

Continuous cervical epidural block

Treatment for intractable hiccups

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Abstract

Intractable hiccups, although rare, may result in severe morbidity, including sleep deprivation, poor food intake, respiratory muscle fatigue, aspiration pneumonia, and death. Despite these potentially fatal complications, the etiology of intractable hiccups and definitive treatment are unknown. This study aimed to evaluate the effectiveness of continuous cervical epidural block in the treatment of intractable hiccups.

Records from 28 patients with a history of unsuccessful medical and invasive treatments for hiccups were evaluated. Continuous cervical epidural block was performed with a midline approach at the C7–T1 or T1–T2 intervertebral space with the patient in the prone position. The epidural catheter was advanced through the needle in a cephalad direction to the C3–C5 level. Catheter placement was confirmed using contrast radiography. A 6-mL bolus of 0.25% ropivacaine was injected, and a continuous infusion of 4 mL/h of ropivacaine was administered through the epidural catheter using an infuser containing 0.75% ropivacaine (45 mL ropivacaine and 230 mL normal saline). When the hiccups stopped and did not recur for 48 hours, the catheter was removed.

Cumulative complete remission rates were 60.71% after the first cervical epidural block, 92.86% after the second, and 100% after the third. One patient complained of dizziness that subsided. No other adverse effects were reported.

Continuous C3–C5 level cervical epidural block has a successful remission rate. We suggest that continuous cervical epidural block is an effective treatment for intractable hiccups.

Abbreviations: CNS = central nervous system, ECG = electrocardiography, GABA = gamma-amino-butyric acid, GERD = gastroesophageal reflux disease, SpO₂ = saturation of peripheral oxygen.

Keywords: continuous cervical epidural block, intractable hiccups, phrenic nerve

1. Introduction

A hiccup is the sudden, erratic contraction of diaphragmatic and intercostal muscles immediately followed by closure of the larynx. Most hiccups are common, transient, harmless, and self-limiting and can be treated with medications and physical maneuvers. Although rare, hiccups lasting beyond 48 hours are considered persistent hiccups; intractable hiccups are defined as hiccups lasting more than 1 month or recurrent hiccups despite treatment.^[1–3] Intractable hiccups can lead to severe medical problems, including sleep deprivation, respiratory fatigue, nutritional depletion, and aspiration pneumonia, and can be fatal. Due to the long trajectory of afferent and efferent nerves and the diffuse central processes of the hiccup reflex arc, the

accurate diagnosis of the lesion in the arc is complicated, and terminating the pathological processes is difficult.^[4] Although a number of treatments have been recommended,^[5–11] optimal therapy for intractable hiccups is still debatable.

The hiccup reflex arc involves the peripheral phrenic, vagal, and sympathetic pathways and central midbrain modulation. The phrenic nerve is essential for normal function and phrenic nerve blockade has been used to treat intractable hiccups.^[11,12] However, selective bilateral block of the phrenic nerves is technically difficult and bilateral phrenic nerve block can result in dyspnea or hypoxia.^[13]

To overcome these limitations, in this study, we describe a continuous upper cervical epidural block as a new treatment method for intractable hiccups and evaluate the effectiveness of this treatment.

2. Material and methods

Data from 35 patients treated for intractable hiccups at the Pain Center from January 1, 2008 to July 1, 2014 were obtained. The records of clinical symptoms and signs were retrospectively reviewed. Appropriate approval was obtained from institutional review board of the Korea University Medical Center (KUGH14137).

Prior to presentation at the Pain Center, all 35 patients had previously received oral medication for intractable hiccups at other hospitals. Two patients had prior invasive treatment, including cervical epidural block (n = 1) and phrenic nerve block during thoracic surgery (n = 1). Information on previous treatment and the medical history of the 35 patients was

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obtained. The 35 patients who visited the Pain Center discontinued previously prescribed medications and were started on gabapentin (300 mg, daily) and baclofen (5–10 mg, 3 times daily) for 1 week. This drug combination was successful in 5 patients, who had complete remission of their hiccups. Two patients with obvious organic causes of hiccups requiring specific treatment (severe hiatal hernia, $n=1$; lung cancer involving the diaphragm, $n=1$) were excluded from the study and referred to the surgical service. Twenty-eight patients with intractable hiccups and a history of unsuccessful medical treatment with gabapentin and baclofen were included in this study.

