

## **BLOOD PRESSURE MANAGEMENT FOLLOWING ACUTE SPINAL CORD INJURY**

### **RECOMMENDATIONS**

Standards: There is insufficient evidence to support treatment standards.

Guidelines: There is insufficient evidence to support treatment guidelines.

Options:

- Hypotension (systolic blood pressure < 90 mm Hg) should be avoided if possible or corrected as soon as possible following acute SCI.
- Maintenance of mean arterial blood pressure at 85 – 90 mm Hg for the first seven days following acute SCI to improve spinal cord perfusion is recommended.

### **RATIONALE**

Acute traumatic spinal cord injury is frequently associated with systemic hypotension. Hypotension may be due to associated traumatic injuries with hypovolemia, direct severe spinal cord trauma itself, or a combination. The occurrence of hypotension has been shown to be associated with worse outcomes after traumatic injury, including severe head injury.(1,2,8,16,20,24) While a prospective controlled assessment of the effects of hypotension on acute human SCI has not been performed, laboratory evidence suggests that hypotension contributes to secondary injury after acute SCI by further reducing spinal cord blood flow and perfusion.(1,3,4,8,16,18,19,20-22,24) Hypotension in animal models of spinal cord injury results in worse neurological outcome.(13,14,23,26,28,29) Several clinical series of human patients with acute SCI managed in an aggressive fashion with attention to blood pressure, oxygenation and hemodynamic performance report no deleterious effects of therapy and suggest improved neurological outcome. (13,14,23,26,28,29) Despite these observations, the majority of patients with acute SCI treated in contemporary practice are not routinely monitored nor treated

with blood pressure augmentation following injury. For these reasons the issues of routine blood pressure support and threshold levels of mean arterial pressure maintenance following acute SCI have been raised.

## **SEARCH CRITERIA**

A National Library of Medicine computerized literature search from 1966 to 2001 was undertaken using Medical Subject Headings in combination with “spinal cord injury: medical management, non-operative management, hypotension and spinal cord blood flow. Approximately 3000 citations were acquired. Non-English language citations were deleted. Titles and abstracts of the remaining publications were reviewed and relevant articles were selected to develop the guidelines. We focused on two specific topics concerning human patients with acute spinal cord injuries: hypotension (22 articles reviewed) and spinal cord blood flow (no articles identified). Additional references were culled from the references lists of the remaining papers. Finally, members of the author group were asked to contribute articles known to them on the subject matter that were not found by other search means. Articles describing non-human laboratory investigations germane to the topic, related general review articles, and relevant studies of hypotension and human traumatic brain injury referenced in the Scientific Foundation are included in the bibliography. These efforts resulted in six manuscripts describing clinical case series (Class III evidence), which form the foundation for this review. They are summarized in Evidentiary Table format.

## SCIENTIFIC FOUNDATION

Ischemia of the spinal cord is felt to be one of the most important contributors to neuronal injury and neurologic deficit after acute spinal cord injury. Both local and systemic vascular alterations can contribute to ischemia after acute SCI by further reducing spinal cord blood flow which can exacerbate and extend the principle spinal cord insult.(1,6,8,16,20,24)

In the normal, non-injured spinal cord, arterial blood supply is diffuse, primarily delivered via a single anterior spinal artery and two posterior spinal arteries. A variable number of anterior and posterior radicular arteries provide segmental contributions over the length of the cord.(24,25) They feed anastomotic arterial channels over the pial surface that supply the outer half of the cord, and penetrating central arteries from the anterior spinal artery, which supply the central portion of the cord. Terminal branches of the central arteries extend rostral and caudal to overlap with adjacent terminal arteries, yet the terminal arterioles that originate from the terminal arteries do not interconnect within the cord. They in turn give rise to an extensive capillary network, which does interconnect within the deep gray and white matter of the cord. Capillaries are much more numerous and extensive in the gray matter than the white matter reflecting the increased metabolic needs of cell bodies compared to axons.(24,25) Perfusion of the spinal cord under normal physiological circumstances is maintained over a wide range of systemic blood pressure by autoregulatory mechanisms that appear identical to those which regulate cerebral blood flow. (1,3-5,7,9,10,15,16,18,19-21,24)

