Def Sci J, Vol 34, No 4, October 1984, pp 417–428

Studies on Prevention of Cold Injuries

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Received 16 July 1984

Abstract. Studies were carried out to find out suitable measures for prevention of cold injuries. These include methods to screen out individuals who are more prone to cold injuries; and to evaluate the effect of cold acclimatization and use of certain drugs and vitamins in its prevention. Studies were also conducted to evaluate the peripheral vascular responses to cold on a group of young men who suffered from cold injury at high altitude. Experiments on monkeys have shown that the animals with higher peripheral vascular responses under local cold stress are better protected against frost bite. Cold acclimatization also was found to be effective in raising these responses and thereby lessening the degree of injury, in experimental animals. Role of certain drugs and vitamins were tried in animals.

1. Introduction

Deleterious effects of extreme cold are commonly seen in the high altitude areas of our Himalayan regions. Hypothermia and local cold injuries are the two main problems encountered due to severe cold conditions. In our country occurrence of hypothermia is rare but cold injuries, specially frost bite, are more frequent during military operations in the snow bound areas. Many cases of frost bite have also been reported during various mountaineering expeditions and hence the problem of cold injuries has gained considerable importance for the civil population too.

It is known that the peripheral tissues cool more rapidly than the central tissues on exposure to cold, and hence they are more liable to cold injuries[1]. As the extremities contain very little muscle mass, the capacity for heat production during cold exposure is less. In the cold areas of high altitude the problem becomes more intense since hypoxia is superimposed over cold stress which results in marked reduction of extremity blood flow[2,3]. Besides frost bite, trench foot and chill blains are other forms of cold injuries generally seen in our mountaineous areas.

2. Etiological Factors and Pathogenesis

Severity of atmospheric cold and exposure to such environment for considerable duration is the main factor for the occurrence of cold injuries. Wind movement, hastens tissue cooling. The effect of the severity of wind at a particular ambient temperature on the causation of frost bite, the "Wind Chill Factor" has been worked out by Siple[4]. Moisture is a good thermal conductor and, therefore, interferes with the natural insulating power of the skin. Hypoxia of high altitude adds to this due to increased vasoconstriction as pointed out earlier.

Besides these environmental factors, physical inactivity, lack of adequate nutrition, physical exhaustion, fatigue, fear and anxiety, local injury of the skin, excessive use of alcohol, smoking and lack of personal hygiene,are the other important factors in the causation of cold injuries[5].

The most important initial protective response to cold is peripheral vasoconstriction which reduces the heat dessipation. When this becomes intense the blood supply to the tissues is reduced. Generally, when the temperature of the extremities falls below 10 °C or so, the cold induced vasodilatation occurs which allows a surge of blood flow to the areas, at least for a short period[6]. However, in some cases this phenomenon is inadequate and the severe vasoconstriction continues for prolonged periods[7]. Thus the vascular disturbance due to severe vasoconstriction appears to be the most important etiological factor for the causation of frost bite[8]. Before the tissue freezes the contriction is maximum and the blood flow in the tissue is practically stagnant. Aggregation of platelets form occlusive masses at this stage and then the blood supply will be totally cut off[9]. These changes will induce necrosis of the affected part, if blood circulation is not restored immediately. Besides, crystal formation and high concentration of electrolytes in partially frozen tissues add to the damage[10]. Upon thawing, considerable hyperaemia will be present and the permeability of the vessels is increased; and as a result, fluid leaks out from the blood.

3. Preventive Measures

Proper clothing, adequate nutrition, and intelligent field operations are probably the most important factors of prevention. The clothing should be worn in many layers and should be impervious and wind proof. A multilayer clothing which can be removed or added on, and which has the possibility of being opened or closed easily, is the ideal type of clothing to wear in the cold[9]. Damp clothing should be immediately changed. Similarly proper foot gear and socks are also essential. The feet and hands should be kept clean, must be washed in warm water and thoroughly dried. Application of vaseline can be of benefit. Use of foot powder can decrease the dampness, as feet are more prone to sweating.

Regular and moderate exercise will keep the circulation intact. People should avoid sitting in a cramped position without any movement. Contact with cold metal objects should be avoided. Adequate nutrition and physical fitness are equally important[11]. Excessive smoking and use of alcohol immediately before a cold exposure will have damaging effect and therefore should be avoided. However, application of all these preventive measures are very difficult during military operations, and often inadequate.

