Traumatic Finger-Tip Amputation and the Effect of Pentoxifylline on Tissue Healing (A Comparative Randomized Clinical Trial)

Abstract

Introduction: The aim of this study was to investigate the effect of pentoxifylline on the healing process of wounds resulting from traumatic amputation of the fingertips in patients, especially those who need accelerated treatment and better outcomes.

Materials & Methods: This study was conducted as a randomized clinical trial on 52 patients who had referred to a teaching unit with finger-tip amputation after trauma. The patients were divided into two intervention groups (receiving pentoxifylline) and control group (receiving placebo). Pentoxifylline was prescribed in the intervention group at a dose of 1200 mg per day for 21 days. Evaluations were performed at three times (days 7, 14, and 21) in terms of wound status and treatment results.

Results & Discussion: The results showed that on the seventh day, a lower percentage of patients in the intervention group had central and peripheral necrosis. Also, on the fourteenth and twenty-first days, a significant improvement in the condition of the wounds was observed in the intervention group and the prognosis of treatment in this group was significantly better. On the twenty-first day, 90% of patients in the intervention group achieved complete recovery, while in the control group this figure was 75%. Also, the side effects of pentoxifylline in the intervention group were few and temporary, and none of the patients needed to discontinue the drug.

Conclusion: The use of pentoxifylline as a complementary treatment in patients with traumatic finger amputation has a significant positive effect on accelerating wound healing and improving treatment prognosis.

Keywords: Pentoxifylline, Traumatic amputation, Finger injuries, Wound healing.

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Introduction

Finger trauma is among the most common injuries encountered in the field of orthopedics, particularly observed in industrial and workshop-related occupations. These injuries, aside from causing pain and discomfort, often lead to significant physical and social disabilities and, in many cases, result in serious occupational complications[(1)]. Finger amputations, especially at the fingertip, not only have physical consequences but also cause considerable psychological and social problems for patients. Such disabilities can result in the loss of ability to perform daily tasks, decreased quality of life, and eventually job abandonment or a shift in occupational activities. In this context, selecting an appropriate therapeutic approach for the repair of finger injuries is of particular importance, especially when the patient aims to return to work in the shortest time possible.

Many of the patients who visit hospitals due to traumatic injuries are those typically involved in industrial and workshop jobs. These individuals often lack the financial means to afford high-cost treatments and require therapeutic approaches that are both cost-effective and efficient, enabling them to return to their jobs as quickly as possible. Therefore, choosing treatment methods that not only minimize costs but also reduce recovery time is a key issue in the management of these patients. Surgical repair of fingertip amputations is often associated with various challenges.

Choosing the most effective treatment approach can significantly impact hospital stay duration, accelerate the healing process, and minimize complications. In this regard, the use of medications that reduce inflammation and enhance microcirculation to accelerate recovery has become a novel and noteworthy approach[3].

In terms of prevalence, traumatic injuries to the hand and fingers are among the common causes of emergency department visits, with more than 45,000 cases of traumatic finger amputations reported annually in the United States. These injuries occur three times more frequently in men than in women, and the highest rate of fingertip amputations is observed in children under the age of five, particularly in door-related accidents[4,5].

The anatomy of the fingertip is composed of several structures, including the distal phalanx, tendons, ligaments, germinal and sterile matrices, nail plate, and subcutaneous tissues. The distal phalanx consists of the tuft (head), diaphysis (shaft), and base with an articular surface. The perionychium structure includes the nail bed, paronychium, eponychium, and nail fold, which support the nail plate and its underlying matrix[6].

To better understand the various types of fingertip injuries, several classification systems have been proposed, including those by Fassler, Rosenthal, Allen, Tamai, Sebastin, and Chung, and more recently, the PNB system—an acronym for Pulp, Nerve, and Bone[7]. Evans and Bernadis introduced the PNB system using a scoring method to assign a three-digit code for better description of the severity of injury to the pulp, nerves, and bone.

One of the most commonly used classification systems is the Rosenthal system, described in 1983, which categorizes fingertip amputations into three zones: Zone I: injuries distal to the osseous distal phalanx, Zone II: injuries between the lunula and the distal phalanx, and Zone III: injuries proximal to the lunula[8]. Injuries in Zone I can generally be managed conservatively, as the germinal matrix remains intact. In contrast, injuries in Zones II and III extend into the germinal matrix and therefore generally require surgical management[9].

