Treatment of Intractable Hiccups With an Oral Agent
Monotherapy of Baclofen
-A Case Report-

Ju Hwan Lee, MD, Tai Yo Kim, MD, Hyun Wook Lee, MD, Yu Sun Choi, MD*, Seo Young Moon, MD*, and Yong Kwan Cheong, MD

Hiccups are an involuntarily powerful spasm of the diaphragm, followed by a sudden inspiration with a closure of the glottis. Hiccups that are caused by gastric distention, spicy foods and neural dysfunction can resolve themselves without any treatment. Some hiccups are associated with certain diseases or they occur postsurgically, and life-restricting intractable hiccups should be treated. The cause of hiccups should be quickly determined so as to administer the proper treatment. Hiccups often remit spontaneously within a short period of time, but they may also occur without remission for a prolonged period in some cases. We report here on a 36-year-old man who suffered with intractable hiccups for 5 years. We administered a single oral dose of baclofen, and then the hiccups disappeared. We conclude that a single dose of baclofen is a good treatment for intractable hiccups. (Korean J Pain 2010; 23: 42-45)

Key Words:
baclofen, intractable hiccups.
who had previously received medical treatments at several other medical institutions without favorable results. We report this successful case with a review of the relevant literature.

**CASE REPORT**

A 35-year-old, 62 kg, male patient presented with a 5-year history of hiccups. Until visit to our hospital, the patient had been receiving medical treatment for chest discomfort and nausea caused by dyspepsia and gastro-esophageal reflux that had developed since the intractable hiccup began. In addition, he had been under psychological treatment due to the hiccups over the last five years. Brain magnetic resonance imaging (MRI) performed at the neurologist department at another university hospital under the suspicion of a brain lesion showed normal findings. Before visit, he had been treated at several medical institutions, but to no avail. Except for the hiccups, the patient had no significant prior medical history and no abnormality findings, including a blood test, electrocardiography (EKG), and chest X-ray. One noticeable change since the onset of his chronic hiccup was that he had lost 8 kg in weight.

Since one year before the visit, his hiccups had worsened and on visit, he hiccupped approximately 30 times per minute. He was a college lecturer and complained of severe discomfort and embarrassment caused by hiccups during lecture. The hiccup also disturbed his sleep. He was referred to our hospital from a private physician clinic for treatment with a phrenic nerve block. However, he requested medical treatment rather than interventional treatment. Accordingly, 10 mg of baclofen was administered twice daily. On an out-patient visit after 2 days, the patient reported that the bout of hiccups had decreased one hour after taking the first dose of the medication and stopped completely by 2 hours. In addition, the symptoms of dyspepsia and gastroesophageal reflux had also disappeared. One week after the same dose of medication had been prescribed, the hiccups resumed with a lower frequency and intensity 1 day before the outpatient visit. Baclofen 10 mg was then administered 3 times a day. On the next out-patient visit 1 week later, his hiccups had stopped completely. Two months after the same dose was given, the quantity of the dose was reduced over the next 2 weeks and then stopped. At a follow-up performed 3 months after termination of his medication, the hiccups had not recurred and the patient is currently free from hiccups and gastrointestinal symptoms.

**DISCUSSION**

Hiccups are repeated involuntary, spasmodic, transient contractions of the diaphragm, followed by a sudden closure of the glottis [4]. The precise mechanism of hiccup is unclear [5]. Most studies on the mechanisms of hiccup have been performed on animal experiments. The hiccup reflex is complex and composed of the following: on the afferent limb: the vagus nerve, the pharyngeal branch of the glossopharyngeal nerve, the pharyngeal nerve plexus of C2-C4, the sympathetic nerve of T6-T12; and on the efferent limb: the phrenic nerve, the inspiratory accessory muscle, and effenter nerve fibers leading to the expiratory muscle [6,7]. The reflex center consists of the spinal cord between C3-C5, brain stem and midbrain [8-10].

The longest recorded attack of hiccups lasted for more than 60 years and such intractable hiccups are often difficult to cure due to the complex involvement of many factors [11]. In particular, the most common cause of hiccups is gastroenteric disease, such as gastric distension or gastroesophageal reflux disease. If the hiccups are not persistent, many patients can be cured simply by medication for gastroenteric disease [9]. Other commonly reported causes of hiccups are metabolic disorders (diabetes mellitus, hypotension, hypokalemia, etc), medication problems (deoxymethasone, chloroalizapoxide, short-acting barbiturate, etc), and surgical operations on the skull, chest, abdomen, urinary tract, etc [3,12]. The lower part of the esophagus is believed to also trigger hiccups because the afferent limb can be irritated by the presence of an esophageal endoprosthesis or malignant tumor. Moreover, there is a case report of the development of intractable hiccups caused by an esophageal endoprosthesis [13]. Even more than 100 underlying disorders are believed to be responsible for hiccups. Therefore, the treatment of intractable hiccups requires an evaluation of the underlying disorders [3,5].