4. Susceptibility to Cold Injuries

Individual susceptibility to the occurrence of cold injury is well known. When a body of troops are exposed to identical environmental conditions, only a few suffer from frost bite. The susceptibility may be due to various factors such as the individual's tolerance to cold stress, physical fitness, age, status of acclimatization, and racial and ethnic factors[12]. It was suggested that individuals with high peripheral vascular responses might be less susceptible to the occurrence of cold injuries[13]. This is most likely due to variation in the extremity blood flow under severe cold stress. This variation can be assessed by the estimation of heat output, cold induced vasodilation (CIVD) response and by calculating the peripheral blood flow from the temperature changes of the finger during cold water immersion[14]. Hence, these parameters were chosen to evaluate the individuals' proneness to cold injuries in a series of experiments.

To begin with, studies were conducted to evaluate the peripheral vascular responses such as heat output, CIVD, peripheral blood flow on cold immersion, cold pressor response, and mean skin temperature changes on a group of young men who suffered from frost bite at high altitude. Their responses were compared with that of a group of subjects who were exposed with them under identical conditions but did not suffer from any injury; and also with another group of subjects from the plains who had never been to the high altitude. It was observed that responses were significantly less in those who had earlier suffered from frost bite as compared to the other two groups (Table 1). More detailed experiments were then carried out on rhesus monkeys which have shown that animals with higher peripheral vascular responses under local cold stress are better protected against cold injury. Monkeys with very good CIVD response had the highest mean heat output values and practically escaped from frost bite, whereas monkeys with very poor CIVD responses had lowest values of heat output and suffered from severe to very severe type of injuries (Table 2). The product moment coefficient of correlation ($r = -0.79$) between heat output and degree of cold injury was highly significant[15] ($p < 0.001$).

These observations suggest that individuals with higher peripheral vascular responses, on exposure to severe cold, are comparatively better protected against cold injuries. In another study, it was shown that the South Indians are more susceptible to the occurrence of cold injuries, as compared to North Indians and Gorkhas, and the high altitude natives are most resistant[16].

Table 1. Comparison of peripheral vascular responses in frost bite cases with other two groups

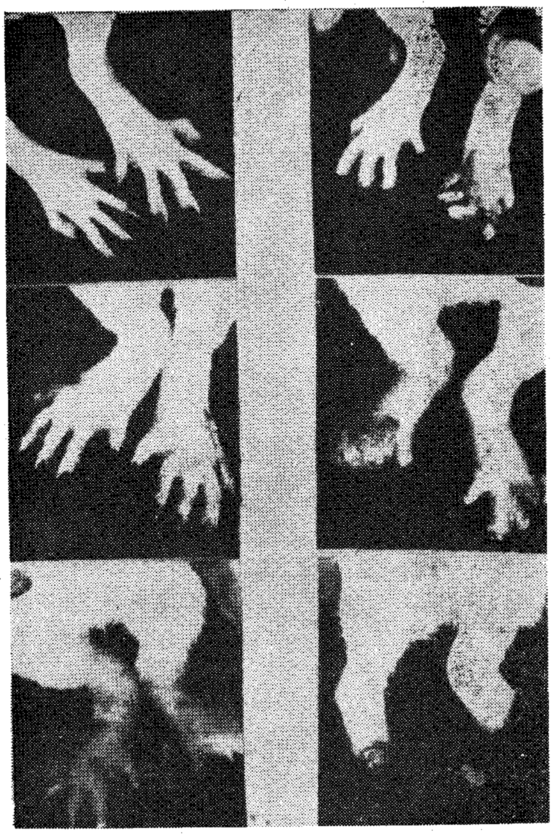
Parameters	Group A	Group B	Group C	Statistical Significance Group A Vs Group B	Group A Vs Group C	Group B Vs Group C
Heat Output cal/100ml tissue/min	98.34	134.64	142.03	$p<0.001$	$p<0.001$	NS
Cold induced vasodilation response (CIVD)	Poor CIVD response	Good hunting response of CIVD		—	—	—
Peripheral blood flow during cold immersion ml/cm²/min	1.12	1.87	1.98	$p<0.001$	$p<0.001$	NS
Cold pressor response (CPR) Sys/Dia mm Hg	10.2/8.7	12.0/10.3	12.6/10.2	NS	NS	NS
Mean skin temperature°C	30.32	31.07	30.99	NS	NS	NS

Table 2. Relation of CIVD response with heat output and degree of cold injury in monkeys (15).