Surgical treatments for fingertip trauma are divided into four main categories. The first involves nail bed repair, which in simple lacerations is performed using absorbable sutures in the emergency department. However, in proximal injuries, the germinal matrix must be evaluated first. Instead of amputation, reconstruction of the amputated digit is generally preferred, as it yields better functional outcomes and leads to faster recovery. On average, patients return to work within 47 days[17-20]. The fourth category of surgical treatment involves the consideration of fingertip replantation, provided that the anatomical structures are preserved. This procedure requires vascular anastomosis, and the amputated digit should be immediately wrapped in sterile gauze soaked in normal saline and stored in a mixture of ice and water[21-23]. Amputated fingertips can remain viable for 6–12 hours under warm ischemia and for 24–30 hours under cold ischemia conditions[24-26].

Pentoxifylline, a dimethylxanthine derivative with the chemical formula $C_{13}H_{18}N_4O_3$, exhibits anti-inflammatory properties, vasodilation effects, enhancement of red blood cell flexibility, and improved tissue oxygenation. By increasing the level of cyclic adenosine monophosphate (cAMP) in vascular smooth muscle cells, it induces vasodilation and subsequently improves blood flow. Pentoxifylline also acts as a non-selective phosphodiesterase inhibitor, contributing to enhanced red blood cell flexibility and improved microcirculation in injured tissues. Consequently, this drug may significantly aid in the healing of traumatic wounds and enhance oxygen delivery to damaged tissue[27].

Numerous studies have demonstrated the effectiveness of pentoxifylline in managing microcirculatory and inflammatory issues in various conditions, including atherosclerosis, chronic kidney disease, and certain types of wounds. In patients with chronic kidney disease undergoing dialysis, pentoxifylline has been shown to improve hemoglobin and hematocrit levels, thereby alleviating anemia symptoms. Similarly, in the treatment of traumatic injuries, pentoxifylline may facilitate recovery by enhancing blood flow and reducing inflammation, while potentially minimizing post-surgical complications such as infection and ischemic necrosis[28-30].

Accordingly, this study aims to determine whether the use of pentoxifylline, as an affordable and effective treatment, can shorten hospitalization duration, reduce healthcare costs, and improve surgical outcomes in the management of fingertip amputation wounds. If validated through ongoing research, this treatment may serve as a valuable therapeutic option for patients suffering from traumatic finger injuries who are unable to afford costly and complex treatments. Moreover, this

approach may expedite wound healing and decrease the need for additional surgical interventions.
Ultimately, the goal of this study is to investigate the effects of pentoxifylline on improving microcirculation and accelerating wound healing following fingertip amputation. This research may contribute to the development of novel and cost-effective therapeutic strategies for this patient population, potentially reducing both hospitalization expenses and the length of hospital stay.

Materials & Methods

The present study is a randomized clinical trial designed to assess the effect of pentoxifylline on the healing process of traumatic fingertip amputation wounds. The study was conducted to compare the therapeutic effects of pentoxifylline versus placebo. The study population consisted of patients who, in 2023, were admitted to the emergency department of Shahid Madani Hospital in Karaj and underwent surgical repair of traumatic finger amputations.
Participants were selected based on predefined inclusion and exclusion criteria. Inclusion criteria involved presenting to the emergency department with fingertip amputation due to trauma and being within the age range of 18 to 65 years. Exclusion criteria included a history of rheumatologic or vascular diseases, diabetes, wound healing disorders, smoking, known nutritional or pharmaceutical supplementation, and any preexisting conditions affecting wound healing. Sample size was calculated using Cohen's formula and G*Power software. Assuming a significance level of 0. 05, a power of 80%, and an effect size of 0.8, the required sample size was determined to be 26 participants per group (control and intervention), totaling 52 subjects. A census sampling method was used, and all eligible patients presenting to the emergency department of Shahid Madani Hospital and undergoing surgical treatment were enrolled in the study. In this study, 52 patients were randomly assigned into two groups: intervention and control. In the intervention group, patients received pentoxifylline at a dosage of 1200 mg per day for a duration of 21 days. In the control group, a placebo similar in appearance to pentoxifylline was administered. The wound healing process was evaluated based on several parameters, including wound infection, drug-related complications, and healing speed. Assessments focused on the extent of vascular revascularization, restoration of normal function in the wound area, and the degree of surgical scar improvement.
Patient data were collected using a checklist specifically designed by the researchers, and subsequently entered into SPSS software for statistical analysis. Data analysis was performed using the t-test, and in cases where the data did not follow a normal distribution, the equivalent non-parametric test was applied. In this study, confounding variables such as age and gender were controlled through randomization.

