make a generic statement such as 'leeches should be applied every 6 hours', even if this is based on an evidence-based medical point of view. However, evidence in the literature suggests that more than 90% of passive bleeding occurs within 5 hours [15-17]. Based on that finding, we perform the first application on average after 8 hours according to the type of case and the surgeon's predictions of the operation. The question we most frequently encounter is how many leeches are used and how often they are used. There is no definite or satisfactory answer to this question. There is no clear answer to those questions in the literature either and a wide range of regimens are used. Another issue is the length of leech application in a session and treatment length. In our series, the average length of leech application in a session was 14 minutes and the treatment lasted 6.2 days (range 3-14). When leeches are the only source of venous outflow, it is obvious that their use should continue until inoculation occurs. On the basis of experimental animal models, this process takes 3 to 5 days; however, limited clinical data suggest that 6 to 10 days are necessary [12]. According to a previous meta-analysis, the average duration of leech therapy is 4.2 days [19].

Our practices are still evolving and we are still learning. However, it will not be possible to use any standard leech treatment protocol that might be expected in the near future for flap or replantation cases.

There were some limitations of this study. Firstly, this hirudotherapy was applied by the same surgical team that operates on and clinically follows up all patients. Secondly, a control group could not be included due to the ethical concern mentioned above. Lastly, but most critically, patients and characteristics of hirudotherapy, the volume/number of leeches used per unit of reconstructive surgery, the time of initiation, the duration of administration, and the number of leeches cannot be optimized homogeneously. In addition, the findings of this paper will encourage orthopedic surgeons to apply and popularize hirudotherapy for reconstruction cases. Therefore, planning new studies that are multicentric and different in etiology will contribute to clarifying the reliability and practicability of hirudotherapy.

