brief communications

Steroids after cardiac arrest: A retrospective study with concurrent, nonrandomized controls

Article abstract—We retrospectively examined the effect of steroid treatment on the outcome of 458 consecutive patients admitted after out-of-hospital cardiac arrest. Of those given steroids, 128/213 (60%) regained consciousness, and of those not given steroids, 150/245 (61%) regained consciousness. Findings remained unchanged using logistic regression to adjust for differences in the two treatment groups. These results suggest that there is no role for steroids in the treatment of global brain ischemia.

Scott T. Grafton, MD, and W.T. Longstreth, Jr., MD, MPH

Does steroid treatment affect outcome from brain ischemia? A recent trial of steroids for ischemic stroke could demonstrate no benefit.[1] There are no randomized trials for global brain ischemia, such as follows cardiac arrest. Experiments in animals with global brain ischemia suggested that steroids have no effect[2,3] or may even be harmful.[4] We decided to search for beneficial or deleterious effects of steroid treatment after cardiac arrest using a previously reported cohort.

Methods. The cohort studied[5,6] consisted of 459 consecutive patients admitted to a single hospital over a 10-year period after out-of-hospital cardiac arrest. All experienced asystole or ventricular fibrillation documented by ECG, and thus all had global brain ischemia. From the initial review of the records,[5,6] we could determine in all but one patient whether steroids were received during the hospitalization; this left 458 patients for analysis. Outcome was determined in all patients. Two outcomes were assessed: awakening and survival to hospital discharge. Awakening was defined as mention in the records of the patient having been able to follow commands or to have comprehensible speech at any time following the cardiac arrest.

We ascertained details of steroid use by a second review of the patient's medical records. Six of the charts could not be located for the second review. The additional information collected included the delay after cardiac arrest until steroids were given, the initial dose, the total dose in the initial three 24-hour periods, total duration of treatment, the type of steroid used, and the medical indication for steroid administration. To allow comparisons, the doses of glucocorticoids given were all expressed in equivalent amounts of dexamethasone.

Both univariate and multivariable analyses were performed. For discrete variables the chi-squared statistic was used; for continuous variables, the t test. We used a multivariable technique, logistic regression,[7] to control for differences in severity between treatment groups. In the logistic regression, we used seven variables previously shown to be independently related to outcome in this cohort.[6] Information on these seven variables was available around the time of admission and would have been available to clinicians making decisions about the use of steroids. The variables were: whether the arrest had been witnessed, whether epinephrine or norepinephrine had been used during the resuscitation, and on admission to the hospital the motor examination, the presence of the pupillary light response, the presence of spontaneous eye movements, and the blood glucose level. We used logistic regression to see if, controlling for these variables, the use of steroids was significantly related to outcome.

Results. Of the 458 consecutive patients admitted after cardiac arrest, 213 (47%) received steroids and 245 (53%) did not. For those receiving steroids, dexamethasone was the most common agent given (76%). We could determine the reason for steroid treatment in 169 patients. In 52% it was for treatment of the ischemic brain injury; in 31% for lung disease, usually aspiration; and in 16% for both. Only three patients were taking steroids prior to their cardiac arrest: one for arthritis and two for pulmonary disease. One with pulmonary disease never awoke; the other two patients did.

The median delay until beginning treatment was 2.7 hours after the cardiac arrest. The first dose of steroids was given within 6 hours in 79% of patients and within 10 hours in 90%. The median duration of treatment was 3.4 days, 87% receiving steroids for 1 week or less. The median doses in the initial three 24-hour periods were 22, 16, and 16 mg of dexamethasone or its equivalent, reflecting the most common dosing regimen of 10 mg of dexamethasone as the initial dose followed by 4 mg every 6 hours. Neither awakening nor survival to hospital discharge were significantly related to type of steroid administered, initial or subsequent steroid dosage, duration of treatment, or reason for treatment.

Table. Steroid treatment and outcome after out-of-hospital cardiac arrest

Outcome	Steroids given	Steroids not given	Difference in proportions	95% CI
Ever awakening*				
All patients	128/213 (60%)	150/245 (61%)	−0.01	−0.10 to 0.08
Patients not awake on admission	115/200 (58%)	94/189 (50%)	0.08	−0.02 to 0.18
Survival to discharge				
All patients	118/213 (55%)	134/245 (55%)	0.007	−0.08 to 0.10
Patients not awake on admission	106/200 (53%)	88/189 (47%)	0.06	−0.03 to 0.16

* "Ever awakening" is defined by the patient's being able to follow commands or having comprehensible speech at some time following the cardiac arrest.

Considering all 458 patients or only the 389 not awake on admission, steroid treatment was not significantly related to ever awakening or survival to hospital discharge (table). To control for differences in the treatment groups, we used logistic regression. The outcome variable was awakening, and the predictor variables were the seven described above and steroid treatment. We first performed the analysis on all patients and used the coefficient to estimate the odds ratio. The odds ratio for steroids was 1.18, 95% CI of 0.83 to 1.61 ($F = 1.06$ and $p >> 0.05$). Considering only patients not awake on admission, the odds ratio for steroid treatment was unchanged at 1.18, 95% CI of 0.85 to 1.61 ($F = 0.88$ and $p >> 0.05$). Thus, the risk of never awakening for patients treated with steroids was slightly greater (1.18 times) than the risk for patients not treated with steroids regardless of their status on admission. These analyses excluded 76 patients with one or more missing values. Most of these patients had multiple missing values and died soon after admission of recurrent arrhythmias or cardiogenic shock.

Discussion. This retrospective study with concurrent, but not randomized, controls found no beneficial or deleterious effects of steroids given after cardiac arrest. A major criticism is that, without random assignment of treatment, a systematic bias influencing treatment decisions is possible. We tried to correct for this potential bias by using a multivariable technique to control for differences in severity. We chose logistic regression in part because the coefficient for a particular variable can be converted to an estimate of the odds ratio and is thus more clinically interpretable. Beneficial effects of steroids would then be indicated by an odds ratio of less than one, and deleterious effects by an odds ratio greater than one. The variables used in this model to control for severity in this cohort were independent predictors of outcome.[6] They were all available at the time a clinician made decisions about steroid treatment. Using this multivariable analysis, the risk of never regaining consciousness for patients treated with steroids was 1.18 times the risk for patients not treated with steroids. This slightly increased risk is not statistically significant.

The design of this study is no substitution for a well-done, controlled clinical trial.[8,9] In nonrandomized trials, the adjustments for severity can never be complete and there may be important factors that are not measured or not recognized. Nevertheless, in the absence of a controlled clinical trial, this study becomes the best available clinical evidence upon which to base decisions about steroid treatment after cardiac arrest. Perhaps a study similar in design to this one could be done using

data from the trial of thiopental loading after cardiac arrest.[10] In that study, 73% of patients received steroids at the discretion of their treating physician. The analysis would still involve nonrandomized controls, but it would have an advantage over the present study of having the predictors and outcomes determined prospectively.

Unless future studies suggest otherwise, steroids should not be used after cardiac arrest to improve neurologic outcome. The evidence does not justify proceeding with an expensive and time-consuming controlled clinical trial. Thus, studies with concurrent, but not randomized, controls are likely to be the best evidence to address this clinical question. This study did not show a deleterious effect of steroid treatment as has been suggested in experimental animals.[4] Consequently, if steroids need to be administered for some other reason, the setting of recovery after cardiac arrest is not a contraindication.

References

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