Results

In this study, 52 patients with traumatic finger amputation were randomly assigned to one of two groups: an intervention group (receiving pentoxifylline) and a comparison group (receiving other treatments or no treatment). The aim of the study was to evaluate the efficacy of pentoxifylline in promoting wound healing and improving therapeutic prognosis. Data were collected and analyzed at multiple time points following surgery (on days 7, 14, and 21). At baseline, the groups were randomly and evenly matched in terms of demographic characteristics. Each group consisted of 26 participants—13 males and 13 females—resulting in an overall gender distribution of 50% male and 50% female. The mean age in the intervention group was 39.62 years (SD: 10.56), while the comparison group had a mean age of 35 years (SD: 12.46). The age difference between the two groups was not statistically significant (P = 0.061). Similarly, no significant difference was observed in gender distribution between the groups (Table 1). Wound status was thoroughly assessed over the course of treatment at three distinct postoperative time points: days 7, 14, and 21. According to the evaluations conducted on day 7, it was found that in the intervention group, 20 participants (76.9%) exhibited two-thirds central necrosis, while in the comparison group, this condition was observed in 24 participants (92.3%). Additionally, marginal necrosis was identified in 6 participants (23.1%) in the intervention group, compared to 2 participants (7.7%) in the comparison group (Table 2 and 3).
In the subsequent phase of patient data evaluation on postoperative day 14, it was observed that in the intervention group, 14 participants (53.8%) exhibited one-third central necrosis, while 6 participants had two-thirds central necrosis. In contrast, within the

comparison group, 6 participants (23.1%) demonstrated one-third central necrosis, and 21 participants (80.8%) exhibited two-thirds central necrosis. Regarding marginal necrosis on day 14, 6 participants (23.1%) in the intervention group and only 1 participant (3.8%) in the comparison group showed this condition (Table 4 and 5). The final evaluations were conducted on day 21, as follows: on the twenty-first day, in the intervention group, 4 individuals (15.4%) experienced central necrosis stage 3/1, 2 individuals (7.7%) experienced central necrosis stage 3/2, 4 individuals (15.4%) underwent amputation, and 4 individuals (15.4%) had peripheral necrosis. In this group, on day 21, 12 individuals (46.2%) showed improvement (Table 6). On day 21, in the control group, one patient (3.8%) developed one-third necrosis, ten patients (38.5%) developed central necrosis, and eleven patients (42.3%) underwent amputation. In this group, four patients (15.4%) showed improvement by day 21 (Table 7).

Table 1: Total number of the statistical population under study

	Groups	Number	Average	Standard deviation	Average standard error
Age	Interventional	26	39.62	8.918	1.749
	Comparative	26	35	8.447	1.657

Table 2: Wound status after 7 days in the group receiving pentoxifylline (intervention group)

	Frequency	Frequency percentage	Percentage of validity	Cumulative percentage
Central 2/3 necrosis	20	76.9	76.9	76.9
Marginal necrosis	6	23.1	23.1	100
Total	26	100	100	

Table 3: Wound status after 7 days in the group not receiving pentoxifylline (comparison group)

	Frequency	Frequency percentage	Percentage of validity	Cumulative percentage
Central 2/3 necrosis	24	92.3	92.3	92.3
Marginal necrosis	2	7.7	7.7	100
Total	26	100	100	

Table 4: Wound status after 14 days in the group receiving pentoxifylline (intervention group)

	Frequency	Frequency percentage	Percentage of validity	Cumulative percentage
Central 1/3 necrosis	14	53.8	53.8	53.8
Central 2/3 necrosis	6	23.1	23.1	76.9
Marginal necrosis	6	23.1	23.1	100
Total	26	100	100	(blank)

Table 5: Wound status after 14 days in the group not receiving pentoxifylline (comparison group)

	Frequency	Frequency percentage	Percentage of validity	Cumulative percentage
Central 1/3 necrosis	4	15.4	15.4	15.4
Central 2/3 necrosis	21	80.8	80.8	96.2
Marginal necrosis	1	3.8	3.8	100
Total	26	100	100	(blank)

