Neurological Prognosis of Acute Cervical Spinal Cord Injury Patients Requiring Catecholamine Administration

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Abstract

Study Design: Retrospective cohort study using aggregated data from our institute.

Objective: To examine the effects of hypotension requiring catecholamine (dopamine and epinephrine) administration on neurologic recovery in acute cervical spinal cord injury (SCI).

Summary of Background Data: Following spinal cord injury, traumatic blood loss and spinal shock can occur causing low blood pressure resulting in secondary damage to the spinal cord. Surgical intervention and strict blood pressure control have been reported to assist neurological recovery in acute spinal cord injury. However, no reports have examined the neurological prognosis of patients requiring hemodynamic control with a catecholamine.

Methods: American Spinal Injury Association (ASIA) Impairment Scale (AIS) grades at the initial examination on admission and at one-month follow-up were compared between the catecholamine administration group (group C) and the no-catecholamine administration group (group N).

Results: A total of 229 acute cervical SCI patients were treated and 175 patients (130 males, 45 females; mean age 59.1 years) were finally included in this study. Mean blood pressure was maintained at >85 mmHg, and heart rate was maintained at >45/min for 7 days after injury. The percentage of initial AIS grade A was higher in group C (n=28) than in group N (n=147). No patient in group C was AIS grade D. AIS grade improved in 21.4% of group C and 54.4% of group N. The percentage of neurologically improved patients was significantly higher in group N than in group C (p=0.013). In AIS grade C patients, neurological improvement was greater in group N than in group C (p=0.007).

Conclusions: This study showed that neurological improvement is poor in acute cervical SCI patients requiring catecholamine administration. Further studies examining the neurological prognosis and ideal hemodynamics are needed.

INTRODUCTION

Recently, patients with spinal cord injury (SCI) with or without bone injury are increasing due to aging population. SCI is neurological and musculoskeletal trauma, and may influence autonomic neural transmission. Patients’ lives are affected by the combination of consequent general physiological impairment, a wide range of potential complications, and sensory impairment [1-3]. Treatments of SCI are stabilization of the hemodynamic and respiratory system, and the stabilization of spinal column. High-dose methyl prednisolone succinate (MPSS) has been introduced and used to improve neurological status [4-7]. However, its application is still controversial due to a high
complication rate [8-11]. Many investigators research about the mechanism of progression of neural damage. Also, experiments on transplantation of neural / mesenchymal stem cells or injection of granulocyte colony-stimulating factor are conducted [12-15]. Specific therapies for SCI may be developed in the near future.

The functional prognosis of SCI may almost pre determined according to the severity at the time of injury. SCI progresses due to secondary effect following external force at the time of injury. SCI results in low blood pressure because of traumatic blood loss and/or spinal shock. Also, SCI may cause impairment of sympathetic innervations, which may influence blood pressure and heart rate from the acute phase and thereafter [2,3,16]. Experimentally, low blood pressure decreases spinal cord blood flow [17-20] and causes secondary damage to the spinal cord [21-26]. Early aggressive volume resuscitation and maintaining mean arterial blood pressure higher than 85 mmHg have been shown to be beneficial for cerebral ischemia caused by subarachnoid hemorrhage and stroke [27]. Surgical intervention and strict blood pressure control have been reported to be helpful for neurological recovery in acute SCI [17,24,28-30]. Some reports have examined neurological prognosis in patients requiring hemodynamic control with a catecholamine [31-34]. In this study, the effects of hypotension requiring catecholamine (dopamine and epinephrine) administration on neurologic recovery in acute cervical SCI were examined.

MATERIALS AND METHODS

Patients

From October 2003 to September 2012, 229 acute cervical SCI patients were treated in our institute. The following cases were excluded from the analysis: more than 8 hours after injury; patients with no medical record at 1-month follow-up; severe head injury that precluded accurate American Spinal Injury Association (ASIA) Impairment Scale (AIS) grade estimation; hemorrhagic injury that required interventional radiology; and AIS E cases. A total of 175 patients (130 males, 45 females; mean age 59.1 years) were finally included in this study.

These patients were divided into 2 groups: group C (catecholamine treatment) and group N (no catecholamine treatment). AIS grade was compared between the two groups at the initial examination on admission and at one-month follow-up.

This study has been approved by the ethics committee in our institute.