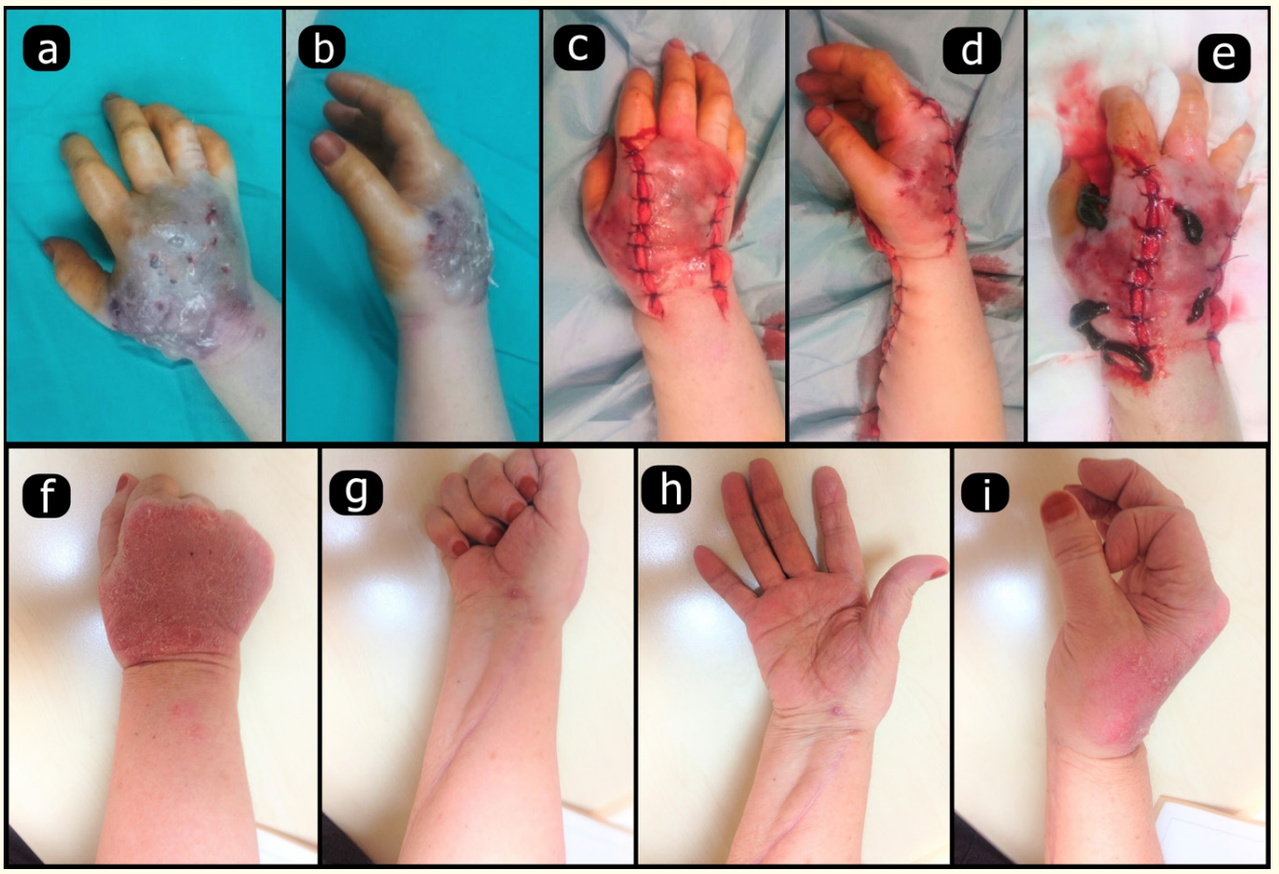

Figure 1: Clinical Presentation of Case 17; Extravasation of radiological contrast material leads to Compartment Syndrome of hand and forearm.

a, b: Preoperative views of the case AP and lateral, respectively. **c, d:** Early postoperative views of the case just after faciatomy of hand and forearm. **e:** The view of first hirudotherapy application in operating theatre. **f, g, h. and i:** Postoperative functional view of the case at 6th week before rehabilitation.

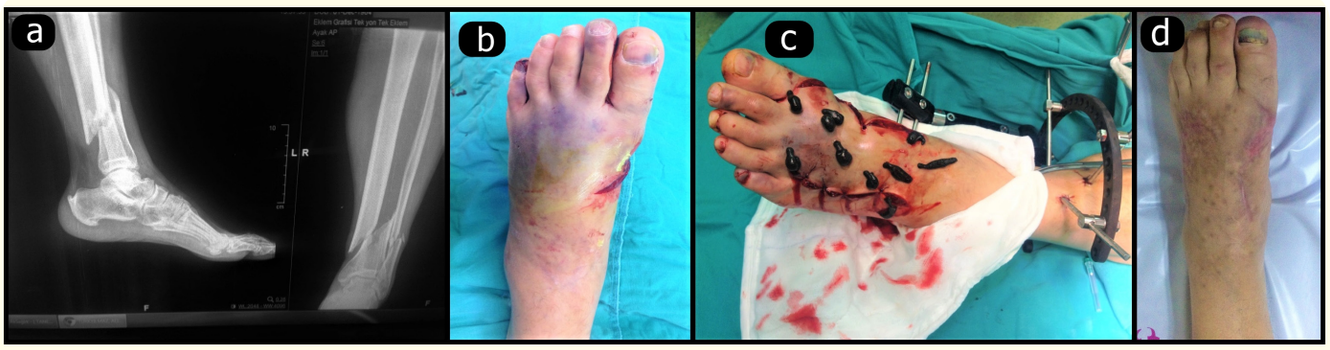

Figure 2: Clinical Presentation of Case 19; Crush injury of foot and ankle leads to Compartment Syndrome.

a: Preoperative radiological view of the lower extremity. **b:** Preoperative clinical view of the foot. **c:** Intraoperative hirudotherapy application after faciatomy of the foot and closed reduction and external fixation of the fracture. **d:** Postoperative view of the case at 9th weeek.