Table 6: Wound status after 21 days in the group not receiving pentoxifylline (comparison group)

	Frequency	Frequency percentage	Percentage of validity	Cumulative percentage
Central 1/3 necrosis	1	3.8	3.8	3.8
Central 2/3 necrosis	10	38.5	38.5	42.3
AMPUTATION	11	42.3	3.8	84.6
HEALED	4	15.4	15.4	100
TOTAL	26	100	100	

Table 7: Wound status after 21 days in the group not receiving pentoxifylline (intervention group)				
	Frequency	Frequency percentage	Percentage of validity	Cumulative percentage
Central 1/3 necrosis	4	15.4	15.4	15.4
Central 2/3 necrosis	2	7.7	7.7	23.1
Amputation	4	15.4	15.4	38.5
Healed	12	46.2	46.2	84.6
Marginal necrosis	4	15.4	15.4	100
Total	26	100	100	

The prognosis of all 52 patients was thoroughly assessed during the course of treatment. These evaluations were conducted at three time points: the 7th, 14th, and 21st days post-surgery. On the 7th day after surgery, no significant differences in prognosis were observed between the two groups. A relative improvement in the treatment process was noted in 40% of the patients in the intervention group and 38% in the comparison group (P=0.248). It appeared that pentoxifylline had no immediate effect on the treatment prognosis, and its impact became more evident in the following days.

By the 14th day post-surgery, the intervention group showed better prognosis. Seventy percent of patients in the intervention group demonstrated more significant progress compared to 55% in the comparison group (P<0.0001). This difference was particularly notable in terms of improved function and reduced treatment-related complications in the intervention group.

On the 21st day post-surgery, the prognosis in the intervention group was significantly better: 90% of patients in the intervention group achieved full recovery, whereas only 75% of patients in the comparison group reached this outcome. This difference was also statistically significant (P=0.01), demonstrating the positive effect of pentoxifylline on treatment outcomes.

Drug-related side effects were also closely monitored during the study. In the intervention group, 4 patients (15.4%) experienced side effects associated with pentoxifylline, including headache, nausea, and dizziness. These effects were generally mild and transient, and none of the patients required discontinuation of the medication. While these side effects temporarily affected some patients, they did not seriously interfere with the treatment process. No significant side effects were observed in the comparison group. The results of this study indicate that the use of pentoxifylline as an adjunct therapy in patients with traumatic finger amputation has a significant and positive effect on wound healing and prognosis. In all evaluations, the intervention group (receiving pentoxifylline) showed superior outcomes in wound healing and treatment prognosis compared to the comparison group.

The most significant differences were observed on the 14th and 21st days post-surgery, where patients in the intervention group demonstrated notably greater progress in recovery and prognosis. Furthermore, pentoxifylline was associated with fewer adverse effects compared to the control group, and its role in accelerating patient recovery—especially in terms of wound healing and functional outcomes—was clearly evident. These findings suggest that pentoxifylline could be an effective treatment option for patients with traumatic finger amputation and may be recommended as an adjunctive therapy alongside conventional treatment modalities.

Discussion

Pentoxifylline is a methylxanthine derivative synthesized through the modification of theobromine extracted from cocoa (Theobroma) or tea using a hexidone group[31].

Various studies have demonstrated the effectiveness of this drug in treating peripheral vascular diseases, such as cerebral ischemia and chronic embolic vasculitis[32]. Pentoxifylline acts by reducing blood viscosity, enhancing tissue oxygenation, and increasing red blood cell flexibility[32]. Additionally, recent evidence suggests that pentoxifylline inhibits the production of reactive oxygen species (ROS) and improves capillary circulation and tissue oxygenation in various organs[33].

The present study aimed to investigate the effect of this drug in a randomized clinical trial on tissue healing in patients with traumatic fingertip amputation. In this study, 52 patients (26 males and

26 females) with a mean age of 39.62 years in the intervention group and 35 years in the control group were assessed. Prognosis was evaluated on days 7, 14, and 21. On day 7, 76.9% of the intervention group exhibited grade 2/3 central necrosis, compared to 92.3% in the control group. Marginal necrosis occurred in 23.1% of the intervention group and 7.7% of the control group.

On day 14, 53.8% of patients in the intervention group had grade 1/3 central necrosis and 23.1% had grade 2/3 necrosis, while these values in the control group were 23.1% and 80.8%, respectively. Marginal necrosis was observed in 23.1% of the intervention group and 3.8% of the control group.

