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The Experience of the Total Intravenous Anesthesia of Patient with Noonan Syndrome

– A case report –

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Noonan syndrome is a condition involving facial, cardiovascular and skeletal abnormalities that may pose problems to anesthesiologists during surgery. Propofol, which is used as an induction agent for noncardiac surgery, produces little or no change in the heart rate. Remifentanil decreases the sympathetic and somatic responses to noxious stimuli and can be given in high doses without negative inotropic effects. We report successful management of a patient with Noonan syndrome, hypertrophic cardiomyopathy, and atrial fibrillation, undergoing laparoscopic cholecystectomy using the the total intravenous anesthesia with propofol and remifentanil. **(Korean J Anesthesiol 2007; 52: S 82～5)**

Key Words: hypertrophic cardiomyopathy, Noonan syndrome, propofol, remifentanil.

Noonan syndrome is a clinical entity that resembles Turner syndrome but with a normal karyotype. These patients have facial, cardiovascular and skeletal abnormalities that may pose problems to anesthesiologists during surgery. There is no case report of anesthesia for laparoscopic cholecystectomy in a patient with Noonan syndrome using the total intravenous anesthesia (TIVA) with propofol and remifentanil. We report the management of a patient with Noonan syndrome, hypertrophic cardiomyopathy and atrial fibrillation, and describe the successful use of propofol and remifentanil in the TIVA technique for laparoscopic cholecystectomy.

CASE REPORT

A 17-year-old male (weight 45.7 kg, height 155 cm) with known Noonan syndrome, hypertrophic cardiomyopathy and atrial fibrillation was referred for an anesthetic opinion. There was no family member with characterstics of Noonan's syndrome. He had been under cardiological review throughout childhood and was admitted whenever he suffered an arrhythmic attack. His current medication consists of oral atenolol 25 mg twice daily. On the abdominal ultrasonography, the gall bladder was not distended but appeared as a multilayered wall with a small amount of fluid collection in the gall bladder fossa. Acalculous cholecystitis was suspected and he was planned to undergo an emergency laparoscopic cholecystectomy.

The hemoglobin level was 14.5 g/dl, and the serum electrolytes, creatinine, glucose, aspartate trasaminase (serum glutamic oxaloacetic transaminase), alanine transaminase (serum glutamic pyruvatic transaminase), and alkaine phophatase were within the normal limits. A hematological investigation revealed no coagulation or platelet defects. Echocardiography indicated hypertrophic cardiomyopathy and no left ventricular outflow tract obstruction. The basal septum and left ventricular posterior wall showed increased echogenic foci but the regional wall motion appeared normal. The left ventricular outflow tract maximal velocity was approximately 3 m/sec and there was no evidence of systolic anterior motion of the mitral valve. The patient had not received anesthesia previously.

At operation room, his blood pressure was 100/70 mmHg, his heart rate was 126 beat/min, and oxygen saturation was 98%. The patient was premedicated with intravenous glycopyrrolate 0.2 mg before surgery and there was little change in heart rate. Preoperative monitorings such as electrocardiography,

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pulse oxymeter, and direct arterial pressure monitoring via the radial arterial cannula was instituted. After preoxygenation, anesthesia was induced in the supine position using a target-controlled infusion of propofol (target blood concentration 2.5 μg/ml) and remifentanil (target blood concentration 2.0 ng/ml). Rocuronium 50 mg was administered after the loss of a verbal response to achieve muscle relaxation. The patient was intubated with an 8.0 mm internal diameter following a grade II view on laryngoscope. He has the short, hypoplastic and rounded shaped epiglottis that covered the vocal cord, and showed only inferior border of the commissure fissure. The tracheal tube was smoothly carried into the trachea and its position confirmed by stethoscope. The patient was ventilated with an air/oxygen mixture (FiO_2 0.5). After induction, the systemic blood pressure decreased to 80/50 mmHg but increased to 100/55 mmHg after receiving intravenous phenylephrine 50μg. Anesthesia was maintained by the continuation of the target-controlled infusion propofol (target blood concentration 2.0μg/ml) and remifentanil (target blood concentration 2.5 ng/ml). The arterial blood gas analysis revealed the following: pH 7.43, PaO_2 285 mmHg, $PaCO_2$ 34 mmHg, bicarbonate 22.6 mM, base excess -1.7 mM, saturation 100%. The procedures were started. After the pneumoperitoneal state, end-tidal carbon dioxide tension was maintained at 30-31 mmHg. During the perioperative period, the patient remained hemodynamically stable, his heart rate ranged from 118 and 127 beats/min that was regarded sinus tachycardia and his systolic and diastolic arterial pressure varied from 100 to 109 mmHg and from 55 to 60 mmHg, respectively. The oxygen saturation was stable at 99-100%.