Initial Treatment

All patients were admitted to our intensive care unit. The patients' hemodynamic status was continuously monitored with peripheral arterial catheters and controlled strictly. Oxygen was administered to keep SpO2 at >95%. Mean blood pressure was maintained at >85 mmHg, and heart rate was maintained at >45/ min for 7 days after injury. Catecholamine was administered via central venous catheter in group C patients. Patients with hypotension (mean blood pressure <85 mmHg) received rapid infusion of 1000 mL of extracellular fluid (ECF), which contains Na+:131mEq/L, K+:4mEq/L, Ca++:3mEq/L, Cl-:109mEq/L, and Acetate: 28mEq/L. When the ECF administration did not maintain hemodynamics, dopamine was administered. Fluid infusion was continued to maintain adequate urine volume (0.5 to 1.0 mL/kg/h) even after introduction of catecholamine. When the dopamine infusion rate was higher than 15µg/kg/ min, epinephrine was added. Hemodynamic parameters were maintained at target values with this treatment flow in all patients. After starting enteral alimentation, intravenous catecholamine administration was gradually converted to enteral docarpamine administration. Catecholamine conversion was performed within 7 days after injury. Enteral docarpamine was started at 2250mg/ day and gradually increased up to 4500 mg/day as required. In our institute, high dose MPSS was not administered. In our past study [9], we have shown that high-dose steroid usage has limited neurological efficacy with some side effects; diabetes mellitus, infection, and delay of wound healing.

Vertebral fractures and/or dislocations were reduced manually with halo ring traction, and surgical fixation was performed within 48 hours after injury. When manual reduction was not achieved with a halo ring, open reduction and fixation were performed within 12 hours after admission. Patients with no fracture and/or dislocation were treated with conservative management at first. Surgical decompression of the cervical spinal cord by laminoplasty was applied when the cervical spinal canal stenosis was apparent and the AIS grade improvement was not achieved.

For secure reduction and rigid fixation, all surgical methods involved posterior fixation with pedicle screws and/or lateral mass screws with intra operative CT and navigation. Basically, anterior decompression and/or fixation surgery were not selected because SCI patients were at risk of tracheotomy for respiratory management.

Vertebral artery injury (VAI) was diagnosed by contrast enhanced Computed Tomography (CT) scan and/or Magnetic Resonance Imaging (MRI) in our institute. We took whole body contrast enhanced CT scan for all poly-trauma patients or patient suspected spinal trauma, and MRI for paraplegic or tetraplegic patients. When VAI was diagnosed or suspected, angiography was performed for detail examination. Unilateral VAI was treated with artery embolization and bilateral VAI was treated with stenting or bypass surgery.

Early rehabilitation including early ambulation was started and continued after admission when the patients' general condition allowed.

![Figure 1 AIS improvement by group. AIS improved in 6 of 28 patients (21.4%) in group C and 80 of 147 patients (54.4%) in group N. The percentage of neurologically improved patients was significantly higher in group N than that in group C.](image-url)
Statistical data analysis

In this study, we made statistical analysis by Fisher’s exact test and the Mann-Whitney U test, using SPSS® 15.0 for Windows (SPSS Inc., Chicago, IL, USA). P<0.05 was defined as statistically significant.

RESULTS

There were 28 patients (23 males, 5 females) in group C and 147 (107 males, 40 females) in group N. In group C, 25 patients received only dopamine, and 3 patients received both dopamine and epinephrine F. Steroids were administered to 4 patients in group C and 29 patients in group N before admission to our hospital. The patients’ mean age was 59.1 years in group C and 59.0 years in group N. There were no significant differences in sex and age between the 2 groups (sex: Fisher’s exact test, p=0.35, age: Mann-Whitney U test, p=0.75). Furthermore, regarding cervical spine medical histories of cervical spine, ossification of posterior longitudinal ligament was observed in 2 patients in group C (7.1%) and 20 patients in group N (13.6%), and cervical disk hernia was observed in 3 patients in group N (2.0%). Major combined injuries were observed at admission to our institute: vertebral arterial injury in 8 patients in group C (28.6%) and 7 patients in group N (4.7%), thoracic and/or lumbar spine fracture in one patient in group C (3.6%) and 9 patients in group N (6.1%), extremity fractures in 3 patients in group C (10.8%) and 9 patients in group N (6.1%), pelvic fracture in 3 patients in group N (2.0%), pneumothorax or hemothorax in 2 patients in group C (7.2%) and 2 patients in group N (1.4%), and pancreas injury in one patient in group N (0.7%) (Table 1).

AIS improved in 6 of 28 patients (21.4%); one patient in 15 AIS grade A, 4 patients in 6 AIS grade B, one patient in 7 AIS grade C in group C and 80 of 147 patients (54.4%; 8 patients in 22 AIS grade A, 14 patients in 20 AIS grade B, 40 patients in 57 AIS grade C, 18 patients in 48 AIS grade D) in group N. The percentage of neurologically improved patients was significantly higher in group N than that in group C (Fisher’s exact test, p=0.013). When examining the patients by AIS grade at admission, the rate of AIS grade improvement in each group had no significant differences in AIS grades A and B. In AIS grade C, however, group N patients improved more frequently than group C patients (Fisher’s exact test, p=0.007) (Table 2). No significant difference was found in the mean point gain of the Motor Score between group C (16.6) and group N (17.0).

