Hyperkalemia

A Prognostic Factor During Acute Severe Hypothermia

Marie-Denise Schaller, MD; Adam P. Fischer, MD; Claude H. Perret, MD, FCCP, FCCM

When hypothermic patients appear to be dead, the decision to resuscitate may be difficult due to lack of reliable criteria of death. To discover useful prognostic indicators, we reviewed the hospital charts of nine hypothermic victims of snow avalanches (group A: median value of rectal temperature, 29.6°C; range, <12°C to 34°C) and of 15 patients with hypothermia following acute drug intoxication and/or cold exposure (group B: 28.8°C; range, 25.5°C to 32°C. In group A, plasma potassium level on admission was extremely high (14.5 mmol/L; range, 6.8 to 24.5 mmol/L) compared with that obtained in group B (3.5 mmol/L; range, 2.7 to 5.3 mmol/L). All patients in group A were in cardiorespiratory arrest. None could be successfully resuscitated despite effective rewarming by cardiopulmonary bypass or peritoneal lavage. In contrast, all of the patients in group B recovered from hypothermia, including two in cardiorespiratory arrest. Thus, extreme hyperkalemia during acute hypothermia appears to be a reliable marker of death. It might be used to select those patients in whom heroic resuscitation efforts can be useful.

(*JAMA*. 1990;264:1842-1845)

A BETTER understanding of the pathophysiology of hypothermia[1] accounts for the recent development of sophisticated rewarming techniques, such as gastrointestinal, peritoneal, and mediastinal irrigation or extracorporeal blood warming.[2-9] Among these, rapid core rewarming using cardiopulmonary bypass has been reported to be of particular interest in patients experiencing severe hypothermia who have suffered cardiorespiratory arrest for 1 to 3 hours.[7] Ideally, such radical treatment should be applied only to those patients in cardiocirculatory arrest who have a chance of recovery. Hypothermia greatly modifies clinical and biochemical factors so that it becomes difficult to determine the chance of survival or even to establish if a patient is dead or alive. Reliable indicators of death in patients with hypothermia would be of great help in making hospital triage decisions, to limit any delay in the treatment of those who have a chance of survival, and to avoid rewarming patients who are dead.

For editorial comment see p 1856.

From the Intensive Care Unit, Department of Medicine (Drs Schaller and Perret) and Division of Cardiovascular Surgery (Dr Fischer), University Hospital, Lausanne, Switzerland

Reprint requests to Intensive Care Unit, Department of Medicine, University Hospital, CH-1011 Lausanne, Switzerland (Dr Schaller).

MATERIALS AND METHODS

The hospital charts of all hypothermic victims of snow avalanches who were admitted to the University Hospital of Lausanne (Switzerland) between 1984 and 1988 were reviewed. Charts of all patients admitted to our medical intensive care unit during the same period with a diagnosis of hypothermia following acute drug intoxication and/or cold exposure were also reviewed. Hypothermia was defined as a core temperature below 35°C. The circumstances leading to hypothermia, clinical findings, and biochemical alterations, as well as outcome, were analyzed in search of a possible prognostic indicator. In another group of patients with normothermia who died in the intensive care unit, blood was drawn up to 1 hour after death and plasma potassium was measured. Lactate was measured using a lactate analyzer (23 L; Yellow Springs Instrument, Yellow Springs, Ohio). Arterial pH was measured with a blood gas analyzer (AVL 995; AVL, Schaffhausen, Switzerland). Nonparametric tests (Kruskal-Wallis, Mann-Whitney, and Spearman's rank correlation coefficient) were performed comparing biochemical variables between the different groups. Results are expressed as median (range) unless otherwise specified.

