Successful Treatment with Biperiden for Extrapyramidal Reactions from Droperidol

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Abstract
Although extrapyramidal reactions have been reported as a side effect from droperidol, information to management for this side effect is not well known.

We report herein 2 cases of extrapyramidal reactions associated with droperidol administration in the postoperative period.

In Case 1: 27-year-old man underwent orthopedic surgery under spinal anesthesia. After the surgery, acute dystonia developed after droperidol administration for intraoperative sedation. 5 mg of biperiden resolved these extrapyramidal signs completely.

In Case 2: 11-year-old girl underwent laparotomy under combined epidural and general anesthesia. Oculogyric crisis occurred after starting continuous epidural infusion of droperidol to treat postoperative nausea and vomiting. 3 mg of biperiden diminished these reactions completely.

Extrapyramidal reactions such as acute dystonia and oculogyric crisis are occasionally treated as transient postoperative psychic symptoms, since such reactions are not commonly known among medical staff in the perioperative period. Anesthesiologists should be aware of the risk of developing extrapyramidal symptoms to droperidol. In addition, biperiden can be successfully used as treatment.

Key Words
droperidol, extrapyramidal reactions, biperiden, acute dystonia, oculogyric crisis

Introduction
Droperidol has been widely used as a powerful anti-emetic for postoperative nausea and vomiting (PONV), and as a sedative and/or adjuvant agent for general anesthesia¹. Excessive drowsiness, hypotension, prolongation of the QT interval², and, on rare occasions, extrapyramidal reactions³⁴⁵ have been reported as side-effects for this drug.

Extrapyramidal reactions such as involuntary movements are occasionally treated as transient postoperative psychic symptoms, since such reactions are not commonly known among medical staff regarding perioperative period. However, patients can suffer from serious mental trauma following involuntary movements that cannot be controlled by the patient.

We report that biperiden, an anti-parkinsonism agent, was remarkably effective to terminate extrapyramidal reactions developing in a case with an
intravenous administration of droperidol for sedation and a case with a continuous epidural administration against PONV in the postoperative period.

Case Report

Case 1

A 27-year-old man, weight 59 kg, ASA (American Society for Anesthesiologists) physical status 1, was scheduled for removal of implanted orthopedic materials in the left patella. Past medical history was unremarkable. Caudal anesthesia was initially induced with 12 ml of 1.0% carbocaine, but adequate analgesic level was not obtained. Subarachnoid administration of 3 ml of 0.5% bupivacaine was therefore performed. Although level of analgesia was sufficient (Th6) for the operation, the patient became very anxious because of the experience with failed caudal anesthesia. As a result, 5 mg of droperidol was intravenously administered for sedation. Surgery ended without any problems within 75 min. About 3 h after the operation, the patient developed spasm of the lips, tongue, and eyeballs. He said, “I cannot stop my cheeks from moving or my eyeballs rolling upward”. At that time, vital signs were normal and consciousness did not seem impaired. We therefore considered these symptoms as acute dystonia due to droperidol and administered 5 mg of biperiden by intramuscular injection, resolving these extrapyramidal signs completely within 30 min.

Case 2

An 11-year-old girl, weight 40 kg, ASA physical status 2, underwent emergency operation for traumatic pancreatic transaction and duodenal perforation. Past medical history was unremarkable. General anesthesia was induced using 200 mg of thiopental and endotracheal intubation was facilitated with 6 mg of vecuronium. Anesthesia was maintained with nitrous oxide in oxygen and sevoflurane ranging from 0.4–1.5%. After induction of anesthesia, an epidural catheter was inserted via Th7/8 for postoperative analgesia. Surgical procedures were completed uneventfully within 6 h. An endotracheal tube was removed in the operating room. In the recovery room, analgesic mixture of 0.2% ropivacaine 57 ml and 0.3 mg of fentanyl was continuously infused at rate of 3 ml/h through the epidural catheter. On postoperative day 2, she complained of nausea and vomiting. In an attempt to control these symptoms, the analgesic mixture was changed to ropivacaine 110 ml, fentanyl 0.3 mg, and droperidol 2.5 mg. About 9 h after restarting infusion, she expressed strong anxiety regarding involuntary movement of the eyeballs. She complained, “My eyeballs are rolling upward”. Abdominal abscess and acute pancreatitis, which sometimes result in mental disorders, were excluded based on laboratory testing and abdominal computed tomography. Since symptoms involved typical oculogyric crisis that is often seen as a part of acute dystonia from neuroleptic agents, we considered symptoms must represent a reaction to epidural droperidol. Epidural infusion was stopped and 3 mg of biperiden in 50 ml of normal saline was drip infused over 30 min. Symptoms soon resolved completely. She was discharged on postoperative day 57 without any problem.

