Alcohol as an injury-aggravating factor

A. Donelson, R. Schmidt-Hargrave, K. Kennett, K. Ramachandra, L. Cheng, and L. Thibault
Failure Analysis Associates, Inc., Menlo Park, California 94025 USA

Introduction and overview

The US now suffers over 10,000 new cases of traumatic spinal cord injury (SCI) each year. Motor vehicle accidents, especially rollover crashes, are the leading cause of SCI in the US (e.g., Thurman et al. 1995). Large percentages of persons who sustain SCI evidence use of beverage alcohol at the time they sustain injury. Most studies of nonfatal SCI indicated that between 25% and 50% of patients had consumed alcohol, and a large majority of persons who had been drinking had alcohol concentrations of 0.10% w/v or higher. Decades of research have established alcohol as the single most frequent contributing factor in motor vehicle crashes causing serious injury or death. The role of alcohol as an injury-aggravating factor, however, is less well understood. As a consequence, relationships among the presence and amount of alcohol, the severity of injury — in particular, injury to the spinal cord or head — and outcomes of treatment and rehabilitation are not well characterized.

This paper focuses on alcohol (i.e., ethanol) as a factor that can aggravate SCI. We first highlight findings of a much more extensive review of the state of knowledge. Experimental and epidemiologic studies provide converging lines of evidence supportive of hypotheses that elevated concentrations of alcohol hinder functional recovery from SCI. We then suggest some directions for future research to advance understanding of alcohol’s role as an injury-aggravating factor.

Experimental Research.

In research spanning several decades, investigators have studied pathophysiological mechanisms of acute SCI. Reviews of the literature (e.g., Tator et al. 1991; Janssen et al. 1989) reflect the great amount of work done to describe and explain functional and biochemical changes observed after experimental SCI. Aims of research on SCI include the discovery of ways to preserve or restore neurological function. The development of experimental models of SCI was — and still is — critical to this endeavor. Of particular importance here, experimental research has shown that, after initial damage due to trauma, a delayed, progressively destructive process causes further damage to the spinal cord (Janssen et al. 1989). Much of the secondary
damage after experimentally induced trauma to the spinal cord seems to result from reactive changes in biochemistry after the initiating insult (Halt et al. 1992).

Experimental studies have also demonstrated (1) that the presence of alcohol in elevated concentrations aggravates SCI and (2) that acute intoxication at the time of injury also affects long-term histologic and functional outcomes of SCI. Ethanol, its principal metabolite acetaldehyde, and free-radical intermediaries can cause many adverse intracellular reactions. Ethanol may also alter critical relationships among the membrane biomolecules by physical forces or chemical reactions, resulting in cellular dysfunction and death.

In vivo experimental studies have investigated the aggravating effects of alcohol on SCI in the ferret, rat, and cat (Halt et al. 1992; Anderson 1986; Brodner et al. 1981; Flamm et al. 1977; and Seligman et al. 1977). Anderson used a controlled-compression technique; the other four studies used weight-drop techniques to produce SCI. Measurement of somatosensory evoked potentials (SEP) has become an important tool in assessing severity of experimental SCI. Peripheral nerves distal to the injured site are stimulated, and recordings at cortical or brainstem levels measure conduction through the injured site. Measurements of SEP several hours after injury lead to reasonably good predictions of ultimate functional outcomes, assessments conventionally done four or more weeks after injury (Anderson and Stokes 1992).

In studies cited above, both acute and chronic effects of alcohol on SCI were investigated. Measurements of SEP showed clear differences between those animals sustaining SCI with alcohol and those given no alcohol. In these studies, the return of evoked responses by 3 hours was a positive indicator for functional outcome. Evoked responses did not return within 2 or 3 hours in alcohol-treated injured animals, whereas injured animals serving as controls all regained evoked responses. Exceptions were the 360 and 500 gm-cm contusions in the study by Brodner et al. (1981); no differences between alcohol-treated and untreated injured animals were observed. Such contusions were thought to cause such extensive structural disruption that secondary pathophysiologic effects were masked. Longer-term effects of alcohol were also observed. Functionally, the alcohol-treated animals in these studies had poorer outcomes. All of the alcohol-treated injured animals remained paraplegic, whereas the injured controls regained some level of gait. Halt et al. (1992) did not measure evoke potentials but did assess functional recovery in the rat via angleboard and modified Tarlov motor scores. The alcohol-treated injured animals had a worse neurologic outcome at 4 weeks than did the control animals.