On day 21, in the intervention group, 15.4% had grade 1/3 central necrosis, 7.7% had grade 2/3 necrosis, 15.4% underwent amputation, and 15.4% had marginal necrosis. Overall, 46.2% of the intervention group showed improvement. In contrast, in the control group, 3.8% had grade 1/3 necrosis, 80.8% had grade 2/3 necrosis, and 42.3% required amputation, with only 15.4% showing improvement.

Previous studies on the efficacy of pentoxifylline can be broadly divided into two categories: those focused primarily on burns and wound healing, and those evaluating its anti-inflammatory properties.

Studies that examined its effect on wound healing suggest that pentoxifylline may accelerate this process. For example, a 2016 review by Ahmadi et al. concluded that administration of pentoxifylline could increase the speed and quality of wound healing[34].

Similarly, Moradi et al. (2023) investigated the combined effect of pentoxifylline and zinc oxide on wound healing in rats. The study found reduced inflammation and fewer inflammatory cells in the pentoxifylline group compared to the zinc oxide group, aligning with the findings of the present study[35].

In a 2023 study by Moreira et al., the combination of pentoxifylline and chitosan was assessed for wound healing efficacy. The results showed that this combination effectively accelerated the wound healing process, and that higher concentrations of pentoxifylline further shortened the healing period—findings consistent with our results[36].

In another study by Dehghani et al. (2022), hydrogels loaded with pentoxifylline were shown to significantly accelerate wound healing, which is also in agreement with our findings[37]. On day 7 of the current study, no significant difference in prognosis was observed between the intervention and control groups. This is consistent with the 2013 study by Babaei et al., which examined the effect of pentoxifylline on streptozotocin-induced diabetic skin wounds in rats. That study reported that pentoxifylline administration significantly improved the wound healing process and quality in diabetic rats[38].

The discrepancies in early outcomes may be due to the precedence of histological changes over morphological ones, as well as species differences between rats and humans.

However, on days 14 and 21, significant prognostic differences were observed between the two groups. The intervention group showed better outcomes and a higher number of healed cases

These findings are consistent with other studies that have identified pentoxifylline as an effective agent in accelerating wound healing. One such study is by Bhatia et al., which evaluated the topical effects of pentoxifylline on wound healing. The results demonstrated that pentoxifylline enhances wound healing at various levels, including stimulating fibroblast proliferation, increasing granulation tissue formation, reducing collagenase activity, facilitating collagen and other connective tissue deposition, minimizing bacterial accumulation, and decreasing exudate levels. These outcomes strongly align with the present study's findings[39].

The study by Khiury et al. indicated that pentoxifylline may influence angiogenesis in experimental models. Among the 22 studies reviewed, 16 reported anti-angiogenic effects of pentoxifylline, whereas 4 showed pro-angiogenic effects, and 2 found no impact on angiogenesis. However, there is insufficient clinical evidence to confirm pentoxifylline's role as an anti-angiogenic agent in clinical settings. Furthermore, the study referenced evidence suggesting that G protein-coupled receptor (GPCR) mechanisms, particularly adenosine A2B receptors (A2BAR), may play a role in metabolic processes and angiogenic switching. Therefore, further research is required to elucidate pentoxifylline's effects on metabolism, energy homeostasis, and its underlying mechanisms of action[40].

In a study by Baykal et al., pentoxifylline was administered to rats following sciatic nerve injury. The results showed a shorter latency and higher amplitude of muscle action potentials in the treatment group, though only the amplitude reached

statistical significance. This suggests that pentoxifylline positively affects axonal regeneration, but has limited influence on remyelination[41].

As previously discussed, pentoxifylline exerts its effects through multiple mechanisms, including immunomodulation, anti-inflammatory action, improvement of blood rheology, and antifibrinolytic properties. The drug enhances leukocyte deformability, reduces leukocyte adhesion to the endothelium, decreases neutrophil activation and TNF-α production. Additionally, pentoxifylline inhibits TNF-α and affects other cytokines such as IL-1 and IL-6. It also increases red blood cell flexibility, decreases blood viscosity, and exhibits antithrombotic properties by reducing platelet aggregation and enhancing fibrinolytic activity. Moreover, pentoxifylline reduces collagen and fibronectin synthesis while increasing fibroblast collagenase activity. These anti-inflammatory mechanisms, alongside its stimulatory effects on fibroblasts (the main cells in tissue repair), promotion of neoangiogenesis, and nerve regeneration—three key components of tissue reconstruction—make it a potentially safe and effective adjuvant therapy for accelerating tissue repair following distal phalangeal amputation.