RESULTS

During a 5-year period, nine patients were hospitalized for accidental hypothermia due to snow avalanches (group A) and 15 patients were admitted with hypothermia occurring after drug or alcohol intoxication and/or prolonged cold exposure (group B). Patient characteristics, treatment, and outcome are summarized in Tables 1 and 2. In group A, rectal temperatures ranged from <12°C to 34°C (29.6°C) compared with 25.5°C to 32°C (28.8°C) in group B (not significant [NS]). All nine patients in group A were in cardiorespiratory arrest on admission and none of them responded to

Table 1.—Hypothermic Patients After an Avalanche (Group A): Admission Data, Treatment, and Outcome*

Patient No./Sex/Age, y	Cold Exposure Time, h	Rectal Temperature, °C	pH_a† at 37°C	Lactate, mmol/L	Potassium, mmol/L	Relevant Clinical Findings	Rewarming Method	Outcome
1/M/15	0.5	24.2	6.68	ND	6.8	CRA	CPB	Dead
2/M/17	5.3	24.5	6.24	ND	16.2	CRA	CPB	Dead
3/M/35	2?‡	31.5	6.55	18	18	CRA	. . .	Dead
4/M/27	2	29.6	6.59	20	12.6	CRA	CPB	Dead
5/M/24	<1	31	ND	ND	13.5	CRA	CPB	Dead
6/F/51	2	30.9	6.69	21	14.5	CRA	PL	Dead
7/M/28	<1	34	6.54	ND	9.4	CRA	CPB	Dead
8/M/20	>18	<12	ND	ND	24.5	CRA	. . .	Dead
9/M/18	>18	<12	ND	ND	24.2	CRA	CPB	Dead

*ND indicates not determined; CRA, cardiorespiratory arrest; CPB, cardiopulmonary bypass; and PL, peritoneal lavage.
†pH_a indicates arterial pH not corrected for actual temperature. Since temperature-corrected pH values have no established physiological reference values, it was considered that pH measured at 37°C would best reflect the in vivo acid-base status.
‡Question mark indicates not precisely known.

Table 2.—Hypothermic Patients After Drug Intoxication and/or Cold Exposure (Group B): Admission Data, Treatment, and Outcome*

Patient No./Sex/Age, y	Precipitating Factors	Cold Exposure Time, h	Rectal Temperature, °C	pH_a† at 37°C	Lactate, mmol/L	Potassium, mmol/L	Relevant Clinical Findings	Rewarming Method	Outcome
1/F/59	Drug intoxication	24	27.8	7.29	0.6	4.0	Coma	MV	Survivor
2/F/27	Drug intoxication	24?§	31.4	7.44	0.8	3.8	Stupor	Passive‡	Survivor
3/F/78	Fall in apartment	24-36?	25.5	7.19	1.1	3.2	Stupor; HR, 32 beats/min	GL	Survivor
4/M/44	Drug intoxication	4.5?	30.5	7.31	7.9	3.3	None	MV	Survivor
5/F/47	Immersion	2	30	7.17	7.5	3.0	None	Passive	Survivor
6/M/45	Alcohol, subdural hematoma	4-9?	27.8	7.30	ND	2.7	Coma/RA	MV	Death, day 2
7/F/35	Anorexia nervosa	0	30.4	7.37	ND	3.6	None	Passive	Death, day 8
8/M/52	Terminal cancer	12?	27.3	7.39	10.3	4.0	Coma; HR, 40 beats/min	Passive	Death, day 8
9/F/40	Drug intoxication	36?	31.2	7.28	1	3.5	Coma; RR, 8/min	MV	Survivor
10/M/68	Immersion	0.75	27	6.45	3	2.7	CRA	PL/MV	Survivor
11/F/48	Immersion	2.5	28.2	7.18	1.6	4.5	Coma	PL/MV	Survivor
12/M/32	Floating on lake, overnight	12	31.5	7.39	2.1	3.7	None	Passive	Survivor
13/F/48	Drug intoxication	13.5	27	7.20	7.8	3.0	CRA	MV	Survivor
14/F/55	Drug intoxication	12	32	7.42	ND	5.3	None	Passive	Survivor
15/M/49	Drug intoxication	96?	28.8	7.12	2.5	3.1	Coma and shock	GL	Death, day 3