Local vascular alterations after acute SCI are multiple and the precise mechanisms of injury-induced ischemia of the cord have yet to be elucidated. Most investigators cite direct vascular injury at the site of the primary trauma as the earliest component of the ischemic injury process.(1,6,8,20-22) The principal spinal cord injury leads to not only white and gray matter injury at the insult site, but because of sulcal vessels and collateral terminal arteries which pass

through the primary injury site, creates white matter ischemia distal to the direct injury site.(8,19,20,24) In addition, the primary SCI creates intraluminal thrombosis, vasospasm and initiates a variety of secondary injury biochemical phenomena that further reduce blood flow, injure endothelium or increase edema, microvascular compression and contribute to microvascular collapse.(1,8,19,20,22,27) Post-traumatic spinal cord ischemia has been shown to become progressively worse over the first several hours after injury in animals.(1,4,6,7,16,20)

Laboratory models of spinal cord injury have convincingly demonstrated that autoregulation of spinal cord blood flow is lost after injury, exacerbating local spinal cord ischemia and rendering the spinal cord vulnerable to systemic hypotension.(1,3-5,7,8,16,18,20,27) This is analogous to that which often occurs in regional cerebral vasculature after acute traumatic brain injury. (1,4,5,7,8,10,15,16,20,22,24,27)

Systemic hemodynamic alterations after acute SCI have been well documented and include hypotension, cardiac dysrhythmias, reduced peripheral vascular resistance and reduced cardiac output.(1,12,13,14,17,20,26) Patients with the most severe injuries, particularly those with severe cervical spinal cord injuries are at greatest risk for cardiac, hemodynamic and respiratory disturbances in the first week following acute SCI.(11,12,17) These untoward occurrences, which may be episodic in nature, can result in hypotension and hypoxia. If, as many investigators suspect, acute SCI with loss of spinal cord autoregulation is analogous to acute traumatic brain injury, hypotension and hypoxia can worsen the severity of the original insult and can be disastrous for potential neurological recovery.(1,8,20,21) While the relationship between systemic hypotension and outcome following acute SCI has not been directly studied in human patients, inference from studies of patients with traumatic brain injury (TBI) appears appropriate.(2,8,20) Prospectively collected data from the Traumatic Coma Data Bank (Class II evidence) demonstrates that hypotension (systolic blood pressure < 90 mm Hg) or

hypoxia ( $\text{paO}_2 < 60 \text{ mm Hg}$ ) were independently associated with significant increases of morbidity and mortality following severe TBI.(2) A single episode of hypotension was associated with a 150% increase in mortality. It is in this very setting that therapeutic intervention aimed at correcting hypotension and maintaining threshold levels of MAP to improve cerebral or spinal cord perfusion has its greatest potential.

Several reports of case series suggest that treatment of hypotension and resuscitation to maintain mean arterial blood pressure at high-normal levels, 85 to 90 mm Hg, may enhance neurological outcome following acute traumatic SCI. (13,14,23,26,28,29)

Zach et al, utilized a prospective aggressive medical management paradigm in the treatment of 117 consecutive acute SCI patients.(28) All patients were treated in the intensive care unit with central venous pressure monitoring and were treated with volume expansion (Rheomacrodex 40, 500 ml/day) for maintenance of systemic blood pressure for seven days. Patients were stratified by injury level, degree of deficit (Frankel grade) and by time of admission after injury. The authors reported that 62% of cervical level SCI patients they managed in this way improved at last follow-up, including eight of 18 Frankel grade A patients, two by two grades and a third patient by three grades. No patient with a cervical injury worsened, 38% were unchanged from admission. Of patients who arrived within 12 hours of injury, 67% improved compared to their admission neurologic exam. Of patients admitted between 12 and 48 hours of injury, only 59% improved. When admission occurred after 48 hours of injury, improvement was seen in only 50% of patients. The authors concluded that early transfer and “immediate medical specific treatment of the spinal injury” with attention to maintenance of acceptable blood pressure appeared to improve neurologic recovery.