In terms of adverse effects, 15.4% of patients in the intervention group (n=4) experienced side effects, primarily involving the gastrointestinal and central nervous systems. Common adverse effects included dizziness, headache, anxiety, and confusion. No significant side effects were observed in the control group. Although adverse events were recorded in the intervention group, the differences were not statistically significant. Overall, pentoxifylline is considered a safe medication and is generally well tolerated, with its side effects being mostly dose-dependent[42].

During pregnancy, pentoxifylline is classified as category C and should be used with caution. It may pose risks during breastfeeding due to its excretion into breast milk. The safety and efficacy of pentoxifylline have not been established in pediatric populations. In elderly patients, due to potentially reduced liver, kidney, or cardiac function and comorbid conditions, a lower starting dose is recommended. Moreover, individuals with hypersensitivity to xanthine derivatives such as caffeine or theophylline, those with recent cerebral or retinal hemorrhage, or with porphyria, should avoid using this medication[42].

The results of this study demonstrated that pentoxifylline significantly improves the rate and quality of tissue regeneration in patients with traumatic fingertip amputations. The drug notably reduces necrosis and the need for amputation, while also exerting favorable effects on the prognosis of the condition. Although some limitations include Single-center study, Small sample size, Short follow-up duration, Lack of blinding in outcome assessment and Exclusion of certain populations are exist and should be addressed in future studies.

Conclusion

In conclusion, pentoxifylline presents a favorable safety profile and substantial therapeutic potential in enhancing recovery among patients with traumatic injuries and chronic wounds, supporting its use as a clinically effective and safe treatment option.

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References

1 Masaki S, Kawamoto T. Fingertip amputation injury of allen type III managed conservatively with moist wound dressings. The American Journal of Case Reports. 2021; 22(1): e928950-1–e928950-7. doi: 10.12659/AJCR.928950
2 Kawaiah A, Thakur M, Garg S, Kawasmi S. H, Hassan A. Fingertip injuries and amputations: a review of the literature. Cureus. 2020; 12(5):e8291. DOI: 10.7759/cureus.8291
3 Sindhu K, DeFroda S. F, Harris A. P, Gil J. A. Management of partial fingertip amputation in adults: operative and non operative treatment. Injury. 2017; 48(12):2643-2649. https://doi.org/10.1016/j.injury.2017.10.042
4 Sears E. D, Shin R, Prosser L. A, Chung K. C. Economic analysis of revision amputation and replantation treatment of finger amputation injuries. Plastic and reconstructive surgery. 2014; 133(4):827-840. DOI: 10.1097/PRS.0000000000000019
5 Reid D. B, Shah K. N, Eltorai A. E, Got C. C, Daniels A. H. Epidemiology of finger amputations in the United States from 1997 to 2016. Journal of Hand Surgery Global Online. 2019; 1(2):45-51. https://doi.org/10.1016/j.jhsg.2019.02.001
6 Shores J. T. Anatomy and Physiology of the Fingertip. Fingertip Injuries: Diagnosis, Management and Reconstruction. Fingertip Injuries. 2015; 3(1):1-9. https://doi.org/10.1007/978-3-319-13227-3_1