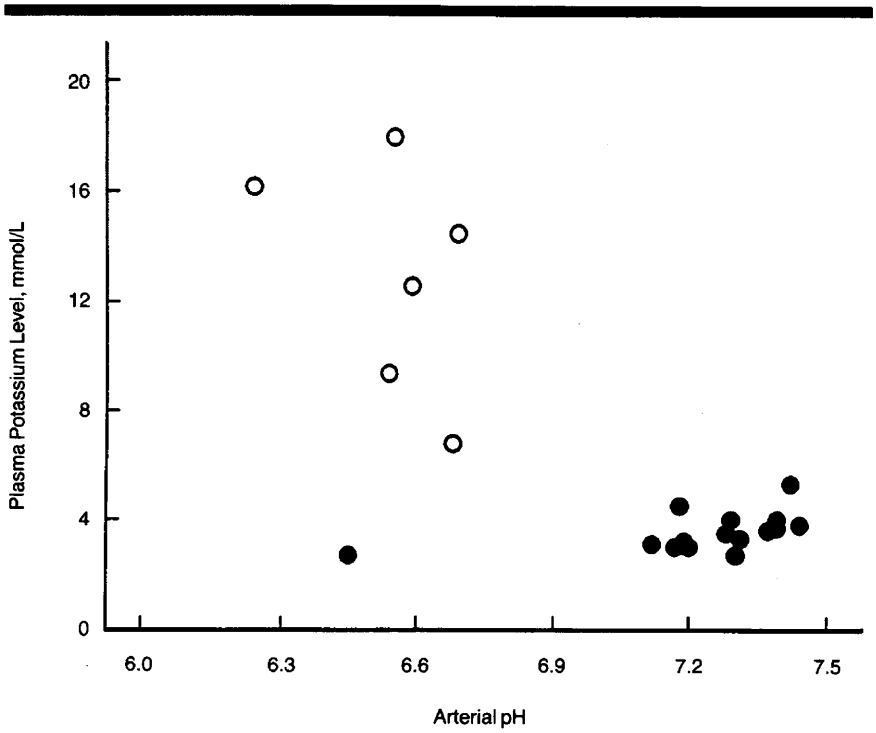
*ND indicates not determined; HR, heart rate; RA, respiratory arrest; RR, respiratory rate; CRA, cardiorespiratory arrest; MV, mechanical ventilation; GL, gastric lavage; and PL, peritoneal lavage.
†pH_a indicates arterial pH not corrected for actual temperature. Since temperature-corrected pH values have no established physiological reference values, it was considered that pH measured at 37°C would best reflect the in vivo acid-base status.
‡Passive rewarming involved putting isolating blankets over the thorax and abdomen and the administration of warmed perfusions and heated air inhalation.
§Question mark indicates not precisely known.

cardiopulmonary resuscitation and active core rewarming with cardiopulmonary bypass in six patients or peritoneal lavage in one patient.

In contrast, all of the 15 patients with hypothermia in group B recovered. However, there were four late deaths due to associated conditions; these included bilateral subdural hematoma with severe brain compression and skull fractures (patient 6), sudden death in a patient with anorexia nervosa (patient 7), metastatic cancer (patient 8), and septic shock and pneumonia (patient 15). In this group, it is noteworthy that the two patients who suffered cardiorespiratory arrest were successfully resuscitated. Intravascular disseminated coagulation was noticed in several patients of both groups. Arterial pH values that were measured at 37°C ranged from 6.24 to 6.69 (6.57) in six patients of group A and were significantly lower than those obtained in group B (7.29; 6.45 to 7.44; $P<.002$). It is interesting to note that patient 10 from group B recovered in spite of an extremely severe acidosis (pH 6.45). Arterial blood lactate was 18, 20, and 21 mmol/L in patients 3, 4, and 6, respectively, of group A (ie, higher than any value determined in the patients from group B). The most striking finding was the high plasma potassium levels measured in group A (14.5 mmol/L; 6.8 to 24.5 mmol/L) compared with those obtained in group B (3.5 mmol/L; 2.7 to 5.3 mmol/L; $P<.001$). When comparing patients with moderate hypothermia (rectal temperature of 28°C to 34°C), kalemia was 13.5 mmol/L (9.4 to 18 mmol/L) in group A ($n=5$) and 3.6 mmol/L (3 to 5.3 mmol/L) in group B ($n=9$; $P<.01$). In those patients with severe hypothermia (rectal temperature <12°C to 28°C) the difference is still significant, with a median value of kalemia of 20.2 mmol/L (6.8 to 24.5 mmol/L) in group A ($n=4$) and 3.1 mmol/L (2.7 to 4.0 mmol/L) in group B ($n=6$; $P<.05$). There was no correlation between arterial pH and plasma potassium in group A ($r=.31$) or in group B ($r=.58$, Figure).