Discussion

Droperidol, a butyrophenonic anti-psychotic agent that antagonizes dopamine D2 receptors, has been used as an anti-emetic for PONV induced by narcotic agents. Extrapyramidal reactions as a side effect can be classified into 3 categories: 1) acute dystonia; 2) akathisia; and 3) Parkinsonism. Acute dystonia is mainly characterized by physical symptoms such as localized involuntary movement of the face, neck or back, and is not commonly accompanied by any psychotic symptoms. Akathisia is similar to acute dystonia in that the patient is incapable of maintaining a resting position, such as a sitting position. However, concomitant psychotic symptoms such as aggressiveness, agitation or suicidal attempts also appear. With Parkinsonism, patients present with identical symptoms to Parkinson’s syndrome, such as pill-rolling or mask-like facies. Most extrapyramidal symptoms induced by droperidol have been reported as acute dystonia and akathisia.

In both of our cases, symptoms were limited to the lips, tongue, and eyeballs, and consciousness was unimpaired, thus appearing to represent typical acute focal dystonia. Occurrence of extrapyramidal reactions induced by droperidol has been considered dose-dependent. However, relatively higher doses of droperidol (5–10 mg) are common in anesthetic practice, yet the development of extrapyramidal reactions during the postoperative period remains rare. This may well be because any symptoms that develop might be masked by residual effects of
Drugs such as benzodiazepines have been reported. Drug treatments such as through thoracic epidural administration.

remains unclear. We speculate that concentration starting administration kg might have accumulated in the central nervous system such as the shortened duration of hospitalization for day surgery.

To prevent PONV, changes in anesthetic methods, such as using propofol instead of inhalational anesthetics and nitrous oxide, avoid the use of opioids have been recommended. As anti-emetic agents, 5-HT3 inhibitors, metoclopramide, steroids or droperidol have been reported. Of these, droperidol is used most frequently due to cost advantages.

Generally, the dose of droperidol in adults has been recommended as 0.625–1.25 mg for intravenous bolus and 2.5 mg/day for continuous infusion. Little information is available regarding pediatric doses for continuous infusion, even though children are susceptible to developing extrapyramidal reactions to droperidol. Habre described 2 cases of extrapyramidal reactions in 10- and 9-year-old children following continuous intravenous administration of droperidol. Symptoms developed at total doses of 0.14 mg/kg and 0.17 mg/kg, respectively. A cumulative dose of < 0.1 mg/kg was thus suggested for children.

In Case 2, symptoms appeared about 9 h after starting administration (cumulative dose, 0.027 mg/kg). Why this occurred with such a small dose remains unclear. We speculate that concentration might have accumulated in the central nervous system through thoracic epidural administration.

Various treatments for reactions to droperidol have been reported. Drug treatments such as benzodiazepines, anti-histamines, and anti-psychotic agents have been described. However, these methods control extrapyramidal symptoms by sedating the patient, not by antagonizing the symptoms themselves. A risk of respiratory suppression or circulatory changes is also present. We instead used biperiden, which can work against involuntary movements induced by butyrophenonic anti-psychotic agents. Biperiden has frequently been prescribed in conjunction with butyrophenonic anti-psychotic agents in the psychiatric field.

In addition, this drug has an advantage in terms of diagnostic treatment for extrapyramidal reactions of unclear origin. According to the search results, only one German study has described biperiden treatment for extrapyramidal symptoms induced by a droperidol-fentanyl mixture. In terms of adverse drug reactions, mild and transient thirst and urinary retention that occur along with the anti-cholinergic characteristics of biperiden have been described.

Clinicians must recognize the risk of developing extrapyramidal symptoms following use of droperidol, and all medical staff should be made aware of this possibility. In addition, biperiden can be successfully used as treatment.

References

8) Hung YC, Ho YY and Shen CL. Delayed Akathisia and Suicidal Attempts following


ビペリデンによるドロベリドール投与後の錐体外路症状に対する治療

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抄録

ドロベリドールの副作用には錐体外路症状があるが、その対処に関する報告は少ない。今回、脊椎麻酔中の鎮静と、術後の嘔気対策に使用した症例で錐体外路症状を発症したが、ともにビペリデンが著効したので報告する。症例1) 27歳男性の整形外科手術が脊椎麻酔で行われた。術中鎮静にドロベリドール5 mgを投与したところ術後に急性ジストニアが出現したがビペリデン5 mg投与により症状は完全に消失した。症例2) 11歳女児の開腹手術後、麻薬による鎮痛により嘔気が生じたためドロベリドールを硬膜外カテーテルから持続投与したところ眼球回転発作が出現した。ビペリデン3 mg投与によって症状は速やかに消失した。

急性ジストニアや眼球回転発作などの錐体外路症状は、周術期の医療従事者にはあまり知られていないため、一旦発症したとしても単なる一過性の術後精神症状として扱われてしまうことがある。麻酔科医はドロベリドール投与後には錐体外路症状が出現する危険性があることを常に認識すべきである。また、その治療にはビペリデンが有用であると思われた。

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