### INTRODUCTION

The term "hiccup" derives from the sound of erroneously the event "Hiccough" implies association with respiratory reflexes. Also called "synchronous diaphragmatic flutter". An involuntary, intermittent, spasmodic contraction of the diaphragm and intercostal muscles accompanied by sudden inspiration that ends with abrupt closure of the glottis, making the classic hiccup sound. Considered pathologic because serves no useful function. Normally brainstem action that closes the glottis never activated when brainstem stops respirations (one inhibited/one activated). Abnormal when both activated. Medulla controls both actions; damage to medulla can cause intractable hiccups. May involve dopamine, serotonin, opioid, calcium channel, GABA pathways. The causes and aetiology of hiccups are given in Table 1.

# **MECHANISM OF HICCUPS**

The reflex arc for hiccups include the afferent pathway (periphery to central)-vagus, phrenic or thoracic sympathetic fibers; the central connection, phrenic nerve nuclei, inspiratory and glottis control centers in posterior lower medulla, reticular part of brainstem and hypothalamus. Efferent pathway is phrenic nerve to diaphragm. Involves the accessory respiratory muscles as well.

### **TREATMENT**

Understanding the cause of hiccup is important in treatment aspect. For example hiccups due to cerebral ischemia or injury may improve with anti-coagulants, whereas due to meningitis may improve with antibiotics.

# NON-PHARMACOLOGIAL

- Hold breath
- Hyperventilate (re breath into paper bag)
- Sneeze
- Gargle
- Pressure on eyeballs or carotid sinus
- Chest compression by pulling knees to chest or leaning forward
- Rubbing 5<sup>th</sup> cervical vertebrae

# **PHARMACOLOGICAL**

- Dopamine antagonists.
- Chlorpromazine is approved for treating hiccups.

- Blocks dopaminergic neurotransmission. Recommended dose; 25-50 mg PO/IM q6-8 hours
- Haloperidol –Recommended; 1-4 mg PO/SL q8 hour.
- Droperidol.
- Calcium channel blockers -anti- spasmotic effect on smooth muscle
- Nifedipine (Adalat)
- Nimodipine (Nimotop)
- Carvedilol –non –cardio selective beta blocker, Ca channel blocker and antioxidant
- Amantadine -weak antagonist of NMDA receptor
- Zyprexa, serotonergic antagonist useful in brain injury
- Metoclopramide, antiemetic with central antidopaminergic effect like, Recommended; 5-10 mg PO/IV q8 hours
- Baclofen, which is a GABA(B) receptor agonist.
  Acts primarily at the spinal cord level by inhibiting spinal afferent pathways.
- Other useful drugs include-ketamine, valproic acid, lidocaine, benzodiazepines.
- Combo therapy ie COB (cisapride, omeprazole, baclofen) and COBG (add gabapentin)

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Table 1: Causes of Aetiology of Hiccups	
Etiology	Examples
CNS	
Vascular	Stroke, Infarct, SLE, Vascular disorder, Aneurysm, Basllar artery insufficiency
Tumor	Astrocytoma, Carvenoma, Brainstem tumors, Glloblastomas, Metastasis
Inflammation	Neuromyelltis, Multiple sclerosis, Pneumonia, Encephallitis, Meningitis
Trauma	Brain injury
Miscellaneous	Seizure, cranial herpes infection, hydrocephalus, parkinsons, tobacco use, multiple sclerosis
Peripheral Pathway	
Chest cavity	Mediastinal diseases, lymphadenopathy/diaphragmatic tumors, Mediastinal tumor, pleurisy, pulmonary edema
Heart	Myocardial ischemia
GIT	Esophageal tumors, GERD & gastritis, stomach volvulus, H-pylori, hepatomegaly, pancreatitis, gastric distention
Lower Abdomen	Gynecologic tumors, prostate cancer, intra-abdominal tumors, bowel obstruction
Miscellaneous	Cancers, nephrosis, UTI, psychological

#### Causes

Extrinsic Causes	
Surgery	Anesthetic agents, post-op disturbances
Chemotherapy	Chemotheraputics, steroids
Drugs	Anti-parkinson treatment, psychiatric meds, azithromycin, bisphosphonates (hypocalcemia), morphine (hypocapnea) sulfonamides, steroids, methydopa, diazapam, barbiturates, librium
Instrumental	Atrial pacing, catheter ablation, central venous cath, esophageal stent, bronchoscopy, tracheostomy, shaving beards
Miscellaneous	Electrolyte imbalance, ethanol users, TB, chronic renal failure, stress, anorexia

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