In the third nonhypothermic group (two women, 11 men, 33 to 75 years old) dying in the hospital, plasma potassium levels progressively increased from 5.44 ± 0.33 mmol/L (mean ± SEM) at time of cardiac arrest to 5.85 ± 0.46 mmol/L, 6.11 ± 0.44 mmol/L, and 6.92 ± 0.40 mmol/L at 15-minute intervals, subsequently up to 7.2 ± 0.47 mmol/L after 1 hour ($P<.001$). The mean level achieved 1 hour after death was significantly higher than that measured in patients from group B (3.56 ± 0.18; $P<.001$).

In group A, patient 1, who had the lowest potassium level (6.8 mmol/L), was the only one to recover sinus rhythm and a pulse pressure during rewarming. However, he could never be



Plasma potassium and arterial pH were measured in hypothermic victims of snow avalanches (group A: open circles) and in patients with hypothermia following acute drug intoxication and/or cold exposure (group B: closed circles). No correlation was found in group A ($r = .31$) or in group B ($r = .58$) between plasma potassium and pH.

weaned off the heart-lung machine and died of severe pulmonary hemorrhage.

COMMENT

One of the main problems in the treatment of hypothermia is identifying those patients in cardiorespiratory arrest who have a chance of being successfully resuscitated, particularly when several victims are admitted simultaneously. Temperature itself is not a reliable index, as demonstrated by reports of successful resuscitation in patients with extreme hypothermia.[10-13] Unconsciousness due to hypothermia rarely occurs with a core temperature above 28°C, so that an associated cause should be sought if coma appears with a higher temperature.[14] However, resuscitation cannot be withheld solely on the basis of coma and asystole associated with a too mild degree of hypothermia; successful resuscitation has been reported in comatose and asystolic patients with relatively moderate hypothermia after immersion.[15-17] Furthermore, it is well established that prolonged cardiorespiratory arrest during hypothermia does not per se predict outcome.[7,15-17] Patients 10 and 13 in group B confirm this. Therefore, at this time, the only definite criterion of death is failure to respond to resuscitation and rewarming.[18-20]

Although there is still controversy concerning the effect of hypothermia on plasma potassium levels,[14,15,21-23] it is generally accepted that prolonged induced hypothermia usually produces hypokalemia by shifting potassium from extracellular to intracellular compartments.[24,25] This could account for our finding of plasma potassium levels below 3.5 mmol/L in almost 50% of the patients in group B. In contrast, all patients in our series who were hypothermic secondary to an avalanche accident had an extremely high plasma potassium level and, when measured, a severe acidosis, although the "normal" range of pH for low temperatures is presently unknown.[26] Acute acid-base disturbances are known to produce changes in plasma potassium concentration that largely reflect transmembrane flux of the ion.[27,28] When experimentally induced by infusion of mineral acids, acute acidosis is associated with increments in plasma potassium concentration.[28,29] In sharp contrast, no modification in kalemia is observed when metabolic acidosis is due to organic acids.[28,30] Thus, lactic acidosis cannot be responsible for the extremely high potassium levels observed in group A. Acute hypercapnia elicits a too moderate increase in kalemia (0.04 to 0.3 mmol/L for each 0.1 U of pH decrease[28]) to account for the extreme values reached in this group. Common causes of hyperkalemia, such as chronic renal failure or hypoaldosteronism, could not be evoked. Although patients in group A were skiing when swept away by an avalanche, the extreme levels of plasma potassium measured on admission are much higher than those reported in crush syndrome or after strenuous exercise,[31-33] even when associated with hypothermia.[34] The most likely mechanism is a transfer of cellular potassium in extracellular fluid, reflecting acidosis and tissue damage following death. This is in agreement with the progressive rise in plasma potassium levels observed after death in our series of patients with normothermia.