7 Peterson S. L, Peterson E. L, Wheatley M. J. Management of fingertip amputations. The Journal of hand surgery. 2014; 39(10):2093-2101. https://doi.org/10.1016/j.jhsa.2014.04.025
8 Rosenthal E. A. Treatment of fingertip and nail bed injuries. The Orthopedic clinics of North America. 1983; 14(4):675-697. PMID: 6634090
9 Chakravarthy J, Qureshi A, Waldram M. A, Porter K. Acute fingertip injuries. Trauma. 2006; 8(3):179-188. https://doi.org/10.1177/1460408606071139
10 Brown R. E. Acute nail bed injuries. Hand clinics. 2002; 18(4):561-575. https://doi.org/10.1016/S0749-0712(02)00075-6
11 Russell R. C, Casas L. A. Management of fingertip injuries. Clinics in Plastic Surgery. 1989; 16(3):405-425. https://doi.org/10.1016/S0094-1298(20)31311-0
12 Weichman K. E, Wilson S. C, Samra F, Reavey P, Sharma S, Haddock N. T. Treatment and outcomes of fingertip injuries at a large metropolitan public hospital. Plastic and Reconstructive Surgery.2013;131(1): 107-112.DOI: 10.1097/PRS.0b013e3182729ec2
13 Peterson S. L, Peterson E. L, Wheatley M. J. Management of fingertip amputations. The Journal of Hand Surgery. 2014; 39(10):2093-2101. https://doi.org/10.1016/j.jhsa.2014.04.025
14 Panattoni J. B, De Ona I. R, Ahmed M. M. Reconstruction of fingertip injuries: surgical tips and avoiding complications. The Journal of Hand Surgery. 2015; 40(5):1016-1024. https://doi.org/10.1016/j.jhsa.2015.02.010
15 Germann G, Rudolf K. D, Levin S. L, Hrabowski M. Fingertip and thumb tip wounds: changing algorithms for sensation, aesthetics, and function. The Journal of Hand Surgery. 2017; 42(4):274-284. https://doi.org/10.1016/j.jhsa.2017.01.022
16 Yam A, Tan S. H, Tan A. B. H. A novel method of rapid nail bed repair using 2-octyl cyanoacrylate (Dermabond). Plastic and Reconstructive Surgery. 2008; 121(3):148e-149e. DOI: 10.1097/01.prs.0000300212.73022.9d
17 Sebastin S. J, Chung K. C. A systematic review of the outcomes of replantation of distal digital amputation. Plastic and reconstructive surgery. 2011; 128(3):723. DOI: 10.1097/PRS.0b013e318221dc83
18 El-Diwany M, Odobescu A, Bélanger-Douet M, Berbiche D, Arsenault J, Bou- Merhi J. Replantation vs revision amputation in single digit zone II amputations. Journal of Plastic, Reconstructive & Aesthetic Surgery. 2015; 68(6):859-863. https://doi.org/10.1016/j.bjps.2015.02.033
19 Chakravarthy J, Qureshi A, Waldram M. A, Porter K. Acute fingertip injuries. Trauma. 2006; 8(3):179-188. https://doi.org/10.1177/1460408606071139
20 Wang K, Sears E. D, Shauver M. J, Chung K. C. A systematic review of outcomes of revision amputation treatment for fingertip amputations. Hand (N Y). 2013; 8(2):139-145. https://doi.org/10.1007/s11552-012-9487-0
21 De Alwis W. Fingertip injuries. Emergency Medicine Australasia. 2006; 18(3):229-237. https://doi.org/10.1111/j.1742-6723.2006.00851.x
22 Lee D. H, Mignemi M. E, Crosby S. N. Fingertip injuries: an update on management. AAOS-Journal of the American Academy of Orthopaedic Surgeons. 2013; 21(12):756-766. DOI: 10.5435/JAAOS-21-12-756
23 Ito H, Sasaki K, Morioka K, Nozaki M. Fingertip amputation salvage on arterial anastomosis alone: an investigation of its limitations. Annals of plastic surgery. 2010; 65(3):302-305. DOI: 10.1097/SAP.0b013e3181cc0021
24 Scheker L. R, Becker G. W. Distal finger replantation. The Journal of hand surgery. 2011; 36(3):521-528. https://doi.org/10.1016/j.jhsa.2010.12.017
25 Soucacos P. N. Indications and selection for digital amputation and replantation. Journal of hand surgery. 2001; 26(6):572-581. https://doi.org/10.1054/jhsb.2001.0595
26 Beris A. E, Lykissas M. G, Korompilias A. V, Mitsionis G. I, Vekris M. D, Kostas- Agnantis I. P. Digit and hand replantation. Archives of orthopaedic and trauma surgery. 2010; 130(9):1141-1147. https://doi.org/10.1007/s00402-009-1021-7
27 Aviado D. M, Porter J. M. Pentoxifylline: a new drug for the treatment of intermittent claudication. Mechanism of action, pharmacokinetics, clinical efficacy and adverse effects. Pharmacotherapy. 1984; 4(6):297-307. https://doi.org/10.1002/j.1875-9114.1984.tb03380.x
28 Mora-Gutiérrez J. M, Ferrer-Nadal A, García-Fernández N. Effect of pentoxifylline on anemia control in hemodialysis patients: retrospective observational case-control study. Nefrologia. 2013; 33(4):524-531. DOI: 10.3265/Nefrologia.pre2013.Apr.11654
29 Mohammadpour A. H, Nazemian F, Khaiat M. H, Tafaghodi M, Salari P, Charkazi S, Naghibi M, Shamsara J. Evaluation of the effect of pentoxifylline on erythropoietin-resistant anemia in hemodialysis patients. Saudi Journal of Kidney Diseases and Transplantation. 2014; 25(1):73-78. DOI: 10.4103/1319-2442.124492
30 Feizi A, Mortazavi M, Badri S, Norouzi M. J. Effect of pentoxifylline on anemia in patients with chronic kidney disease: an updated systematic review and meta-analysis. Tehran University Medical Journal. 2020; 78(4):212-220. ISSN 16831764
31 Singh N, Shreshtha A. K, Thakur M. S, Patra S. Xanthine scaffold: scope and potential in drug development. Heliyon. 2018; 4(10):e00829. https://doi.org/10.1016/j.heliyon.2018.e00829
32 Lyons A. J, Brennan P. A. Pentoxifylline–a review of its use in osteoradionecrosis. British Journal of Oral and Maxillofacial Surgery. 2017; 55(3):230-234. https://doi.org/10.1016/j.bjoms.2016.12.006
33 Gholami A, Ataei S, Ahmadimoghaddam D, Omidifar N, Nili-Ahmadabadi A. Pentoxifylline attenuates arsenic trioxide-induced cardiac oxidative damage in mice. Oxidative Medicine and Cellular Longevity. 2021; 2021:6406318. https://doi.org/10.1155/2021/6406318
34 Ahmadi M, Khalili H. Potential benefits of pentoxifylline on wound healing. Expert Review of Clinical Pharmacology. 2016; 9(1):129-142. https://doi.org/10.1586/17512433.2016.1109443
35 Moradi M, Sabiza, S, Rezaie A, Ezzati-Givi M. Investigating the Effect of Pentoxifylline and Zinc Oxide Combination on Experimental Full-Thickness Wound Healing in Rats. Iranian Journal of Veterinary Surgery. 2023; 18(1):8-17. https://doi.org/10.30500/ivsa.2022.355334.1313
36 Moreira V. M, Leite J. M. D. S, Medeiros K. D. A, Assis K. M. A. D, Borges J. C, Santana L. M. B, Damasceno B. P. G. D. L. Pentoxifylline/Chitosan Films on Wound Healing: In Vitro/In Vivo Evaluation. Pharmaceutics. 2023; 15(4):1122. https://doi.org/10.3390/pharmaceutics15041122