In the case of our patient, although basic tests, such as blood test, chest x-ray, EKG, etc, were performed at our institution and a brain MRI and gastrofiberscopy were conducted at other hospitals before, no abnormal findings were observed except for the gastroesophageal reflux.
After the hiccup ceased, the digestive symptoms improved and the patient’s appetite and sleep patterns returned to normal.

Hiccups can adversely affect the quality of a patients’ life considerably due to irritation and discomfort if they persist. In addition, a prolonged attack may cause fatigue, sleep disorders, dehydration, depression and wound dehiscence during the perioperative period, etc., and may be associated with even death because the progress of the underlying disorders would be further complicated [9].

The treatment of this ailment can be divided into pharmacological, non-pharmacological and nerve block treatments, and efforts to investigate the organic etiology should be made as a treatment is employed [11].

Non-pharmacological treatment includes breath holding, drinking cold water, inserting a nasal or nasogastric tube. However, this treatment is ineffective in persistent hiccups and is commonly used along with a pharmacological treatment. Metoclopramide, chlorpromazine, baclofen, amitriptyline, phenytoin, valproic acid, carbamazepine, haloperidol, nifedipine, etc. are used for pharmacological treatments [3]. Several nerve blocks have been advocated for intractable cases, including phrenic nerve block, cervical epidural block, glossopharyngeal nerve block, etc [14, 15].

Baclofen, which was employed to treat our patient, is a γ-aminobutyric acid (GABA) agonist used primarily to treat spastic movement, particularly in instances of spinal cord injury, spastic paralysis, multiple sclerosis, amyotrophic lateral sclerosis, trigeminal and glossopharyngeal neuralgias, etc. Baclofen is also an effective drug for hiccups and has been used to treat intractable hiccups as in our case. Launois et al. [16] reported that the introduction of baclofen resulted in the complete resolution of hiccups in 5 out of 9 patients, and significant improvement in 2 patients. Guelaud et al. [17] also witnessed the complete resolution of hiccups in 18 out of 37 patients as well as a significant decrease in the frequency and severity of hiccups in 10 patients under baclofen therapy.

The effective action of baclofen in hiccups is due to the fact that baclofen, an analog of GABA, decreases the excitability and inhibits the hiccup reflex, which reduces synaptic transmission at the spinal cord by increasing the threshold of its excitement and producing an anti-spastic effect [18]. Baclofen is absorbed rapidly after oral administration and is eliminated with a half-life of 3–4 hours by renal excretion through the kidney. The common side effects are sedation, insomnia, weakness, ataxia, confusion, etc. The sudden discontinuation of baclofen after long-term use can be associated with withdrawal symptoms, such as convulsions, so it is recommended that the dose be tapered down slowly when discontinuing the medication [18].

Several other agents have been used to cure hiccups. Metoclopramide accelerates gastric emptying and increases the resting tone of lower esophageal sphincter through antagonism of the gastroenteric inhibitory effect of the dopamine receptor on the gastric smooth muscle, while decreasing the secretion of gastric juice. However, it can cause extrapyramidal disorder [19]. Chlorpromazine, also a dopamine antagonist, has an inhibitory effect at the hypothalamus but its use is limited due to its many side effects, while amitriptyline synchronizes the electroencephalographic activity and affects the brain amines [16]. Of the antiepileptic drugs, phenytoin, valproic acid, and carbamazepine effective treatments for intractable hiccups: phenytoin acts on the motor cortex and inhibits the transmission of motor activity; valproic acid increases the function of GABA; and carbamazepine blocks posttetanic potentiation [16].

Intractable hiccups, in general, are not cured as easily as in our patient. The fact itself that he had searched extensively for treatments over the last 5 years highlights the difficulty in treating intractable hiccups. The number of different treatments can be considered as being inversely proportion to the number of causes, and the clinical findings document many cases of patients undergoing a variety of complex treatments. Our patient did not want nerve block and he had been under a range of pharmacologic treatments at several medical institutions, and had taken approximately 10 different medications prior to visit of our hospital. So baclofen could be administered easily with the discontinuation of the other ineffective drugs. However, provided the patient has no underlying diseases various pharmacological treatments with a nerve block are suitable, which are more likely to resolve the problem rapidly. Kim et al. [20] also reported that patients under treatment with baclofen and gabapentin showed satisfactory clinical results.

In conclusion, baclofen is used to treat hiccups, and can be used either as a first-line treatment or if a patient does not respond to other medications. This case supports
the efficacy of baclofen in difficult cases of intractable hiccups. However, further research will be needed to develop a definitive cure for hiccups.

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