In a multicenter hypothermia survey, Danzl et al[35] reported a significantly higher plasma potassium level in the nonsurvivors (4.6 ± 1.57 mmol/L; mean $\pm$ SD) compared with the survivors (4.10 ± 0.8 mmol/L). In that series of 401 patients with hypothermia, which did not include avalanche accidents, potassium values ranged from 1.5 to 9.3 mmol/L and never reached the extreme values obtained in our patients. Similarly, in nine climbers found severely hypothermic after 2 to 3 days of cold exposure on Mt Hood, plasma potassium was noticed to be extremely high in seven nonsurvivors (>8 to 33 mmol/L), while it was 5.3 and 6.7 mmol/L, respectively, in the two survivors.[36] Thus, it appears that profound hyperkalemia (>10 mmol/L) could be used as a prognostic index when other clinical and biochemical changes due to hyperthermia are misleading. Arterial pH seems of limited interest in the absence of established normal ranges during hypothermia. Furthermore, extreme acidosis as an isolated finding does not imply a fatal outcome as demonstrated by the complete recovery of patient 10 in group B. One may argue that, in our study, conditions leading to hypothermia might influence outcome. Actually, successful resuscitation has been reported in hypothermic victims of avalanches admitted to the hospital after prolonged cardiorespiratory arrest.[7]

There are probably multiple independent variables that affect outcome in this setting. Until more detailed data are available, a markedly elevated potassium level (perhaps >10 mmol/L) should be considered as an index of irreversibility. Practically speaking, when a patient presents with hypothermia, cardiorespiratory arrest, and coma, the plasma potassium level should be obtained immediately. It might be used as

a tool for triage decision in the hospital when several patients with hypothermia have to be treated simultaneously, whatever the temperature or the presence of a cardiorespiratory arrest. It is probably even futile to prolong resuscitation in patients experiencing hypothermia with cardiorespiratory arrest when potassium levels reach such extremes.

Since this manuscript was submitted for publication, a 44-year-old woman was admitted to our institution with severe hypothermia (19.6°C) and prolonged cardiorespiratory arrest (3.25 hours) following an avalanche accident. She remained buried under 2 m of snow for 1 hour. Kalemia on admission was 4.5 mmol/L and arterial pH was 7.07. Rapid core rewarming was achieved with cardiopulmonary bypass. The patient recovered uneventfully.

We are grateful to Professor E. Kenneth Weir, MD, Minneapolis, Minn, for his constructive advice in preparing the manuscript. We also want to thank Jérôme Biollaz, MD, for the statistical analysis of the results, Gérard Waeber, MD, and Francis Héritier, MD, for performing blood sampling in normothermic patients after death, and Françoise Bilat for her secretarial help.

