การรักษาภาวะเขียวรุนแรงที่เกิดจากโรคหัวใจพิการแต่กำเนิดชนิดเขียวในผู้ป่วยทารกหลังผ่าตัด ด้วยการให้ fentanyl ทางหลอดเลือดดำอย่างต่อเนื่อง

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Treatment of Immediately Postoperative Hypercyanotic Spell in an Infant With Continuous Fentanyl Infusion

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ภาวะเขียวรุนแรงที่เกิดจากโรคหัวใจพิการแต่กำเนิดชนิดเขียว (TET spell หรือ hypercyanotic spell) เป็นภาวะที่อันตรายถึงชีวิต การให้ยากล่อมประสาทเป็นการรักษาที่สำคัญ มีจุดประสงค์เพื่อให้ผู้ป่วยสงบ ลดการกระตุ้นระบบประสาทส่วนซิมพาเทติก และยับยั้งกลไกพยาธิสภาพของการเกิดภาวะเขียวรุนแรง รายงานผู้ป่วยนี้ต้องการชี้ให้เห็นถึงความสำคัญของการให้ยากล่อมประสาท คือการให้ fentanyl ทางหลอดเลือดดำอย่างต่อเนื่อง เพื่อรักษาอาการเขียวรุนแรงเฉียบพลับหลังจากการผ่าตัด

ผู้ป่วยทารกเพศชายอายุแปดเดือน มีโรคหัวใจพิการแต่กำเนิดชนิดเขียวที่ยังไม่ได้รับการรักษา และมีอาการเขียวเฉียบพลันทันทีหลังการผ่าตัดเสร็จสิ้น ออกซิเจนในเลือดต่ำจนถึงร้อยละ 65 ผู้ป่วยไม่ตอบสนองต่อการรักษาด้วยการจัดท่ายกเข่าชิดอก การให้ยาเพิ่มการหดตัวของหลอดเลือดและการให้สารน้ำเพิ่ม แต่อาการกลับดีขึ้นภายในเวลาอันสั้นหลังจากให้ยาที่มีฤทธิ์กล่อมประสาท และแก้ปวดคือ การให้ fentanyl ทางหลอดเลือดและให้อย่างต่อเนื่อง สุดท้ายผู้ป่วยได้รับการผ่าตัดหลอดเลือดทรวงอกเพื่อเพิ่มเลือดไปที่ปอดวันที่ 20 หลังจากวันผ่าตัดแรก สรุป: การให้ fentanyl ทางหลอดเลือดดำอย่างต่อเนื่อง เป็นอีกการรักษาทางเลือกหนึ่งที่ช่วยรักษาภาวะเขียวรุนแรงที่เกิดจากโรคหัวใจพิการแต่กำเนิดชนิดเขียว อีกทั้งช่วยกล่อมประสาทและบรรเทาหลังจากการผ่าตัด

Hypercyanotic spell or TET spell is an emergency life threatening condition. Sedation is a necessary treatment aiming to calm, attenuating sympathetic activity and breaking pathophysiology of TET spells. This case scenario points out that fentanyl infusion, a commonly used opioid, can be administered for management of immediately postoperative TET spell in infants with Tetralogy of Fallot (TOF).

We present the case of an eight-month old infant with unrepaired TOF who had TET spell immediately after operation, and whose oxygen saturation dropped to 65%. The patient did not respond to knee-to-chest positioning, vasoconstrictor and fluid administration. The symptoms were improved by sedation, fentanyl was bolus intravenously following continuous infusion, within a few minutes. Subsequently, the patient underwent a successful right modified Blalock-Taussig Shunt procedure on 20th postoperative day. Conclusion**:** fentanyl infusion should be considered as an alternative sedation and analgesia of choice for postoperative TET spell patients.

Keywords: fentanyl, postoperative, TET spell

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Introduction

Prevalence of Tetralogy of Fallot (TOF) is estimated in 1 in every 3,600 live births. Moreover, it is the most common cyanotic congenital heart disease[1] which consists of four anatomical components 1) ventricular septal defect (VSD) 2) overriding aorta 3) right ventricular outflow tract (RVOT) obstruction 4) right ventricular myocardial hypertrophy. Atrial septal defect (ASD) was also found in our patient. In these cases, it may be called "Pentalogy of Fallot". However, there is no study defining neither an incidence of children with TOF undergoing non-cardiac surgery nor an incidence of perioperative complication related with TOF. According to the nature of disease, children with congenital heart disease undergoing non-cardiac surgery have an increased risk of morbidity, perioperative cardiac arrest and a higher 30-day mortality[2]. Furthermore, the amount of literature for perioperative management is also limited because few studies exist evaluating anesthetic techniques in children with heart disease for non-cardiac surgery[2]. There is no established single treatment that fits all patients; therefore, we would like to present a sample of successful treatment for a TOF child with an emergency condition.