Tator and colleagues in 1984 described their experience with 144 patients with acute SCI managed between 1974 and 1979 at a dedicated spinal cord injury unit in Toronto, Canada.(23)

They compared their results to a cohort of 358 SCI patients managed between 1948 and 1973 prior to the development of the acute care SCI facility. All 144 patients managed from 1974 to 1979 were treated in an intensive care unit setting with strict attention to the treatment of hypotension and respiratory failure. Hypotension was “treated vigorously” with crystalloid and transfusion of whole blood or plasma for volume expansion. Patients with respiratory dysfunction were treated with ventilatory support as indicated. They reported reduced mean time of injury to admission and treatment, 4.9 hours, compared to greater than 12 hours from the 1948-1973 experience. Neurological improvement was observed in 41 of 95 patients (43%) managed under the aggressive ICU medical paradigm. Fifty-two patients demonstrated no improvement (55%). Only two patients deteriorated (2%). The authors reported lower mortality, reduced morbidity, shorter length of stay and lower cost of treatment with their contemporary comprehensive management paradigm compared to the 1948-1973 experience. They cited improved respiratory management in their ICU as one of the principal factors responsible for reduced mortality and credited the avoidance of hypotension, sepsis and urologic complications for reduced morbidity after injury. These improved management results were realized despite the fact that 28% of the acute SCI patients they treated had additional injuries that increased their risk of morbidity and mortality.

Wolf et al, in 1991 reported their experience with fifty-two patients with acute cervical bilateral facet dislocation injuries managed with an aggressive treatment paradigm that included ICU care, aggressive resuscitation, invasive monitoring and hemodynamic manipulation to maintain mean blood pressure above 85 mm Hg. for five days.(27) Thirty-four patients had complete neurological injuries, 13 had incomplete injuries and five patients were intact. The authors attempted closed reduction within four hours of patient arrival to their center and performed early open reduction on patients who could not be reduced by closed means. The

authors described neurological improvement at discharge in 21% of complete SCI patients and in 62% of patients with incomplete cervical SCI on admission. No intact patient deteriorated. The authors concluded that their protocol of aggressive, early medical and surgical management of patients with acute SCI improved outcome following injury. Treatment in the ICU setting, hemodynamic monitoring with maintenance of mean arterial pressure above 85 mm Hg and early decompression of the spinal cord by open or closed means appeared to reduce secondary complications following acute SCI in their study.

Levi and coworkers treated 50 acute cervical SCI patients in the ICU setting according to an aggressive management protocol which included invasive hemodynamic monitoring and volume and pressor support to maintain a hemodynamic profile with adequate cardiac output and mean blood pressure > 90 mm Hg.(13) Their 1993 report described 31 patients with Frankel grade A injuries on admission, eight patients with Frankel grade B injuries and 11 patients in Frankel C and D grades. Eight patients had shock at the time of admission (systolic BP < 90 mm.), and 82% of patients had volume resistant hypotension requiring pressors within the first seven days of treatment. Volume resistant hypotension was 5.5 times more common among patients with complete motor injuries. Forty percent of patients managed by protocol including several with complete injuries improved, 42% remained unchanged and nine patients died (18%). There was minimal morbidity associated with invasive hemodynamic monitoring. The authors concluded that hemodynamic monitoring in the ICU allows early identification and prompt treatment of cardiac dysfunction and hemodynamic instability and can reduce the potential morbidity and mortality following acute SCI.