References

1. Reuler JB. Hypothermia: pathophysiology, clinical settings, and management. *Ann Intern Med.* 1978;89:519-527.
2. Ferguson J, Epstein F, Leuv J. Accidental hypothermia. *Emerg Med Clin North Am.* 1983;1:619-637.
3. Splittgerber FH, Talbert JG, Sweezer WP, et al. Partial cardiopulmonary bypass for core rewarming in profound accidental hypothermia. *Am J Surg.* 1986;52:407-412.
4. Davis FM, Judson JA. Warm peritoneal dialysis in the management of accidental hypothermia: a report of five cases. *N Z Med J.* 1981;94:207-209.
5. Bristow G, Smith R, Lee J, et al. Resuscitation from cardiopulmonary arrest during accidental hypothermia due to exhaustion and exposure. *Can Med Assoc J.* 1977;117:247-249.
6. Collis ML, Steinman AM, Chaney RD. Accidental hypothermia: an experimental study of practical rewarming methods. *Aviat Space Environ Med.* 1977;48:625-632.
7. Althaus U, Aeberhard P, Schupbach P, et al. Management of profound accidental hypothermia with cardiorespiratory arrest. *Ann Surg.* 1982; 195:492-495.
8. Ledingham IM, Mone JG. Treatment of accidental hypothermia: a prospective clinical study. *BMJ.* 1980;280:1102-1105.
9. Linton AL, Ledingham IM. Severe hypothermia with barbiturate intoxication. *Lancet.* 1966; 1:24-26.
10. Anderson S, Bengt G, Herbring BD, Widman B. Accidental profound hypothermia. *Br J Anaesth.* 1970;42:653-655.
11. Laufman H. Profound accidental hypothermia. *JAMA.* 1951;147:1201-1211.
12. Nozaki R, Ishibashi K, Adachi N, Nishihara S, Adachi S. Accidental profound hypothermia. *N Engl J Med.* 1986;315:1680.
13. Moss JF, Haklin M, Southwick HW, et al. A model for the treatment of accidental severe hypothermia. *J Trauma.* 1986;26:68-74.
14. Paton BC. Accidental hypothermia. *Pharmacol Ther.* 1983;22:331-377.
15. Theilade D. The danger of fatal misjudgment in hypothermia after immersion. *Anaesthesia.* 1977;32:889-892.
16. Dominguez de Villota E, Barat J, Peral G, Juffé A, Fernandez de Miguel JM, Avello F. Recovery from profound hypothermia with cardiac arrest after immersion. *BMJ.* 1973;4:394.
17. Kvittingen TD, Naess A. Recovery from drowning in fresh water. *BMJ.* 1963;1:1315-1317.
18. Gregory RT, Patton JF. Treatment after exposure to cold. *Lancet.* 1972;1:377-378.
19. Gunby P. Cold facts concerning hypothermia. *JAMA.* 1980;243:1403-1409.
20. Zell SC, Kurtz KJ. Severe exposure hypothermia: a resuscitation protocol. *Ann Emerg Med.* 1985;14:339-345.
21. Coniam SW. Accidental hypothermia. *Anesthesia.* 1979;34:250-256.
22. Machida S, Ohta S, Itoh N. Changes in tissue distribution of potassium during simple hypothermia. *Kyobu Geka.* 1977;30:413-418.
23. Black PR, Van Devanter S, Cohn LH. Effects of hypothermia on systemic and organ system metabolism and function. *J Surg Res.* 1976;20:49-63.
24. Koht A, Cane R, Cerullo LJ. Serum potassium levels during prolonged hypothermia. *Intensive Care Med.* 1983;9:275-277.
25. Shida H, Morimoto M, Sugenoya H, Seki T, Inokawa K. Changes of serum electrolytes at open heart surgery with simple profound hypothermia: relation between transient hypopotassemia and metabolic acidosis. *Kyobu Geka.* 1973;26:723-728.
26. Shapiro BA, Harrison RA, Cane RD, Templin R, Wong HY. Temperature correction of blood gases. In: *Clinical Application of Blood Gases.* 4th ed. Chicago, Ill: Year Book Medical Publishers Inc; 1989:176-184
27. Giebisch G, Berger L, Pitts RF. The extrarenal response to acute acid-base disturbances of respiratory origin. *J Clin Invest.* 1955;34:231-245.
28. Adrogué HJ, Madias NE. Changes in plasma potassium concentration during acute acid-base disturbances. *Am J Med.* 1981;71:456-467.
29. Simmons DH, Avedon M. Acid-base alterations and plasma potassium concentration. *Am J Physiol.* 1959;197:319-326.
30. Orringer CE, Eustace JC, Wunsch CD, Gardner LB. Natural history of lactic acidosis after grand-mal seizures: a model for the study of an anion-gap acidosis not associated with hyperkalemia. *N Engl J Med.* 1977;297:796-799.
31. Maughan RJ, Light IM, Whiting PH, Miller JDB. Hypothermia, hyperkalaemia, and marathon running. *Lancet.* 1982;2:1336.
32. van Beaumont W, Strand JC, Petrofsky JS, Hipskind SG, Greenleaf JE. Changes in total plasma content of electrolytes and proteins with maximal exercise. *J Appl Physiol.* 1973;34:102-106.
33. Coester N, Elliott JC, Luft UC. Plasma electrolytes, pH, and ECG during and after exhaustive exercise. *J Appl Physiol.* 1973;34:677-682.
34. Ledingham IM, MacVicar S, Watt I, Weston GA. Early resuscitation after marathon collapse. *Lancet.* 1982;2:1096-1097.
35. Danzl DF, Pozos RS, Auerbach PS, et al. Multicenter hypothermia survey. *Ann Emerg Med.* 1987;16:1042-1055.
36. Hauty MG, Esrig BC, Hill JG, Long WB. Prognostic factors in severe accidental hypothermia: experience from the Mt Hood tragedy. *J Trauma.* 1987;27:1107-1112.