Case report

An eight-month-old male infant presented with abdominal distension after breast feeding and symptoms of gut obstruction including delay passing stool and poor feeding two months ago. He underwent transverse loop colostomy to relieve obstruction uneventfully. The tissue pathologic examination revealed the absence of ganglion cells in the colon. The diagnosis of Hirschsprung's disease was made. Consequently, he was scheduled for transabdominal pull-through operation as the definitive treatment.

He was born at preterm, 35 weeks and 1,835 grams, following cesarean delivery due to maternal severe pregnancy-induced hypertension (PIH) and APGAR score of nine and ten at one and five minutes, respectively. His physical examination found pansystolic murmur at left upper parasternal border on auscultation. The oxygenation saturation showed 94-96% in both pre and post-ductal sites. Transthoracic echocardiography (TTE) demonstrated mild infundibular and valvular pulmonic stenosis, large perimembranous to subaortic ventricular septal defect (VSD) and small atrial septal defect (ASD) secundum. He was diagnosed with Pentalogy of Fallot. Furthermore, his thyroid screening revealed congenital hypothyroidism, but his chromosome study was normal. Upon physical examination on the preoperative visit, the patient was active but still exhibited mild central cyanosis with same baseline oxygen saturation. The otherwise vital signs were within normal ranges (heart rate 90-120 bpm, blood pressure 110/75 mmHg and body temperature 36.5ºC). His weight was 5.8 kg, lower than P5 of growth curve. Chest radiography revealed cardiomegaly with upturned cardiac apex and normal pulmonary vasculature. Laboratory investigations including complete blood count, coagulography and blood chemistry were also within normal range. Neither polycythemia nor coagulopathy had occurred preoperatively. The patient was allowed to have breast milk for four hours and clear liquid two hours before scheduled operation time. No sedative was fed at that morning. The case was accepted for surgery under ASA physical status III and informed consent was obtained.

On the day of surgery, the patient was connected to routine non-invasive monitoring, no invasive monitoring was placed. The patient arrived in operating theatre without intravenous (IV) catheter access, Induction of anesthesia was performed with sevoflurane up to 5% before IV catheterization was established with 22G catheter. Tracheal intubation was facilitated by 4 mg of atracurium and succeeded without adverse event. Caudal anesthesia was performed with 5.8 ml of 0.2% bupivacaine single dose.

Anesthesia was maintained with sevoflurane in air and oxygen (1L :1L), 0.2 mg/kg of atracurium and was continued intermittently. Cefazolin was given for surgical infection prophylaxis. Intraoperatively, hemodynamic parameters were stable. Oxygen saturation was 94-96%. Heart rate was maintained between 120-140 bpm except for the third hour of surgery, at which heart rate gradually increased. Volume status was evaluated before 5 mcg of fentanyl was administrated intravascularly because weaning of caudal anesthesia and pain response was suspected. Ventilation was controlled with semi-closed circuit to maintain end tidal carbon dioxide 35-40 mmHg. The operation lasted for about two hours. The patient remained stable with SpO2 range similar to baseline value. 115 ml of Acetar, 50ml of 5% albumin and 80 ml of 5%D/N/2 were administered and 35 ml of PRC was given for replacement of blood loss. Another 5 mcg of fentanyl were given 30 minutes before extubation.

At the end of the operation, muscle relaxant reversal was given in term of 0.3 mg of neostigmine and 0.1 mg of atropine followed by tracheal extubation after the patient had patent airway reflexes, adequate breathing and active movement. Within a few minutes after extubation, he had become cyanotic while he was crying without sign of airway obstruction. Oxygen saturation rapidly declined from 98% to 65% without bradycardia, heart rate still maintained between 120-130 bpm. TET spell or hypoxic spell was most likely suspected. The patient's position was changed to knee chest position and 100% oxygen was given immediately. However, oxygen saturation did not respond after 1 mcg /kg (5 mcg) of norepinephrine given twice with 1-1.5 mcg/kg/hr of norepinephrine continuous infusion and 10ml/kg (50 ml) of 5% albumin were administered thereafter. 0.5 mcg/kg (3 mcg) of fentanyl was given and he became calm for 5 minutes and oxygen saturation improved to 98% before he cried, after which the oxygen saturation had fallen to 60% again. Finally, 1 mcg/kg/hr of fentanyl was infused continuously, the patient stopped crying, oxygen saturation rose to 95-98%. After the patient was stabilized, 24G catheter was placed in right radial artery and arterial blood gas analysis was done as shown in table 1. 6 ml of 7.5% sodium bicarbonate was given. The patient was observed 30 minutes before being transferred to PICU.