Some studies relevant to SCI have also focused on the cellular and biochemical effects of alcohol. For example, Flamm et al. (1977) discuss a mechanism by which alcohol may enhance the disruption of conduction along the cord. Alcohol was thought to enhance free radical damage to membrane lipids following SCI, thus inhibiting Na+/K+ ATPase activity. Seligman,
Flamm et al. (1977) measured malonaldehyde, a byproduct of free radical peroxidation of polyunsaturated fatty acid, indirectly via lipid soluble fluorescence (LSF) in alcohol-treated SCI cats, injured control cats, and laminectomy control cats. At 3 days post-injury, malonaldehyde rose in all groups. By 5 days, LSF had returned to background in all groups. At 7 days, a second peak of LSF activity occurred only in the alcohol-impact group. This group also developed paraplegia. Authors suggest that the first peak, seen in all groups, is associated with acute, reversible damage related to the surgery and trauma, whereas the second peak is associated with irreversible degeneration within the spinal cord.

Halt et al. (1992) investigated total tissue free fatty acid (FFA) levels following SCI in injured alcohol- and saline-treated rats. They found an increase in total tissue FFA levels at 4 hours, but no significant differences at 24 hours, although levels remained higher than surgical controls. They hypothesized that alcohol-enhanced phospholipid hydrolysis resulting in FFA and thromboxane accumulation, increased release of excitatory amino acids, and decreased tissue magnesium, which promoted secondary tissue damage and poorer outcomes. They also found that total tissue lactate (lactic acid) levels were significantly elevated in alcohol- but not in saline-treated rats 24 hours after injury. This indicated a persistent decrease in tissue oxygen and a sustained shift to anaerobic glycolysis. Other investigations have examined the histological effects of alcohol upon SCI (Halt et al. 1992; Anderson 1986; Brodner et al. 1981; Flamm et al. 1977). Alcohol increased post-injury hemorrhage, edema, and central cavitation. It is thought that aggravation of post-contusion pathology by alcohol impairs functional recovery.

In summary, experimental research has clearly shown that the presence of alcohol in elevated concentrations aggravates SCI and compromises functional recovery from SCI. Extrapolating from animal studies to clinical SCI in humans always requires caution. Great similarities in the neuroanatomy and neurophysiology of mammalian spinal cords, however, increase confidence in findings based on animal models, especially mechanisms by which alcohol may contribute to the secondary destructive responses in human SCI.

**Epidemiologic research.**

It is sometimes said that God protects both fools and drunks. Some studies of relationships between traumatic injury and alcohol did little to dispel this notion. For example, Ward et al. (1982) found a lower mortality rate for drinking patients admitted to a trauma center compared to patients with no alcohol. Other hospital-based studies found little or no differences between drinking and nondrinking patients (Thal et al. 1985; Soderstrom and Eastham 1987; Huth et al. 1984).
Julian Waller (1987) discussed major methodological problems that pervade hospital-based studies of injury severity generally and of injury severity in relation to alcohol specifically. For example, patients of hospitals and trauma centers are not representative of persons involved in traffic crashes, since those that are uninjured, slightly injured, or dead at the scene of motor vehicle accidents are not examined. The severity of crashes that lead to hospitalization often remains unknown. Bias in the detection and reporting of alcohol use by persons injured in motor vehicle accidents further compromises research, as does lack of routine testing for alcohol in hospitals (see also Öström et al. 1992). Among the most confounding of factors in assessing injury severity, however, are alcohol's own debilitating effects. As Waller (1987) showed, alcohol impairment can affect ratings of injury severity based on such standard instruments as the Glasgow Coma Scale (GCS), Abbreviated Injury Scale (AIS), and the Injury Severity Score (ISS). Ratings partly depend on apparent level of consciousness, duration of any loss of consciousness, and responsiveness of the patient to various stimuli — all of which can be directly influenced by alcohol. Ironically, alcohol intoxication can produce not only higher scores for injury severity, but also greater apparent recovery of patients from injury!

