

# Deep Frostbite: the Question of Adjuvant Treatment

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Within the spectrum of peripheral cold injuries, frostbite is the most serious lesion. It is an injury that results from exposure to temperatures that are low enough to cause ice crystal formation in the exposed tissue and develops after exposure to low temperatures for more than 1 hour, usually when protection from the environment is insufficient. While all exposed tissues may be affected, the feet and the hands account for 90% of the injuries reported. The spectrum of injury varies from minimal tissue loss with mild long-term sequelae to major necrosis of the distal limbs with subsequent major amputations [1].

In the past, frostbite was primarily a military problem but it is becoming increasingly prevalent in the civilian population. In addition to the sharp increase in the numbers of homeless people who are vulnerable to cold injuries, the frequency of cold exposures has risen in the last decades along with the growing interest in outdoor activities such as skiing, hiking and mountaineering. It follows that effective treatment of frostbite has become a serious issue not only for rural physicians in extreme climates but also for many urban hospitals. While in the past aggressive rewarming of the affected tissue was the recommended treatment, today adjuvant treatments (e.g., hyperbaric oxygen, thrombolytic agents, and prostacyclin analogues with vasodilatory properties) have

also been suggested [1]. Whether these adjuvant treatments are indeed effective in the case of deep frostbite is highlighted in the present case report.

## PATIENT DESCRIPTION

A group of 11 young Israelis, males and females aged 23 to 32 years, faced a heavy snowstorm while trekking in Nepal along the Annapurna Circuit. In terms of clothing and acclimatization to high altitude, they were well prepared for the trek that ascended to the height of 5416 m at Thorung La (“the Pass”) before descending back to the nearest village at 3800 m. The last lag to the Pass took the group about 5 hours; it usually takes 2–3 hours. Because of poor weather conditions and exhaustion the group started descending at 18:00. However, soon after starting to walk in the waist-high snow they lost the main trail. On the path, four of the travelers succumbed to hypothermia, while the others struggled to continue – walking and crawling alternately. Some of them lost their boots or gloves and were thus unprotected for approximately 8 hours. One member of the group, who fell into a ditch, was covered with snow with one hand kept outside, marking his location.

At 06:00 (24 hours after starting to ascend to the peak) they were rescued by a Nepalese military team and were evacuated by helicopter to a military hospital. The patient, who was fully covered with snow, was rescued 24 hours later (39 hours after starting to descend). The seven travelers were hospitalized in the military hospital for one day before being transferred to the CIWEC Travel Medicine Clinic for frostbite and hypothermia management.

Four of the seven patients were diagnosed as suffering from various grades of frostbite [Table 1] and were treated initially in the military hospital and then in the CIWEC clinic. This involved soaking the affected hands and feet in warm water with povidone-iodine which were then wrapped with puffy dressings. However, we have no information whether this rewarming protocol was optimal. In the CIWEC clinic prostacyclin (iloprost) treatment, according to the protocol suggested by Cauchy et al. [2], was initiated. Other adjuvant treatments upon arrival at the CIWEC clinic included cephalexin (500 mg), a non-steroidal anti-inflammatory drug (ibuprofen, 400 mg 3 times a day) and an anti-tetanus shot. After 2 days, enoxaparin sodium (60 mg x 2/day), and acetylsalicylic acid (aspirin, 300 mg x 4/day) were added.

Within 72 hours after being rescued, the seven patients were transferred to medical centers in Israel accompanied by one of the co-authors (A.R.). Three of the seven patients who were only mildly injured were discharged after a few days of observation. Patients 1, 2 and 3 were hospitalized in the Burn Unit of the Department of Plastic and Reconstructive Surgery, Sheba Medical Center, and the fourth patient was hospitalized in the Plastic and Reconstructive Surgery Department at Hadassah Medical Center in Jerusalem [Table 1].