Type of CIVD Response	No. of subjects	Mean heat output cal/100ml/min	Degree of injury
Very good	6	139.5	0, +
Good	8	122.6	0, +, ++
Poor	8	95.7	++, +++, ++++
Nil	5	69.8	+++++++

5. Cold Acclimatization and Cold Injuries

Studies have shown that people chronically exposed to cold exhibit peripheral heat regulating mechanism which enables them to perform better under a cold environment[17,18]. This physiological adjustment may result from natural cold exposure or by artificial means. It has been reported that deleterious effects of cold on the sensory and neuro-muscular functions of the extremities can be lessened by cold acclimatization[19,20]. This may be partly due to an improved peripheral circulation of the extremities. It is well established that the onset of cold induced vasodilatation is quicker and better in those who are habituated to chronic cold exposure[21,22]. Based on these observations, studies were conducted in rats to see the effect of cold acclimatization in the prevention of cold injuries[23]. The heat output from the hind paw was determined in two groups of (control and cold acclimatized) rats. Later, frost bite was produced in these animals by exposing them to a temperature of—15°C for one hour. After 10 days the severity of cold injury was assessed and classified into very severe, severe, moderate, primary, and no frost bite, on the basis of the extent of tissue necrosis. In the cold acclimatized group the injury was more of primary and moderate type whereas the control group suffered from severe and very severe type of injuries (Table 3). The nature of injury suffered by typical cases from both the groups are depicted in Fig. 1. Thus cold acclimatization was found to be effective in raising the peripheral vascular responses and thereby lessening the degree of injury. This observation is in agreement with other studies both in animals and in man[24,25,26] and is due to better cold tolerance and improved peripheral circulation.



(A) (B)

Figure 1. Typical cases of frost bite in cold acclimatized (A) and control (B) rats

6. Role of Drugs in the Prevention of Cold Injuries

The previous experiments suggest that methods which can improve the peripheral vascular responses and blood flow under severe cold stress can be of use in the prevention of cold injuries. Based on this, role of certain drugs and vitamins were tried experimentally. Three sets of experiments were carried out in rats and monkeys. Even though pilot studies were carried out using a large number of drugs, such as

Table 3. Heat output, changes in rectal temperature and nature of injury in cold acclimatized and control rats (23).

Parameters		Cold acclimatized group		Control group	
Heat output cal/30 min		168.60 ± 37.87*		94.57 ± 28.22	
Fall in rectal temperature °C		17.50 ± 1.30*		19.56 ± 0.86	
Nature of injury			No. of paws injured		
		Rt	Lt	Rt	Lt
0	(No injury)	6	8	3	2
+	(Primary)	5	3	2	2
++	(Moderate)	1	1	2	4
+++	(Severe)	3	2	5	4
++++	(Very severe)	0	1	3	3

*$p < 0.001$

thyroxin, tri-iodothyronine, isoxsuprine hydrochloride, rovigon, xanthinol nicotinate and nicotinic acid, only tolazoline hydrochloride, vitamin C and their combination were tried at experimental levels as these have shown encouraging results[14,27].

Studies were conducted to see the effect of vasodilator drug, tolazoline hydrochloride in six rhesus monkeys, who were made to sit on a monkey chair in a thermoneutral room (27° ± 1°C). Their heart rate was monitored by lead II EKG, the skin and rectal temperature by YSI telethermometer with appropriate probes, heat output by calorimetric method[23], and the CIVD by immersing the right hind limb in a water bath maintained at 4°C[15]. After a weeks interval the animals were administered one tablet (25 mg) of tolazoline hydrochloride (Priscol) orally and two hours later all the above parameters were recorded as earlier.

The administration of tolazoline hydrochloride produced significant ($p < 0.05$) rise in the values of heat output and finger skin temperature. The mean ± SD values of heat output were 120.85 ± 12.63 and 128.79 ± 14.05 cal/100ml/min and that of skin temperatures were 33.36 ± 1.02 and 34.82 ± 0.86°C respectively before and after administration of the drug. Further, there was marked improvement in CIVD response (Fig. 2). The heart rate and rectal temperature, however, had not shown any significant change, the values being 182.0 ± 12.02 and 191.0 ± 14.17 beats/min for heart rate and 39. 33 ± 0.86 and 39.10 ± 0.93°C for rectal temperature respectively before and after the drug therapy.