Mean blood pressure (systolic blood pressure/diastolic blood pressure [mean arterial pressure]) at admission was 107.2±28.5 [80.2] mmHg in group C and 134.1±27.8 [97.6] mmHg in group N. The percentage of initial AIS grade A was higher in group C (15/28: 53.6%) than in group N (22/147: 15.0%). No patient in group A was AIS grade D.

In group C, cervical spine fracture was found at C1-C2 in one patient, at C3-C7 in 17 patients, and at both C1-C2 and C3-C7 in 2 patients. No vertebral fracture was found in 8 patients. In group N, cervical spine fracture was found at C1-C2 in 11 patients, at C3-C7 in 52 patients, and at both C1-C2 and C3-C7 in 2 patients. No vertebral fracture was found in 82 patients.

Table 1: Clinical characteristics at admission by group.

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<th>AIS grade</th>
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Surgical intervention was performed to all patients in group C and 97 patients (66.0%) in group N. In 90 patients with no vertebral fracture and/or dislocation in both groups, 47 patients (52.2%) were treated with conservative management and they were all in group N.

DISCUSSION

The blood supply of the spinal cord consists of one anterior spinal artery and two posterior spinal arteries. The anterior spinal artery turns into the central artery. Terminal branches of the central arteries do not interconnect within the spinal cord [35]. Blood flow within the spinal cord, like cerebral blood flow, is regulated by the autonomic nervous system under physiological circumstances [18,19].

The precise mechanism of ischemia of the spinal cord after acute SCI has not been clarified. Direct injury of the artery within the spinal cord at the injury site has been assumed as the first mechanism of ischemia. Subsequently, peripheral white matter ischemia occurs adjacent to the injury site, followed by intra luminal thrombus, angiospasms, vascular endothelial damage, spinal cord edema, and microvascular compression or collapse.
In animal studies, it has been reported that the auto regulation mechanism of spinal blood flow is disrupted after SCI, and secondary regional aggravation of ischemia might induce hypotension [22-26,28].

Some investigators have studied the effects of hypotension after acute SCI in humans [31-34]. Experimentally, however, hypotension after acute SCI may reduce perfusion within the spinal cord and aggravate the injury [22-26]. In acute SCI, it has been reported that appropriate hemodynamic treatment and early spinal reduction and stabilization may improve the neurological prognosis [27]. The guidelines for the management of acute cervical spine and spinal cord injuries (Section on Disorders of the Spine and Peripheral Nerves of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons) recommend maintaining the mean arterial pressure from 85 mmHg to 90 mmHg to improve the blood flow within the spinal cord for one week after the acute spinal cord injury [36].

In this study, many patients with AIS grade A and no patients with AIS grade D were included in group C. A significant improvement was observed in patients with AIS C in group N (p=0.007) (Table 2). In AIS grade C, group N patients (57/147: 38.8%) improved more frequently than group C patients (7/28: 25%). Adjustment will be difficult due to low numbers of patients, but, this suggests that the improvement of neurological function would be poor in SCI patients with unstable hemodynamics requiring catecholamine treatment, even if early reduction and fixation were performed appropriately. Conversely, the initial spinal cord injury might be so severe that the hemodynamic status becomes so unstable that it requires catecholamine administration. In this study, blood pressure was strictly monitored and controlled in all patients after transfer to our institute, which means low blood pressure before the initial treatment might have contributed to secondary spinal cord damage. Further investigations regarding the time between the injury and the start of hemodynamic control are needed. Because maintaining the mean blood pressure within a high range may be a risk factor for secondary hemorrhage in multiple trauma patients, the ideal blood pressure for spinal cord protection is a further research issue.

In our study, patients with SCI were examined only at the 1-month period. Previous study has reported that neurological status at 1-year is able to predict at the first 15 days after spinal cord injury [37]. We believe that our short-term results would be also relevant to the long-term clinical results.

**SUMMARY**

This study showed that neurological improvement is poor in acute cervical SCI patients requiring catecholamine therapy. In AIS grade C patients, neurological improvement was greater in the no-catecholamine administration group than in the catecholamine administration group.

Further studies examining the neurological prognosis and ideal hemodynamics in acute cervical SCI patients are needed.

**AUTHOR CONTRIBUTIONS**

Koji Uotani conceived of the study, mainly collected data and wrote the manuscript. Tomoyuki Takigawa participated in the design and coordination of the study, and helped to draft the manuscript. Yasuo Ito participated in the analysis and interpretation of data. Toshifumi Ozaki supervised the study. Hideki Ohashi, Shoichiro Mizuno, Takuya Morita, Takeshi Kikuchi helped with data acquisition. All authors read and approved the final manuscript.

**ACKNOWLEDGEMENT**

I have taken efforts in this study. However, it would not have been possible without the kind support and help of many individuals. I would like to extend my sincere thanks to all of them.

**REFERENCES**


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**Table 2: AIS grade changes by group.**

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