Vale et al, in 1997 reported their experience with a non-randomized, prospective pilot study in the assessment of aggressive medical resuscitation and blood pressure management in 77 consecutive acute SCI patients.(26) All patients were managed in the ICU with invasive

monitoring, (Swan Ganz catheters and arterial lines) and blood pressure augmentation to maintain MAP > 85 mm Hg. for seven days post-injury. They reported ten patients with complete cervical SCI, 25 with incomplete cervical injuries, 21 patients with complete thoracic SCI and eight patients with incomplete thoracic level SCI. The average admission MAP for complete cervical SCI patients was 66 mm Hg. Nine of ten complete cervical SCI patients required pressors following volume replacement to maintain an MAP of 85 mm Hg. Fifty-two percent of incomplete cervical SCI patients required pressors to maintain MAP at 85 mm Hg. Only nine of 29 patients with thoracic level SCI required the use of pressors. The authors reported minimal morbidity with the use of invasive monitoring or with pharmacological therapy to augment MAP. At one-year follow-up (mean 17 months) three of ten complete cervical SCI patients regained ambulatory capacity and two regained bladder function. Incomplete cervical SCI patients fared better. Twenty-three of these patients regained ambulatory function at 12 month follow-up, only four of who had initial exam scores consistent with ambulation. Twenty-two of 25 (88%) patients regained bladder control. Thirty-one of 35 cervical SCI patients and 27 of 29 thoracic level SCI patients were treated surgically. The authors statistically compared selection for and timing of surgery with admission neurological function and compared surgical treatment, early and late, with neurological outcome and found no statistical correlation. They concluded that the enhanced neurological outcome identified in their series after acute SCI was optimized by early and aggressive volume resuscitation and blood pressure augmentation and was in addition to and/or distinct from any potential benefit provided by surgery.

The collective experience described in these case series (Class III evidence) strongly suggests that maintenance of MAP at 85 to 90 mm Hg improves spinal cord perfusion or impacts neurological outcome.(13,14,23,26,28,29) Prompt treatment of hypotension and resuscitation to MAP levels of 85 to 90 mm Hg is safe, and it suggests that elevation of MAP to threshold levels

may be beneficial to patients with acute SCI. The seven-day duration of treatment and the threshold levels of MAP maintenance appear to have been chosen arbitrarily by the individual clinical investigators.(13,26,28) They are felt to be analogous to initial duration and threshold MAP level recommendations for management of patients following acute traumatic brain injury. None of the authors provides a specific recipe or an algorithm to guide blood pressure augmentation. All of the manuscripts describe acutely injured patients who have arterial lines and central venous or Swan Ganz catheters in place to monitor pressures and volume status.(13,14,23,26,28,29) Initially crystalloid is given intravenously in response to MAP below 85 mmHg. Colloid is administered if the hematocrit is low (blood) or as a volume expander (albumin). If the patient's volume status is optimal but the MAP remains below threshold, the authors describe the use of pressors, typically (although not exclusively) a beta-agonist (Dopamine) before the addition of an alpha-agonist (Neosynephrine), to elevate the MAP. These agents are titrated to the appropriate dose level to achieve the threshold MAP utilizing volume, pressure, and cardiac performance data provided by the invasive monitoring devices.

## **SUMMARY**

Hypotension is common after acute traumatic SCI in humans. Hypotension contributes to spinal cord ischemia after injury in animal models and can worsen the initial insult and reduce the potential for neurological recovery. Although unproven by Class I medical evidence studies, it is likely that this occurs in human SCI patients as well. Since the correction of hypotension and maintenance of homeostasis is a basic principle of ethical medical practice in the treatment of patients with traumatic neurological injuries, depriving acute SCI patients of this treatment would be untenable. For this reason, Class I evidence about the effects of hypotension on outcome following acute human SCI will never be obtained. However, correction of

hypotension has been shown to reduce morbidity and mortality after acute human traumatic brain injury, and is a guideline level recommendation for the management of TBI. While a similar treatment guideline cannot be supported by the existing spinal cord injury literature, correction of hypotension in the setting of acute human SCI is offered as a strong treatment option. Class III evidence from the literature suggests that maintenance of mean arterial pressure at 85 to 90 mm Hg after acute SCI for a duration of seven days is safe and may improve spinal cord perfusion and ultimately, neurological outcome.