Patients were admitted to the hospital for examination and treatment. To identify underlying diseases and evaluate the causative factor for hiccups, patients underwent chest radiography; an electrocardiography (ECG); a complete blood count and serum chemistry; contrast-enhanced chest and abdominal computed tomography; brain computed tomography; and an upper gastrointestinal endoscopy. Potential causative factors for intractable hiccups were treated and continuous cervical epidural block was performed.

Noninvasive blood pressure, pulse rate, ECG, and saturation of peripheral oxygen (SpO_2) were monitored continuously during the continuous cervical epidural block. The continuous cervical epidural block was performed at the C7–T1 or T1–T2 intervertebral space with the patient in the prone position with the neck flexed. The loss of resistance technique with a midline approach was used for insertion of the needle into the epidural space. Correct placement of the 18-G Tuohy needle in the epidural space was confirmed using contrast radiography. A 22-G epidural catheter (Prefix, B Braun, Melsungen, Germany) was advanced through the needle in a cephalad direction to the C3–5 level. The correct catheter placement was confirmed using contrast radiography in the cervical anteroposterior and lateral views (Fig. 1A and B). Subcutaneous tunneling of the catheter was done for prolonged continuous epidural block. A bolus of ropivacaine (6 mL, 0.25%) was injected followed by a continuous infusion of ropivacaine (4 mL/h 0.75%; 45 mL ropivacaine in 230 mL normal saline) was administered through the epidural catheter using a disposable balloon infuser (Autofuser, ACE Medical, Seoul, Republic of Korea). After the procedure, patients were monitored for at least 30 minutes for the detection

of complications related to the continuous cervical epidural block.

Following cessation of epidural drug administration, when hiccups stopped completely and did not recur for 48 hours, the catheter was removed and the patients were discharged. After discharge, the patients were prescribed (gabapentin 300 mg three times daily, and baclofen 5–10 mg three times daily) for 30 days to prevent hiccups. In the event that hiccups recurred and continued beyond 48 hours, second and third continuous cervical epidural blocks were performed. The follow-up period was 36 months after last continuous cervical epidural block. A complete remission is defined as a case where hiccups do not recur, or are not prolonged >48 hours after taking the medication during the follow-up period.

Data were expressed as the mean \pm standard deviation (SD). Statistical analyses were done with Microsoft Excel (Microsoft Inc., Redmond WA).

3. Results

All 28 patients were male and had an ongoing history of intractable hiccups of 95.19 ± 35.95 days (Table 1). The primary cause of hiccups was gastrointestinal problems ($n=19$), including, gastroesophageal reflux disease (GERD) ($n=10$); gastritis ($n=3$); GERD with gastritis or gastric ulcer ($n=4$); and cholangiocarcinoma ($n=2$). Other causes of intractable hiccups included central nervous system (CNS) disorders (cerebral hemorrhage, $n=1$; cerebral infarction, $n=1$), history of the common cold ($n=2$), laryngitis ($n=1$), and idiopathic hiccups ($n=4$). Problems caused by intractable hiccups were weight loss ($n=4$), insomnia ($n=8$), and dyspnea ($n=6$).

After the first epidural block, 11 patients had recurrent hiccups, and received a second block. After the second block, 2 patients had recurrent hiccups, and received a third block. There was no recurrence of hiccups after the third block. Thus, the cumulative complete remission rates were 60.71% after the first block, 92.86% after the second, and 100% after the third block. The time (in days) until the hiccups stopped gradually shortened after the first (4.22 ± 4.14 days), second (3.63 ± 1.60 days), and third (3.50 ± 0.71 days) blocks. The time to removal of the catheter gradually decreased after the first (7.90 ± 5.35 days),