Another set of experiments were done using five groups of rats (20 each) to evaluate the merits of administration of vitamin C in comparison with the other vasodilator drugs. The experiments were done as follows: The first group of rats (control) were administered 0.5 ml of distilled water (im) as placebo for a period of five days daily prior to cold exposure. In the second group (vitamin C short term) 1 mg of vitamin C (in 0.5 ml) was administered (im) daily for five days before the cold exposure. The third group (vitamin C long term) of animals were injected 1 mg of

Table 4. Comparison of the effects of vitamin C with other drug in cold injury

Groups Sr. No.	Control Rt	Control Lt	Vitamin C (short term) Rt	Vitamin C (short term) Lt	Vitamin C (long term) Rt	Vitamin C (long term) Lt	Priscol Rt	Priscol Lt	Combination of Vitamin C (long term) & Priscol Rt	Combination of Vitamin C (long term) & Priscol Lt
1	++	++	++	+	0	+	+	+	+	0
2	++	+	++	++	+	++	++	++	+	+
3	+++	++	++	++	++	+	+	++	++	++
4	+	++	++	++	++	+	+	0	0	+
5	++	+++	+++	+++	+	0	++	+++	++	++
6	0	++	++	+	++	+	++	+	++	++
7	++	++	0	+	++	++	0	+	+	+
8	+++	++	++	++	++	+++	+++	++	++	+
9	++	++	+	++	+	++	+	0	0	+
10	+	++	++	+	0	+	+	++	+	+
11	++	+++	+++	+++	++	++	++	+	0	0
12	++++	+++	++	++	+	0	+	++	++	++
13	++	0	0	+	++	++	++	++	+	+
14	+	++	+	+	+	++	0	++	+	++
15	++	++	++	++	++	++	++	++	++	+
16	++	++	+	+	0	+	+++	++	++	++
17	++	++	++	+++	++	++	+	+	+	0
18	+++	++++	++	+++	+	+	++	+	+	++
19	++	++	++	++	0	0	++	++	++	+
20	++	+	+	0	++	+	0	+	+	++
Statistical Significance			NS	NS	*	**	*	*	**	**

* $p < 0.05$, ** $p < 0.02$, NS = Not significant
Comparison is done with control group—Rt. paw Vs R_t. paw and Lt. paw vs Lt. paw by Mann Whitney U-test.

60 minutes. Their rectal and paw temperatures were recorded before and during the cold exposure. The degree of injury was assessed and classified. After four weeks the other hind limb was also treated in a similar manner two hours after the administration of 25 mg of tolazoline hybrochloride orally. The extent of injury was statistically compared between the limbs. It was seen that the degree of cold injury was significantly ($p<0.5$) less after the administration of tolazoline hydrochloride. The mean values of rectal temperature and foot skin temperature were significantly ($p<0.001$) reduced after the cold exposure in the normal condition as well as after the administration of the drug. However, the fall in rectal temperature was significantly higher after the treatment (Table 5). The severity of injury suffered by a monkey before and after the drug therapy is shown in Fig. 3.

