Department of Neurology, Henry Ford Hospital, Detroit, MI 48202. In 27 cats treated to vary arterial serum glucose concentrations, we measured cerebral high-energy phosphate metabolite concentration and intracellular pH using in vivo phosphorus-31 nuclear magnetic resonance spectroscopy during transient global cerebral ischemia and reperfusion. Hypoglycemia was induced with 4 units/kg i.v. insulin in six cats before ischemia; hyperglycemia was induced with 1.5 g/kg i.v. glucose in six cats before and in six cats during ischemia. Nine untreated cats subjected to ischemia without manipulation of blood glucose concentration served as controls. During ischemia, intracellular pH fell to similar levels in the control and both hyperglycemic groups. During reperfusion, the hyperglycemic before ischemia group initially exhibited a severe further decline in intracellular pH (p less than 0.003); this further decline was not observed in the control or the hyperglycemic during ischemia groups. Intracellular acidosis was attenuated both during ischemia and early after reperfusion in the hypoglycemic before ischemia group. In all groups, cerebral high-energy phosphate metabolite concentrations were depleted during ischemia and then recovered to the same degree during reperfusion. Our data suggest that brain glucose stores before ischemia determine the severity and time course of intracellular acidosis during ischemia and reperfusion. PMID: 3188123 [PubMed - indexed for MEDLINE]

Katz, L. M., Y. Wang, et al. (1998). "Glucose plus insulin infusion improves cerebral outcome after asphyxial cardiac arrest." Neurorreport 9(15): 3363-7. Hyperglycemia before ischemia worsens cerebral outcome. The aim of this study was to determine the cerebral effects of giving glucose with or without insulin after asphyxial cardiac arrest. Rats underwent 8 min of asphyxial cardiac arrest. After arrest, Group 1 received NaCl; Group 2, insulin; Group 3, glucose; and Group 4, glucose plus insulin, all intravenously. Neurological deficit (ND) scores were 14+/-10%, 22+/-12%, 12+/-10% and 2+/-2% in Groups 1-4, respectively, 72 h after reperfusion. Overall histological damage (HD) scores were 4, 2, 3 and 1, respectively. Group 4 fared significantly better than group 1 on both scores. Glucose after asphyxial cardiac arrest in rats produces no increased brain damage while glucose plus insulin improves cerebral outcome.

RESULTS: In Oslo, Akershus, Ostfold and Stavanger 98, 84, 91 and 186 patients were included, respectively. Hospital mortality was higher in Oslo (66%) and Akershus (64%) than in Ostfold (56%) and Stavanger (44%), P=0.002. By multivariate analysis the following pre-arrest and pre-hospital factors were associated with in-hospital survival: age <or=71 years, better pre-arrest overall performance, a call-receipt-start CPR interval <or=1 min, and no use of adrenaline (epinephrine). The in-hospital factors associated with survival were: no seizures, base excess >-3.5 mmol l(-1), body temperature <or=37.8 degrees C, and serum glucose <or=10.6 mmol l(-1) 1-24 h after admittance with OR (95% CI) 2.72 (1.09-8.82, P=0.033), 1.12 (1.02-1.23, P=0.016), 2.67 (1.17-6.20, P=0.019) and 2.50 (1.11-5.65, P=0.028), respectively. Pre-arrest overall function, whether adrenaline was used, body temperature, the occurrence of hypotensive episodes, and the degree of metabolic acidosis differed between the four regions in parallel with the in-hospital survival rates. CONCLUSION: Both pre-arrest, pre- and in-hospital factors were associated with in-hospital survival after OCHA. It seems important also to report in-hospital factors in outcome studies of OCHA. The design of the study precludes a conclusion on causability.

We examined the interrelations of outcome, time elapsed during cardiopulmonary resuscitation (CPR), and blood glucose levels drawn from 83 patients with out-of-hospital cardiac arrest. Levels rose significantly during CPR. Although slope and intercept of regression lines differed for those dying in the field and those admitted, regression lines were similar for those who awoke and never awoke after admission. These results suggest that the previously reported association between poor neurologic recovery and high blood glucose level on admission after cardiac arrest is best explained by prolonged CPR, leading to both higher rise of blood glucose and worse neurologic outcome.

To develop a model that would forecast neurologic recovery after out-of-hospital cardiac arrest, we reviewed charts on 389 consecutive patients who were not awake on admission to the hospital after resuscitation from asystole or ventricular fibrillation. The outcome variable was "awakening," which was defined as having comprehensible speech or the ability to follow commands. Predictor variables that we considered included both preadmission and admission data. Using discriminant analysis, we derived models from a 60 per cent random sample of cases and tested the models on the remaining 40 per cent. We judged that the best model contained four variables from the admission examination: motor response, pupillary light response, spontaneous eye movements, and blood glucose (levels below 300 mg per deciliter predicted awakening). Overall
correct classification was 80 per cent in the derivation sample and 77 per cent in the test sample. In a simplified form, the model's predictions of awakening had a sensitivity of 0.92, a specificity of 0.65, a positive predictive value of 0.80, and a negative predictive value of 0.84. This rule should be clinically useful in estimating the neurologic prognosis of patients resuscitated after out-of-hospital cardiac arrest.