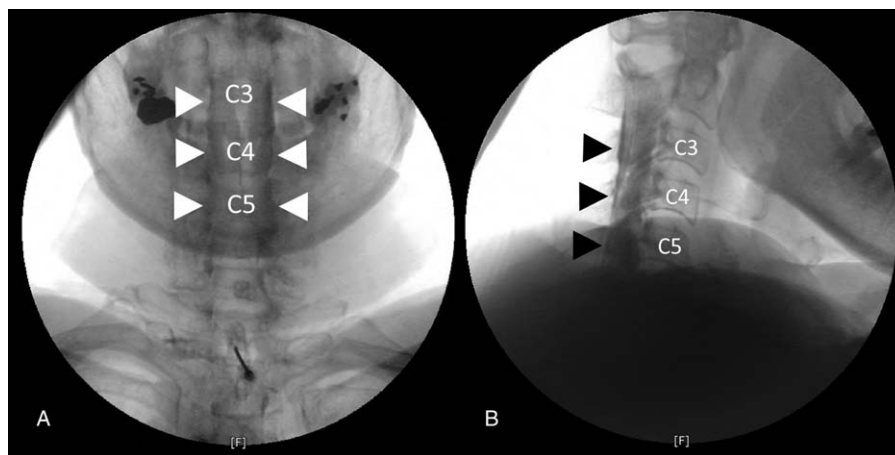


Figure 1. Cervical anteroposterior (AP) and lateral views after injection of 1.5 mL of water-soluble contrast media through the catheter, (A) cervical AP radiograph shows bilateral spread of the contrast media (white arrow). (B) Cervical lateral radiograph shows the spread of contrast media in the upper cervical epidural space including C3–C5 (black arrow).

Table 1**Characteristics of patients with intractable hiccups.**

Basic characteristics (n=28)	
Age, y	56.18 ± 12.78
Sex (male/female)	28/0
Duration of hiccups, d	95.19 ± 35.95
Causative factors (n=28)	
Number of patients (%)	
Gastrointestinal problems	
GERD	19 (67.86%)
Gastritis or gastric ulcer	3 (10.71%)
GERD with gastritis or gastric ulcer	4 (14.29%)
Cholangiocarcinoma	2 (7.14%)
CNS problems	
Cerebral hemorrhage	2 (7.14%)
Cerebral infarction	1 (3.57%)
Common cold	1 (3.57%)
Chronic laryngitis	2 (7.14%)
Idiopathic	4 (14.29%)
Problems caused by hiccup (n=28)	
Weight loss	4 (14.29%)
Insomnia	8 (28.57%)
Dyspnea	6 (21.43%)

Values are expressed as mean ± standard deviation (SD) for age and hiccup duration. CNS = central nervous system, GERD = gastroesophageal reflux disease.

second (6.44 ± 3.40 days), and third (6.00 ± 1.41 days) blocks. One patient complained of dizziness; however, it subsided after removal of the catheter (Table 2).

There was no complication of continuous epidural block and there were no reported adverse drug effects.

4. Discussion

The pathophysiological mechanism of hiccups is related to lesions in the reflex arc. The hiccup reflex arc consists of 3 components: the afferent limb, including the phrenic and vagus nerves, and thoracic sympathetic nerve chain that convey somatic and visceral sensory signals; the central processing unit in the midbrain; and the efferent limb comprised of the motor fibers of the phrenic nerve innervating the diaphragm and the accessory nerves to the intercostal muscles. When the afferent limb receives

Table 2**Parameters related to the continuous cervical epidural block.**

After 1st block (n=28)	
Time till hiccups stopped completely, d	4.22 ± 4.14
Duration of catheterization, d	7.90 ± 5.35
Number of recurrences (%)	11 (39.29%)
Time until 1st recurrence, d	9.67 ± 3.40
After 2nd block (n=11)	
Time till hiccups stopped, d	3.63 ± 1.60
Duration of catheterization, d	6.44 ± 3.40
Number of recurrences (%)	2 (7.14%)
Time until 2nd recurrence, d	9.50 ± 6.36
After 3rd block (n=2)	
Time till hiccups stopped, d	3.50 ± 0.71
Duration of catheterization, d	6.00 ± 1.41
Number of recurrences (%)	0 (0.00%)
Complications (n=28)	
Dyspnea (%)	0 (0.00%)
Infection (%)	0 (0.00%)
Dizziness (%)	1 (3.57%)

Values are expressed as mean ± standard deviation (SD).