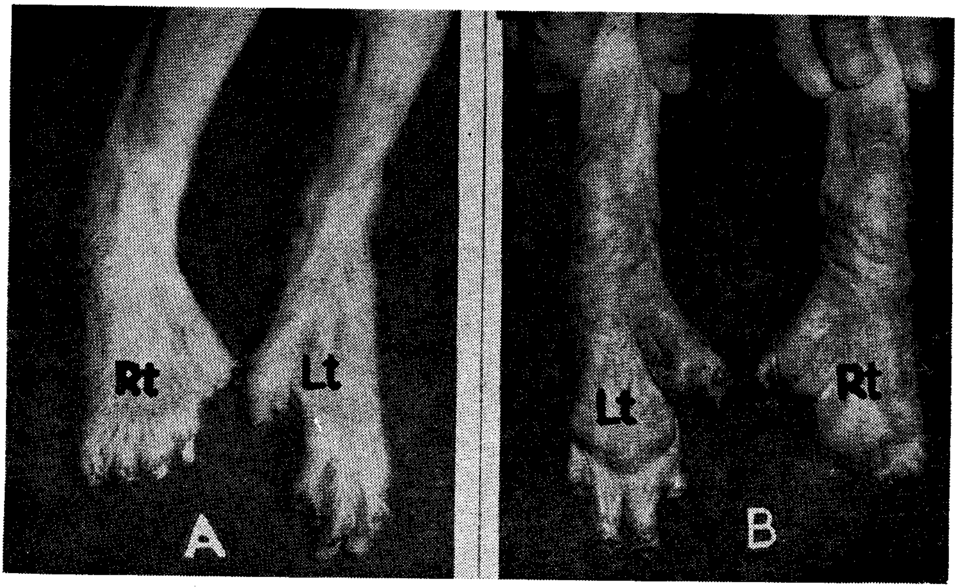


Figure 3. The difference in the severity of frost bite suffered by a monkey before (Rt. limb) and after (Lt. limb) administration of the drug.
(A) Dorsal view (B) Ventral view.

These findings suggest that drugs that can increase the peripheral blood flow during severe cold exposure may be of use in lessening the occurrence of severity of cold injury. It is known that the vasoconstriction resulting from cold exposure affects small arteries and arterioles and lead to diminution of blood flow[30]. This is more severe in the extremities and cold injury in these areas is believed to occur partly due to the anoxia resulting from this circulatory insufficiency and partly due to the direct effect of cold[31,32]. Insufficient circulation leads to stasis in the capillaries and blocks these small blood vessels[33,34], which results in thrombosis. At this stage a slight increase in the extremity blood flow may prevent complete anoxia and necrosis. The drugs were tried for this purpose. Further, even though plenty of research has been done

Table 5. Effect of tolazoline hydrochloride on the occurrence of frost bite in monkeys

Sr. No.	Before Treatment: Rectal Temperature (°C)		Before Treatment: Skin Temperature on Dorsum of the foot (°C)		Degree of injury	After Treatment: Rectal Temperature (°C)		After Treatment: Skin Temperature on Dorsum of the foot (°C)		Degree of injury
	Before cold exposure	After cold exposure	Before cold exposure	After cold exposure		Before cold exposure	After cold exposure	Before cold exposure	After cold exposure	
1	38.5	38.0	30.0	−12.0	++++	38.2	36.8	31.5	−3.5	++
2	38.4	37.8	30.6	− 4.0	++	38.5	37.2	32.0	−1.5	++
3	38.5	38.0	28.5	− 3.5	++	38.8	37.0	30.6	−5.0	++
4	38.9	38.0	30.2	− 8.0	+++	38.8	37.3	31.5	−1.2	+
5	38.3	37.5	28.8	− 2.5	+	38.0	37.0	32.2	−3.0	+
6	38.6	37.8	32.2	− 2.0	+	38.5	36.8	33.5	−2.5	+
7	38.5	37.9	30.5	− 3.5	++	37.8	36.8	29.8	−2.5	++
8.	38.8	37.5	30.0	−11 0	++++	38.6	37.1	30.3	−4.0	++
9	38.2	37.6	29.8	− 2.5	+++	38.8	37.6	30.2	−2.8	++
10	38.5	37.8	31.5	− 4.5	++	38.6	37.2	32.0	−3.8	++
11	38.6	37.8	30.5	− 6.5	+++	38.7	37.4	30.0	−1.0	+
12	38.9	38.0	31.4	− 4.5	+++	38.5	37.5	32.5	−3.5	++
13	38.6	37.8	29.6	−11.2	+++	38.9	37.3	33.0	−3.5	++
14	38.7	37.6	31.5	− 3.5	++	38.4	37.2	32.5	−2.0	++
Mean	38.57	37.79	30.36	− 5.66		38.51	37.16	31.54	−2.84	
± SEM	0.055	0.045	0.280	0.933		0.086	0.069	0.317	0.306	
Significance						NS	***	**	*	*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; NS—Not significant

Comparisons were made between before and after treatment on the treatment of frost bite[35,36,37], data are lacking in the direction of prevention. Frost bite once occurred, treatment is of very little benefit. Therefore, use of drug and other measures for prevention assume immense importance. Out of the various drugs, tolazoline hydrochloride and vitamin C gave some encouraging results. The beneficial effect of tolazoline hydrochloride might be due to an increased blood supply and prevention of stasis in the capillaries at a critical stage of formation of thrombosis. The fall in rectal temperature seen in the case of monkeys may not be so marked in the case of man, who will be protected by proper clothing. Thus the data suggest that these drugs merit attention for field trials under actual situations of hypoxia and cold for the prevention of cold injuries.

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