The treatment course of the four patients included completion of 6 days of iloprost (IV infusion of 2 ng/kg body weight/min for 6 hours/day), clexane (60 mg x 2/day), and aspirin 100 mg/day (for several weeks). The affected areas were dressed daily with vaseline gauze and gauze soaked in mafenid acetate solution. Analgetics was given when

**Table 1.** Patient characteristics, injury and outcome

Patient	Gender	Age (years)	Hours of exposure*	Major injury	Outcome
1	F	32	15	Bilat. H grade 1-2, bilat. F grade 3	Fully recovered, mild coloring of hand and foot
2	M	24	15	Bilat. H grade 3-4, bilat. F grade 2	Amputation, 10 fingers
3	M	31	15	Bilat. H grade 2, L foot grade 1	Fully recovered
4**	M	32	39	R hand grade 4, L hand grade 2, bilat. F grade 2-3	Amputation, right palm & 4 toes (1-2 digits)

\*Time elapsed from starting the descent until reaching the first rescue station

\*\*The patient is chronically treated with acetazolamide for idiopathic intracranial hypertension  
bilat = bilateral

needed. Periodically, debridement of skin from affected areas was performed.

Hyperbaric oxygen (HBO) treatment was started 5 days after the injury according to the following protocol: two treatments a day during the first 3 days followed by a daily treatment for the next 24 days (total of 30 treatments). Each treatment consisted of 90 minutes exposure to 100% oxygen at 2 absolute atmospheres (ATA) with 5 minute air breaks every 30 minutes.

Two of the four patients (patients # 1 and 3) were discharged from the hospital after 4.5 weeks and 3 weeks, respectively, with only minor lesions that did not require surgical intervention. Two patients needed surgical intervention. The palm of patient # 4 was amputated at the metacarpal level after 7 weeks, and four of his toes of the left leg were amputated at the level of necrosis after 11 weeks. Ten fingers of patient # 2 were amputated at the levels of necrosis after 9 weeks.

**COMMENT**

This case series demonstrates the difficulty in reaching a treatment decision regarding frostbite beyond thawing. A number of therapeutic modalities have been investigated and suggested in the attempt to alleviate the progressive ischemia in frostbite and preserve tissue viability by enhancing blood perfusion to the affected limbs and improving oxygenation. These treatments usually include HBO and a prostacyclin analogue infusion (iloprost). The effectiveness of these treatments was questioned during hospitalization of these patients.

Other treatments, such as thrombolytic agents (e.g., tissue plasminogen activator, TPA), is not discussed here.

Treating frostbite with HBO was suggested because of its immediate beneficial effect that results from the increased amounts of dissolved oxygen in plasma. The effect of increased local tissue oxygen tension on wound healing is believed to be due to the enhanced stimulus on angiogenesis and improved neovascularization, as well as to diminishing the inflammatory response and improved post-ischemic tissue survival. Nevertheless, data on HBO treatment in frostbite are anecdotal and very limited; since the first published case over 50 years ago only 18 cases of frost-bitten patients have been reported in the literature with inconclusive results [3]. Therefore, the use of HBO for the treatment of frostbite must be discussed case by case, as demonstrated in our case series, considering the time elapsed from rescue and the degree of the injury.

The physiological rationale of using prostacyclin in the treatment of frostbite is its effect on platelet aggregation that results in decreased microvascular occlusion. Its activity as a vasodilator improves blood supply to collateral vessels. The database with regard to the treatment of frostbite is based on 37 cases, which were described in two clinical studies. Groechenig in 1994 [4] was the first to publish his experience in five patients suffering frostbite (grade 2–3). Although no patient required amputation, this treatment was not routinely used until the recent report in 2011 by Cauchy and

team [2] who described their experience with 32 patients suffering various degrees of frostbite; noteworthy, half the patients were treated also with a thrombolytic agent (TPA). These authors showed a low amputation rate for patients treated with iloprost vs. iloprost and TPA (0% vs. 3.1%, respectively), which probably is due to the severity of cases in the latter group.

In the present case, partial success with iloprost treatment in combination with HBO was noted; two of the four patients, with the less severe grades of injury, were discharged from the hospital with only minor lesions that did not require any surgical intervention and the two other patients needed major surgery.

Based on the clinical outcome in the patients presented here it seems that the success of the adjuvant treatments depends on the grade of the injury. While the lower grades of frostbite (grades 1–3) might be responsive to adjuvant treatment, deep frostbite may not be responsive and will ultimately result in amputation of the affected site. To date, the cumulative data are insufficient to recommend any of the adjuvant treatments. What has proved effective is thawing treatment, namely, immersing the affected limb in hot water, together with conservative treatment using topical dressing [5].

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