a stimulus, the midbrain processes the signal, and the efferent limb signals to the diaphragm and respiratory muscles.^[14] The afferent and efferent limbs are connected centrally between the cervical spine (C3–C5) and the brainstem.^[11] The phrenic nerve, which is part of the afferent pathway and the main efferent pathway of the hiccup reflex arc, is primarily composed of the anterior branch of the spinal root of C3–C5. Considering these anatomical structures and the course of the hiccup reflex arc, Sato et al^[10] reported that a single cervical epidural injection of local anesthetic was successful in treating intractable hiccups. They performed a cervical epidural block that was sufficient to cover the levels supplying the phrenic nerve (C3–C5). However, we had previously experienced a recurrence of hiccups in patients with intractable hiccups after a single continuous cervical epidural block. The recurrence resulted in a repeat of the procedure. Therefore, we postulated that a continuous cervical epidural block, rather than a single epidural bolus, would be more effective in severe hiccup cases. In this study, the cumulative complete remission rate was 100% during the 36-month follow-up period.

The most common causes of intractable hiccups are physical and chemical irritation and inflammation of structures in the hiccup reflex arc. Damage or irritation of the vagus or phrenic nerves results in muscle or direct diaphragmatic stimulation. Continuous cervical epidural block is thought to be effective in preventing the recurrence of hiccups via regulation of the excitation of the nerves in response to these stimuli. Continuous cervical epidural block desensitizes the cervical spinal cord to the stimuli, prevents sensitization, and breaks the cycle.^[15] Boulouffe and Vanpee^[16] reported that administration of local anesthetics blocks the calcium channel, decreases cellular neuronal excitation, and eventually stops hiccups. In our study, the decrease in time until the hiccups stopped, and the decrease in duration of maintaining the catheter could be explained by the inhibition of the cycle and stabilization of the nervous system by the continuous epidural block.

The safety of continuous epidural block has been reported elsewhere.^[17–20] To minimize side effects, including hemodynamic changes and respiratory depression, we initiated continuous epidural block with a low concentration of ropivacaine (0.123%) that had been empirically validated at our hospital and the concentration of ropivacaine was adjusted by titrating according to response and safety. All procedures were performed in the hospital and blood pressure, ECG, SPO₂, and hydration status were monitored during the procedure.

When the hiccups stopped for 48 hours, the cervical epidural catheter was removed and patients were given oral medications (gabapentin and baclofen) to take for 30 days. Although a variety of drugs have been studied, gabapentin and baclofen have a significant effect in preventing the recurrence of hiccups.^[21] Gabapentin blocks calcium channels and increases the release of gamma-amino-butyric acid (GABA), which may reduce neuronal and diaphragmatic excitability.^[22] Baclofen, a GABA analogue, reduces spastic muscle contractions and activates an inhibitory neurotransmitter that is thought to inhibit the hiccup stimulus and prevent the recurrence of hiccups.^[21]

In this study, we evaluated causative factors for hiccups in all patients, and treated those factors while patients received the continuous cervical epidural block. We believe that combining the continuous cervical epidural block with treatment of the causative factors reduced the recurrence of hiccups and increase the cure rate. Due to the relatively rare occurrence of intractable hiccups, the etiology of intractable hiccups has not been

elucidated. Factors that stimulate or damage the hiccup reflex arc or central control of the hiccup reflex can result in intractable hiccups.^[2,3] In this study, the most common cause of intractable hiccups was gastrointestinal problems (67.86%). Interestingly, all the patients with intractable hiccups in this study were men. However, analyzing the causative factors and epidemiology did not provide insight into the preponderance of male patients in this study. We intend to further study this phenomenon.

One limitation of this study relates to its experimental design, which was non-randomized and with a small number of subjects. This was unavoidable not only because it was a retrospective study, but also because patients with intractable hiccups are rare. Intractable hiccups can cause extreme distress to patients and, in rare instances, death. Consequently, it would not be ethical to perform a randomized placebo-controlled study. Treatment methods in the absence of a placebo were chosen according to the severity.

Despite these limitations, the present study represents an important clinical contribution to the treatment of intractable hiccups. When compared with previous studies, our study had a long-term follow-up period and relatively large sample size. It is important to achieve complete remission in patients who complain of severe intractable hiccups in whom other treatments have failed.

In conclusion, continuous cervical epidural block is an excellent treatment for intractable hiccups and is effective in preventing recurrence in patients that do not respond to conventional therapies.

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