Table 1 arterial blood gas analysis

Parameter	Immediate after arterial line access	30 minutes later before PICU transfer
pH	7.214	7.339
$PaCO_2$	30.5	32.8
PaO_2	63.1	68.7
HCO_3	12.4	17.8
BE	-15.7	-8.2
Na	145.9	143.4
K	2.04	2.82
Cl	104.7	108
Ca	0.18	0.56
Lactate	-	2.6

Postoperatively, 1 mcg/kg/hr of fentanyl was infused and oxygen box with oxygen flow 1 LPM was given for 2 days. No TET spell occurred while the patient remained in PICU. On the sixth day after surgery, a cardiac surgeon was consulted. The patient was evaluated and scheduled for a right modified Blalock-Taussig Shunt procedure on the 12th day postoperatively.

Discussion

In unrepaired TOF patient, pathophysiology depends on the degree of RVOT obstruction. TET spell is a result of significant dynamic RVOT obstruction from infundibular spasm causing limited blood flow into the pulmonary artery[3]. It can be activated by catecholamine release due to pain, stress, and light anesthesia.

TET spell is an emergency condition related with significant arterial desaturation. The treatment involves:

1) Fluid administration to increase right ventricular stroke volume

2) 100 % Oxygen administration

3) Increasing systemic vascular resistance (SVR) by knee to chest position and vasoconstrictor administration to decrease right to left blood shunting across the VSD and promote pulmonary blood flow and oxygenation

4) Decreasing sympathetic response

Obviously, this patient developed the spell after extubation and received treatment immediately including intravascular volume expending by 5% albumin, increasing FiO_2, knee to chest positioning and norepinephrine administration. However, the result was unsatisfactory. The patient continued to cry. The team decision was made to administer 1 mcg/kg of fentanyl, the patient became calm and ceased from crying within a few minutes. The oxygen saturation rose up to baseline (96%) before we maintained sedation with 1 mcg/kg/hr of fentanyl infusion.

Base on literature, morphine is recommended for sedating TOF patient with TET spells. However, morphine often causes both arterial and venodilation resulting in paradoxical exacerbation of cyanosis[4]. We selected fentanyl, an alternative of morphine, which is the shortest-acting opioid available in Thailand. Due to its beneficial characteristics such as rapid onset, easy titration and no long period of drug loading required[5], the utility of fentanyl could also address the possibility that morphine might lower the systemic vascular resistance, and potentially worsen the shunting of deoxygenated blood from the right to left heart. Fentanyl is less likely to cause hemodynamic instability and decrease in SVR, which would help alleviate the concerns of potentially exacerbating the hypoxic spell[6,7]. Respiration complications including apnea and ventilatory suppression can be avoided by careful titration. Fentanyl via intranasal route may be alternative treatment of TET spell in patient who has no intravenous catheter access. Danial S. Tsze, et al. reported a three-month old girl with standard TOF who had hypercyanotic spell (oxygen saturation 50%) after crying vigorously. She was transferred to emergency room after her symptoms did not response to knee to chest positioning. She was treated with 2 mcg/kg of intranasal fentanyl and the spell subsided within ten minutes[5].

Additionally, other anesthetics and sedatives have also been reported as effective pharmacologic managements of TET spell, for example ketamine and dexmedetomidine. Ketamine may be used to treat spell due to its vasoconstrictive effect that subsequently promotes SVR increase with sedative effect[4,8]. However, ketamine has relatively high incidence of airway complication and gastrointestinal complications which may potentially bring about adverse effect on unintubated patients. Ketamine can also induce tachycardia by sympathetic stimulation which worsens these spells[4,9]. While dexmedetomidine, the selective α_2-adrenoreceptors agonist, have been reported effective in several clinical situations in pediatric population. Its effects potentially correct the pathophysiologic conditions of TET spell such as sympatholytic effect, maintenance of SVR and minimal depressive effects on respiration[4]. Hideaki S. et al. reported successful management of TET spell by low dose (0.2 mcg/kg/hr) of continuous infusion of dexmedetomidine in an eight-day old newborn with TOF who was brought to hospital with critical cyanosis. The symptoms of the patient were controlled within 30 minutes after starting infusion[4]. However, the duration of TET spell is highly associated with poor outcome, thus the time to correct is crucial. Furthermore, the FDA currently approved only continuous infusion for up to 24 hours in critically-ill adult patients who are initially intubated and receiving mechanical ventilation. At present, there are no FDA-approved indication for its use in children. Consequently, we chose fentanyl infusion to treat the spell immediately and postoperative pain control.

In conclusion, fentanyl infusion should be considered as alternative sedative and analgesic of morphine for hypercyanotic spell patients. Fentanyl may be more useful than other sedatives for postoperative patients because of its properties including rapid onset, ease of titration, analgesic potency and minimal effect on hemodynamic status.

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