### **KEY ISSUES FOR FUTURE RESEARCH**

The issue of whether or not blood pressure augmentation has an impact on outcome following human SCI is important and deserves further study. If augmentation of mean arterial pressure is determined to be of potential benefit, the threshold levels of MAP most appropriate and the length of augmentation therapy need definition. These issues are best analyzed in a multi-institution prospective cohort study or a properly designed multi-institution retrospective case control study.

## EVIDENTIARY TABLE

<b>First Author Reference</b>	<b>Description of Study</b>	<b>Data Class</b>	<b>Conclusions</b>
Vale et al, 1997, J Neurosurg	Prospective assessment of 77 ASCI treated in ICU, aggressive Hemodynamic support, MAP > 85 No control group	CLASS III	Improved outcome with aggressive medical care, distinct from potential benefit from surgery at 1 year follow up.
Levi et al, 1993, Neurosurgery	50 patients treated in ICU, aggressive med treatment, MAP > 90	CLASS III	Improved outcome with aggressive hemodynamic support at 6 weeks post-injury.
Levi et al, 1991, Neurosurgery	103 ACSI, 50 incomplete (Group A), 53 complete (Group B), ICU care hemodynamic support, MAP > 85	CLASS III	Improved neurological outcome, no sig. difference between early and late surgery in either group.
Wolf et al, 1991, J Neurosurg	52 patients with locked facets reduced within 4 hours, ICU care, MAP > 85. 49 operated upon, 23 day 1, 26 delayed..	CLASS III	Closed reduction 61% 52% 1 year follow up. In general, improved neurological outcome with hemodynamic therapy.
Tator, et al, 1984, Canadian J Surg	144 ASCI patients managed per protocol of ICU care, hemodynamic support. Compared to prior cohort	CLASS III	Improved neurological outcome, less mortality with early transfer and ICU care
Zach, et al, 1976 Paraplegia	Prospective assessment of 117 ACSI at Swiss Center, ICU setting Aggressive BP, volume therapy Rheomacrodex x 7d Dexamethasone x 10d No comparison or control group	CLASS III	Improved neurological outcome with aggressive medical treatment and blood pressure management. Better outcome for early referrals.

## REFERENCES

1. Amar AP, Levy ML: Pathogenesis and pharmacological strategies for mitigating secondary damage in acute spinal cord injury. *Neurosurgery* 44(5):1027-1040, 1999.
2. Chestnut RM, Marshall LF, Klauber MR, et al: The role of secondary brain injury in determining outcome from severe head injury. *J Trauma* 34:216-222, 1993.
3. Dolan EJ, Tator CH: The effect of blood transfusion, dopamine, and gamma hydroxybutyrate on posttraumatic ischemia of the spinal cord. *J Neurosurg* 56:350-358, 1982.
4. Ducker TB, Kindt GW, Kempe LG: Pathological findings in acute experimental spinal cord trauma. *J Neurosurg* 35:700-708, 1971.
5. Flohr H, Pöll W, Brock M: Regulation of Spinal Cord Blood Flow. In: Brain and Blood Flow, Russell RWR (ed.), Pitman Medical and Scientific Publishing Co, London, pg 406-409, 1971.
6. Hall ED, Wolf DL: A pharmacological analysis of the pathophysiological mechanisms of posttraumatic spinal cord ischemia. *J Neurosurg* 64:951-961, 1986.
7. Kindt GW, Ducker TB, Huddleston J: Regulation of Spinal Cord Blood Flow. In: Brain and Blood Flow, Russell RWR (ed.), Pitman Medical and Scientific Publishing Co, London, pg 401-405, 1971.
8. King BS, Gupta R, Narayan RK: The early assessment and intensive care unit management of patients with severe traumatic brain and spinal cord injuries. *Surgical Clinics of North America* 80(3):855-870, 2000.
9. Kobrine AI, Doyle TF, Rizzoli HV. Spinal cord blood flow as affected by changes in systemic arterial blood pressure. *J Neurosurg* 44:12-15, 1976.