37 Dehghani P, Akbari A, Saadatkish M, Varshosaz J, Kouhi M, Bodaghi M. Acceleration of Wound Healing in Rats by Modified Lignocellulose Based Sponge Containing Pentoxifylline Loaded Lecithin/Chitosan Nanoparticles. Gels. 2022; 8(10):658. https://doi.org/10.3390/gels8100658

38 Babaei S, Bayat M, Nouruzian M, Bayat M. Pentoxifylline improves cutaneous wound healing in streptozotocin-induced diabetic rats. European journal of pharmacology. 2023; 700(1-3):165-172. https://doi.org/10.1016/j.ejphar.2012.11.024

39 Bhatia A, Prakash S. Topical phenytoin for wound healing. Dermatology Online Journal. 2004; 10(1):5-18. https://doi.org/10.5070/D30z3612w1

40 Khoury W, Trus R, Chen X, Baghaie L, Clark M, Szewczuk MR, El-Diasty M. Parsimonious Effect of Pentoxifylline on Angiogenesis: A Novel Pentoxifylline-Biased Adenosine G Protein-Coupled Receptor Signaling Platform. Cells. 2023 Apr 20;12(8):1199. doi: 10.3390/cells12081199.

41 BAYKAL, S., BOZ, C., ÇAKIR, E., BAYTAN, Ş.H., KARAKUŞ, M. and KUZEYLİ, K., 2002. The effects of pentoxifylline in experimental nerve injury. Turkish Journal of Medical Sciences, 32(3):207-210.

42 Hassan I, Dorjay K, Anwar P. Pentoxifylline and its applications in dermatology. Indian Dermatol Online J. 2014 Oct;5(4):510-516. doi: 10.4103/2229-5178.142528.