Experimental data suggest that postischemic blood glucose concentration plays an important role in modulating both ischemic cerebral infarction and selective neuronal necrosis. This study investigated the association between functional neurological recovery and blood glucose concentrations in human cardiac arrest survivors. A group of 145 nondiabetic patients were evaluated after witnessed ventricular fibrillation cardiac arrest. Data regarding cardiac arrest were collected according to an internationally accepted protocol immediately after arrival. Blood glucose was measured on admission and 6, 12, and 24 h thereafter. To control for duration of cardiac arrest and cardiogenic shock, both known to influence outcome as well as blood glucose, levels, Spearman rank partial correlation was used. In this multivariate analysis, a high admission blood glucose level tended to be associated with poor neurological outcome (rs = -0.16, n = 142, p = 0.06). The association between high median blood glucose levels over 24 h and poor neurological outcome was strong and statistically significant (rs = -0.2, n = 145, p = 0.015). High blood glucose concentrations occurring over the first 24 h after cardiac arrest have deleterious effects on functional neurological recovery. Whether cardiac arrest survivors might benefit from reduction of blood glucose levels needs further investigation.


INTRODUCTION: The impact of the immediate in-hospital post-resuscitation care after out-hospital cardiac arrest is not well known. Based on treatment variables and laboratory findings a multiple logistic regression model was created for the prediction of survival at 6 months from the event. MATERIALS AND METHODS: A retrospective study of the hospital charts of patients successfully resuscitated and treated in one of three community hospitals from 1998 to 2000. In addition to several pre-hospital variables, the mean 72 h values of clinical features such as blood pressure, blood glucose concentration and initiated treatment used, were included in a forward multiple logistic regression model predicting survival at 6 months from the event. RESULTS: The charts of 98 out of a total of 102 patients were sufficiently complete and included in the analysis. Variables independently associated with survival were age, delay before a return of spontaneous circulation, mean blood glucose and serum potassium, and the
use of beta-blocking agents during post-resuscitation care. When those patients who were assigned a ‘do not attempt to resuscitate’ (DNAR) order during the first 72 h of treatment were excluded from the analysis blood glucose, blood potassium and the use beta-blocking agents remained independently associated with survival. CONCLUSION: This study suggests that in-hospital factors are associated with survival from out-of-hospital cardiac arrest. The mean blood glucose and serum potassium during the first 72 h of treatment and the use of beta-blocking agents were significantly and independently associated with survival.

OBJECTIVE: To investigate the relationship between neurologic outcome and blood glucose concentrations in survivors of cardiopulmonary arrest. DESIGN: Retrospective case series chart review. SETTING: Adult multidisciplinary intensive care unit (ICU) of a tertiary referral medical center. SUBJECTS: Consecutive patients over a 12-month period surviving cardiopulmonary resuscitation (CPR). INTERVENTIONS: Variables that were examined that could affect the relationship between the circulating glucose concentration and neurologic outcome included: location of arrest (inpatient/out-of-hospital), age, history of diabetes mellitus, duration of arrest, CPR duration, initial cardiac rhythm, and drugs administered during arrest. Cerebral recovery was evaluated by a 5-point outcome scale (Glasgow Pittsburgh Brain Stem Score) on ICU admission, and 24 and 48 hrs after ICU admission. MEASUREMENTS AND MAIN RESULTS: Observations were made on 85 patients, of whom 67% had inpatient CPR and 33% received out-of-hospital CPR. The duration of arrest of 66 (78%) patients was <5 mins. Mean CPR duration was 13.7 mins. Twenty-one percent of patients had diabetes. The mean blood glucose concentration post-CPR (n = 80) was 272 mg/dL (15.1 mmol/L). A statistically significant association was shown between high glucose concentration post-CPR and severe cerebral outcome among a small subset of patients with CPR lasting >5 min. CONCLUSIONS: The present study does not support an association between the concentration of glucose post-CPR and neurologic outcome. The previously reported casual relationship between hyperglycemia and neurologic prognosis may be an epiphenomenon of the severity of global cerebral ischemia in humans.

BACKGROUND: Hyperglycemia and insulin resistance are common in critically ill patients, even if they have not previously had diabetes. Whether the normalization of blood glucose levels with insulin therapy improves the prognosis for such patients is not known. METHODS: We performed a prospective, randomized, controlled study involving adults admitted to our surgical intensive care unit who were receiving mechanical ventilation. On admission, patients were randomly assigned to receive intensive insulin therapy (maintenance of blood glucose at a level between 80 and 110 mg per deciliter [4.4 and 6.1 mmol per
liter]) or conventional treatment (infusion of insulin only if the blood glucose level exceeded 215 mg per deciliter [11.9 mmol per liter] and maintenance of glucose at a level between 180 and 200 mg per deciliter [10.0 and 11.1 mmol per liter]).