The total anesthetic time was 115 minutes, the estimated amount of blood loss was 10 ml, the total urine output was 90 ml, and a total of 300 ml of 0.9% saline was administered intravenously during surgery. At the end of the surgery, the propofol and remifentanil infusion was stopped. For postoperative pain control, nalbuphine 50 mg and ketorolac 150 mg was administered via intravenous patient-controlled analgesia. The patient received intravenous pyridostigmin 15 mg and glycopyrrolate 0.4 mg, and recovered consciousness 5 minutes later. After extubation, the patient was transferred to the pediatric intensive care unit for continuous hemodynamic monitoring. His postoperative course in the pediatric intensive care unit was uncomplicated.

DISCUSSION

The term of “Noonan syndrome” was first used in 1963 when Noonan and Ehmke reported 9 children with pulmonary stenosis, short stature, and a characteristic facial appearance. It is one of the most common genetic diseases associated with congenital heart defects, being second in frequency to Down syndrome.[1] Its overall incidence is believed to be 1/1,000 and 1/2,000 livebirths. The karyotype of Noonan syndrome is normal.[2] A gene for Noonan syndrome has been mapped by linkage analysis to the long arm of chromosome 12 in several families.[3] The characteristics distinguishing it from Turner’s syndrome include karyotype analysis, gender distribution, fertility, the site of the cardiac lesion, the facial appearance, and the presence of mental retardation.[4]

A diagnosis of Noonan syndrome is purely clinical with no “diagnostic” test being available. The phenotypical features of Noonan syndrome are as follows: 1) Facial features; hypertelorism, ptosis, downward slanting eyes, flattened nasal bridge, epicanthal folds, malar hypoplasia, and low set and anterioly rotated ears. 2) Heart defects; pulmonary valve stenosis, hypertrophic cardiomyopathy, atrial septal defect, ventral septal defect, left-sided obstructive lesion, tetralogy of falot, and patent ductus arteriosus. 3) Other features including short stature, feeding problems, pectus excavatum or carinatum, broad chest, widely spaced nipples, learning difficulties, undescended testes, webbed neck, low posterior hairline (hair may be sparse, but is often coarse and curly), bruising and bleeding, and muscular and skeletal nomalies.[1] The incidence of hypertrophic cardiomyopathy in Noonan syndrome is approximately 20-30% and one-third of cases have a ventricular outflow obstruction.[5]

The potential anesthetic problems presented by a patient with Noonan syndrome relate to an impairment of the cardiopulmonary function, the possibility of a difficult airway and technical difficulties with regional anesthesia due to skeletal abnormalities, such as kyphoscoliosis, short stature, and vertebral anomalies.

In cardiomyopathy, the anesthetic goals are as follows: 1) To minimize sympathetic activation, 2) avoid direct or reflex increases in contractility or HR, 3) to expand the intravascular volume in order to avoid hypovolemia and 4) to minimize the decreases in the LV afterload.[6] The pain and stress of surgery cause sympathetic stimulation, increasing the heart rate and contractility and deteriorating the hemodynamic conditions of

hypertrophic cardiomyopathy.[7]

Inhalation anesthetics are commonly used for patients with hypertrophic cardiomyopathy. Schwartz and Eisenkraft[8] showed that dose-dependent myocardial depression of inhalation anesthetics is ideal because negative inotrophy reduces the degree of systolic anterior motion of the mitral valve - septal contact, which results outflow obstruction. In addition, they allow airway control and the maintenance of a low left ventricular pressure gradient. Campbell and Bousfield[9] reported the management of a patient with Noonan syndrome and hypertrophic obstructive cardiomyopathy. Anesthesia was induced with thiopentone and atracurium, and was maintained with 35% oxygen in nitrous oxide and isoflurane 0.5%.