10. Kobrine AI, Doyle TF, Martins AN: Autoregulation of spinal cord blood flow. In: Wilkins RH (ed.), Clinical Neurosurgery, Volume 21, Congress of Neurological Surgeons, Williams & Wilkins, Baltimore, pg 573-581, 1974.
11. Ledsome JR, Sharp JM: Pulmonary function in acute cervical cord injury. *Am Rev Respir Dis* 124:41-44, 1981.
12. Lehmann KG, Lane JG, Piepmeier JM, Batsford WP: Cardiovascular abnormalities accompanying acute spinal cord injury in humans: Incidence, time course and severity. *JACC* 10(1):46-52, 1987.
13. Levi L, Wolf A, Belzberg H: Hemodynamic parameters in patients with acute cervical cord trauma: Description, intervention, and prediction of outcome. *Neurosurgery* 33(6):1007-1017, 1993.
14. Levi L, Wolf A, Rigamonti D, Ragheb J, et al: Anterior decompression in cervical spine trauma: Does the timing of surgery affect the outcome? *Neurosurgery* 29(2):216-222, 1991.
15. Lewelt W, Jenkins LW, Miller JD: Autoregulation of cerebral blood flow after experimental fluid percussion injury of the brain. *J Neurosurg* 53:500-511, 1980.
16. Osterholm JL: The pathophysiological response to spinal cord injury: The current status of related research. *J Neurosurg* 40:5-33, 1974
17. Piepmeier JM, Lehmann KB, Lane JG: Cardiovascular instability following acute cervical spinal cord trauma. *Central Nervous System Trauma* 2(3):153-160, 1985.
18. Senter HJ, Venes JL: Loss of autoregulation and posttraumatic ischemia following experimental spinal cord trauma. *J Neurosurg* 50:198-206, 1979.
19. Tator CH: Experimental and clinical studies of the pathophysiology and management of acute spinal cord injury. *J Spinal Cord Med* 19(4):206-214, 1996.

20. Tator CH: Ischemia as a secondary neural injury. In: Salzman SK, Faden AL eds. Neurobiology of Central Nervous System Trauma. New York, Oxford University Press, pg 209-215, 1994.
21. Tator CH: Hemodynamic issues and vascular factors in acute experimental spinal cord injury. *J Neurotrauma* 9(2):139-141, 1992.
22. Tator CH: Vascular effects and blood flow in acute spinal cord injuries. *J Neurosurg Sci* 28(3-4):115-119, 1984.
23. Tator CH, Rowed DW, Schwartz MI et al: Management of acute spinal cord injuries. *Can J Surg* 27(3):289-293, 296, 1984.
24. Turnbull IM: Blood supply of the spinal cord: Normal and pathological considerations. In: Wilkins RH (ed.), Clinical Neurosurgery. Congress of Neurological Surgeons, Williams & Wilkins, Baltimore. Volume 20, pg 56-84, 1973.
25. Turnbull IM: Microvasculature of the human spinal cord. *J Neurosurg* 35:141-147, 1971.
26. Vale FL, Burns J, Jackson AB, Hadley MN: Combined medical and surgical treatment after acute spinal cord injury: Results of a prospective pilot study to assess the merits of aggressive medical resuscitation and blood pressure management. *J Neurosurg* 87:239-246, 1997.
27. Wallace MC, Tator CH. Successful improvement of blood pressure, cardiac output, and spinal cord blood flow after experimental spinal cord injury. *Neurosurgery* 20(5):710-715, 1987.
28. Wolf A, Levi L, Mirvis S, Ragheb J, Huhn S, Rigamonti D, Robinson WL: Operative management of bilateral facet dislocation. *J Neurosurg* 75:883-890, 1991.

29. Zach GA, Seiler W, Dollfus P: Treatment results of spinal cord injury in the Swiss Paraplegic Centre. *Paraplegia* 14(1):58-65, 1976.