RESULTS: At 12 months, with a total of 1548 patients enrolled, intensive insulin therapy reduced mortality during intensive care from 8.0 percent with conventional treatment to 4.6 percent (P<0.04, with adjustment for sequential analyses). The benefit of intensive insulin therapy was attributable to its effect on mortality among patients who remained in the intensive care unit for more than five days (20.2 percent with conventional treatment, as compared with 10.6 percent with intensive insulin therapy, P=0.005). The greatest reduction in mortality involved deaths due to multiple-organ failure with a proven septic focus. Intensive insulin therapy also reduced overall in-hospital mortality by 34 percent, bloodstream infections by 46 percent, acute renal failure requiring dialysis or hemofiltration by 41 percent, the median number of red-cell transfusions by 50 percent, and critical-illness polyneuropathy by 44 percent, and patients receiving intensive therapy were less likely to require prolonged mechanical ventilation and intensive care. CONCLUSIONS: Intensive insulin therapy to maintain blood glucose at or below 110 mg per deciliter reduces morbidity and mortality among critically ill patients in the surgical intensive care unit.


OBJECTIVES: Maintenance of normoglycemia with insulin reduces mortality and morbidity of critically ill patients. Here we report the factors determining insulin requirements and the impact of insulin dose vs. blood glucose control on the observed outcome benefits. DESIGN: A prospective, randomized, controlled trial. SETTING: A 56-bed predominantly surgical intensive care unit in a tertiary teaching hospital. PATIENTS AND INTERVENTION: A total of 1,548 patients were randomly assigned to either strict normalization of blood glucose (80-110 mg/dL) with insulin infusion or the conventional approach, in which insulin is only given to maintain blood glucose levels at 180-200 mg/dL. MEASUREMENTS AND MAIN RESULTS: It was feasible and safe to achieve and maintain blood glucose levels at <110 mg/dL by using a titration algorithm. Stepwise linear regression analysis identified body mass index, history of diabetes, reason for intensive care unit admission, at-admission hyperglycemia, caloric intake, and time in intensive care unit as independent determinants of insulin requirements, together explaining 36% of its variation. With nutritional intake increasing from a mean of 550 to 1600 calories/day during the first 7 days of intensive care, normoglycemia was reached within 24 hrs, with a mean daily insulin dose of 77 IU and maintained with 94 IU on day 7. Insulin requirements were highest and most variable during the first 6 hrs of intensive care (mean, 7 IU/hr; 10% of patients required >20 IU/hr). Between day 7 and 12, insulin requirements decreased by 40% on stable caloric intake. Brief, clinically harmless hypoglycemia occurred in 5.2% of intensive insulin-treated patients on median day 6 (2-14) vs. 0.8% of conventionally treated patients on day 11 (2-10). The
outcome benefits of intensive insulin therapy were equally present regardless of whether patients received enteral feeding. Multivariate logistic regression analysis indicated that the lowered blood glucose level rather than the insulin dose was related to reduced mortality (p <.0001), critical illness polyneuropathy (p <.0001), bacteremia (p =.02), and inflammation (p =.0006) but not to prevention of acute renal failure, for which the insulin dose was an independent determinant (p =.03). As compared with normoglycemia, an intermediate blood glucose level (110-150 mg/dL) was associated with worse outcome.

CONCLUSION: Normoglycemia was safely reached within 24 hrs and maintained during intensive care by using insulin titration guidelines. Metabolic control, as reflected by normoglycemia, rather than the infused insulin dose, was related to the beneficial effects of intensive insulin therapy.

Global cerebral ischemia and intracellular pH during hyperglycemia and hypoglycemia in cats. Chopp M, Welch KM, Tidwell CD, Helpern JA. Department of Neurology, Henry Ford Hospital, Detroit, MI 48202. In 27 cats treated to vary arterial serum glucose concentrations, we measured cerebral high-energy phosphate metabolite concentration and intracellular pH using in vivo phosphorus-31 nuclear magnetic resonance spectroscopy during transient global cerebral ischemia and reperfusion. Hypoglycemia was induced with 4 units/kg i.v. insulin in six cats before ischemia; hyperglycemia was induced with 1.5 g/kg i.v. glucose in six cats before and in six cats during ischemia. Nine untreated cats subjected to ischemia without manipulation of blood glucose concentration served as controls. During ischemia, intracellular pH fell to similar levels in the control and both hyperglycemic groups. During reperfusion, the hyperglycemic before ischemia group initially exhibited a severe further decline in intracellular pH (p less than 0.003); this further decline was not observed in the control or the hyperglycemic during ischemia groups. Intracellular acidosis was attenuated both during ischemia and early after reperfusion in the hypoglycemic before ischemia group. In all groups, cerebral high-energy phosphate metabolite concentrations were depleted during ischemia and then recovered to the same degree during reperfusion. Our data suggest that brain glucose stores before ischemia determine the severity and time course of intracellular acidosis during ischemia and reperfusion. PMID: 3188123 [PubMed - indexed for MEDLINE]