To resolve methodological problems inherent in epidemiologic research on alcohol and injury severity, investigators must take into account relevant variables in three domains: (1) the severity of crash and the role of injury-aggravating factors other than alcohol, for example, failure to wear seat belts; (2) the nature and severity of injuries evidenced by persons involved in crashes; and (3) the duration and completeness of recovery from injuries. Several studies have dealt more effectively with these issues, and their findings support hypotheses that alcohol can aggravate traumatic injury (e.g., House et al. 1982; Waller et al. 1985; Dischinger et al. 1988; Stewart 1988; Waller et al. 1989). None of these studies, however, examined the severity of specific types of injuries in relation to the presence of alcohol.

As part of the present study, we analyzed data from the 1988-1995 National Accident Sampling System (NASS) Crashworthiness Data System (CDS), which contains detailed information on both crash severity and the type and severity of injuries to occupants of vehicles towed away from crashes. In general, as severity of injury increased for drivers, so did the likelihood of finding alcohol (see also NHTSA 1997a). Taking into account belt use, ejection, and vehicle rollover, we still found a strong, positive association between alcohol and severity of head injury. The number of cases involving SCI with information on alcohol use was small (n=163). Analysis of the sparse data available suggested a negative correlation between the presence of alcohol and the likelihood a person with SCI would die as a result of crash involvement.

Experimental research suggests, however, that adverse effects of alcohol on SCI will be observed clinically more as diminished function upon recovery than as the severity of injury assessed soon after SCI. A remarkable study of 1,193 patients with SCI, Kiwerski and
Krasuski (1992) provided evidence supporting this thesis. The authors compared neurologic states upon admission to functional status after treatment and rehabilitation. Surviving patients (n=1,084) with cervical or thoracic SCI were characterized as «under the influence of alcohol» or «sober» at the time of injury. Neurologic recovery was about three times as likely for patients judged «sober» compared to patients judged «under the influence of alcohol». Treating the problem as a Markov process, we re-analyzed data reported by Kiwerski and Krasuski. Probabilities that patients judged «under the influence» would ultimately remain in the same functional category assigned upon admission were statistically significantly greater than for patients injured when sober.

Directions for future research.

New sources of data for epidemiologic research and advanced methods for investigating the effects of alcohol in the laboratory point to fruitful lines of research to advance the state of knowledge. For example, in seven states in the US, the Crash Outcome Data Evaluation System (CODES) sponsored by NHTSA (1997b) links statewide data from police reports, emergency medical services, and sources of information on final medical and financial outcomes of involvement in motor vehicle accidents. Data from CODES will likely support more extensive studies of aggravating effects of alcohol on human SCI than those done to date.

For experimental research, laboratory methods have been developed to investigate \textit{in vitro} the effects of mechanical stress on neural cells (NTera-2 cells) in culture. Dynamic mechanical forces are applied to the cell culture population and the resulting strains are measured on individual cells. This simple model permits the investigator to evaluate the dose-response relationships between mechanical injury and cellular trauma without the complicating aspects of in-vivo models. The addition of ethanol to the culture media will provide quantitative data on possible aggravating effects of alcohol given mechanical trauma, which may ultimately determine the injury outcome. Biochemical and metabolic changes induced by alcohol can also be elucidated.

Other models can be applied to study the \textit{in vivo} effects of alcohol on neurovascular elements. We have developed a model for axonal injury in the optic nerve of the guinea pig as a simplified model of the brain and spinal cord. The optic nerve can be stretched at controlled strains and at high strain rates to simulate various levels of mechanical loading that result in central nervous system trauma. Advantages of this model include simplicity of the anatomy, the ability to measure blood flow, and the well-documented histopathology of this injury. Further, measurement of the visual evoked response can be used to assess functional impairment, and transport studies can be conducted to investigate the etiology of the degradation process. We expect that the presence of ethanol will significantly exacerbate these measures of injury.
References