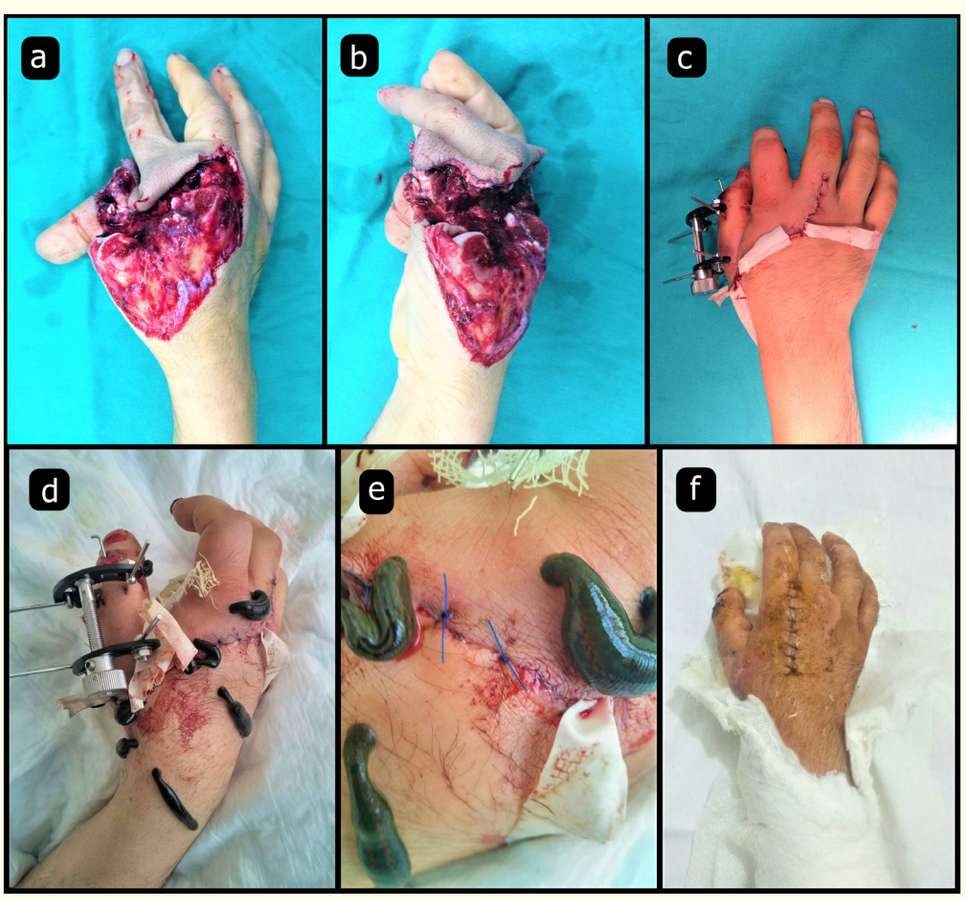

Figure 3: Clinical Presentation of Case 11; Crush injury with ossilated saw, thump and index finger replantation.

a, b: Preoperative views of the case AP and lateral, respectively. **c.** Early postoperative views of the case just after the replantation operation. **d, e:** The view of first hirudotherapy postoperatively at 8th hour. **f:** Postoperative functional view of the case at 3rd week before rehabilitation.

Conclusion

The use of hirudotherapy in crush injuries shortens the patient's hospital stay, minimizes the occurrence of soft tissue problems, and enhances the patient's chances of surviving flap surgery conducted for tissue abnormalities. Despite the lack of high level of evidence-based support in the literature for flap surgery, compartment syndrome, and minor or major replantation, hirudotherapy applied during those surgical procedures will be complementary, morbidity reductive, and adjunctive.

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Conflict of Interest

None of the authors have any conflict of interest.

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