Studies on the use of propofol as an induction agent for noncardiac surgery suggest that a modest decrease or no change in the heart rate is expected. However, systemic vascular resistance and venous return can decrease. Both effects are potentially deleterious in a patient with hypertrophic cardiomyopathy. Bell and Goodchild[10] reported that a slight elevation of the legs and the infusion of colloid as induction can maintain the cardiac output and arterial blood pressure. They concluded that the cardiovascular profile of propofol is compatible with the management of cases with hypertrophic cardiomyopathy. The anesthetic goal includes maintaining the appropriate intravascular volume whilst avoiding the direct or reflex increases in contractility or heart rate.

Remifentanil is used increasingly as an anesthetic agent providing cardiovascular stability in high-risk patients. In 1996, Michelsen and Hug[11] reported that opioids decrease the sympathetic and somatic responses to noxious stimulation and can be given in high doses without negative inotropic effects, even in patients with an impaired cardiac function. They proposed that remifentanil could be an agent that could significantly reduce that stress response and the possible detrimental effects on the systemic vascular resistance. In 2001, McCarroll *et al.*[12] reported the management of patients presenting with peripartum cardiomyopathy and the successful use of remifentanil and propofol. In 2002, Wadsworth *et al.*[13] reported the successful use of remifentanil during general anesthesia for a caesarean delivery in a patient with known hypertrophic cardiomyopathy.

The maintenance of the sinus rhythm is essential since ventricular filling is dependent on the left atrial contraction. Excessive positive pressure ventilation, which interferes with the venous return, was avoided. For the same reason, particular care was taken over the pneumoperitoneum because a reduction in venous return may cause a decrease in coronary arterial perfusion and subsequent attack of arrhythmia. The sympathetic stimulation of painful surgical stress was exacerbated by the prolonged pneumoperitoneal state. An analgesic technique that can reduce sympathetic stimulation and minimize variations in the heart rate, contractility, and filling pressures is required to avoid the precipitating ventricular failure. Remifentanil was used because it has a relative benign effect on myocardial contractility avoiding drug-induced myocardial depression.

TIVA with propofol and remifentanil was found to be safe for patients with Noonan syndrome and hypertrophic cardiomyopathy without a left ventricular outflow tract obstruction.

Phenylephrine was used to treat hypotension that was unresponsive to fluid administration. Phenylephrine can be an ideal vasopressor that has no augment contractility. It increases the systemic vascular resistance, and shortens the duration of action.

Musculoskeletal abnormalities of Noonan's syndrome include a short stature, webbed neck and cubitus valgus. The chest deformity is typical and gives the appearance of a widely spaced nipples. In addition, it might be associated with kyphoscoliosis and respiratory compromise.[8] Other features include joint contractures, cervical spine fusion and lumbar lordosis. The association of Noonan syndrome with malignant hyperthermia has not been substantiated.[14]

There is the potential for airway difficulties in Noonan syndrome because of the high palatal arch, dental malocclusion and webbing of the neck.[15] Although a dental malocclusion was present in our patient, it did not warrant specific precautions, and the trachea was intubated easily.

Abnormal bleeding and bruising are often encountered in Noonan syndrome (56-74%), which is associated with a mixed collection of defects in the platelet and coagulation systems.[16,17] A deficiency in isolated factor VIII is considered the most common single factor deficiency, and may be treated with single factor replacement. Most of the bleeding problems are mild, and may only be revealed during surgical procedures such as dental extraction. Interestingly, cases of severe postoperative bleeding have been reported despite they having normal in vitro clotting assays and platelet counts.[15]

The presence of absence of facial, cardiac or musculoskeletal abnormalities should be determined preoperatively. Anesthesia for patients with hypertrophic cardiomyopathy should avoid tachycardia, hypotension and peripheral vasodilation, and maintain a preload and afterload.

In summary, patients with Noonan syndrome present a mul-

tiplicity of challenges to anesthesiologist. Their fertility and the improving results from cardiac surgery in childhood suggest an increase in their number being treated in anesthetic departments.

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