

Anaesthesia in a patient with Prader-Willi syndrome and severe burn injury: a case report

Peter Biro MD, DESA (Senior Staff Physician)

Institute of Anaesthesiology, University Hospital Zürich, CH-8091 Zürich, Switzerland

Abstract

Prader-Willi syndrome (PWS) is a congenital developmental disorder which is related to severe problems during anaesthesia. Of particular interest are the morphological and patho-physiological alterations which may lead to considerable respiratory complications, including a higher risk of regurgitation and aspiration, and the tendency towards post-surgical hypoventilation. Further difficulties may arise from mental retardation, disturbed thermoregulation, and an unstable glucose metabolism.

In our patient these features have been aggravated by burn injuries exceeding 35% of body surface. Appropriate care of circulatory and respiratory function, as well as supervision of blood glucose level and body temperature during a period of several weeks with repeated operations was necessary to avoid further complications. Additional findings we discovered in our patient were narrow airways not corresponding to the patient's age and a significant resistance to non depolarising muscle relaxants that might have been caused by the burn injuries.

The importance of PWS for anaesthesiologists can be estimated by the circumstance, that it is considered to be nearly as frequent as trisomy-21. PWS in connection with extensive burns has yet not been reported. This case and a recent review of the relevant literature on anaesthetic management of PWS are extensively discussed.

Keywords: Anaesthesia, co-existing disease: Prader-Willi syndrome, burns; Complications: difficult intubation, risk of aspiration, resistance to muscle relaxants.

J Rom Anest Terap Int 2011; 18: 149-152

Introduction

Prader-Willi syndrome (PWS) is a rare congenital disorder of child development. Main clinical symptoms are short stature, reduced muscular tonicity, obesity, mental retardation and hypogonadism [1-3]. Surgical correction of the developmental disorders has to be performed during early childhood. Lack of cooperation on the part of the patient, pathological changes in muscular and reflex activity, as well as other organ manifestations of the disease call for appropriate anaesthetic management.

Case History

A 23-year-old female patient (52 kg, 145 cm) with PWS suffered extensive burns to the body, thorax, neck and face. Of the total body surface, an area of 35% was involved, 25% of which presented third degree burns. There was no evidence of inhalational injury to the respiratory tract. On admission, the patient presented mental retardation, a short stature, acromicria of hands and feet, hypogonadism and diabetes. She had undergone two uneventful general anaesthesias during early childhood for nasal polypectomy and tonsillectomy.

Surgery consisted of wound-cleaning and mesh-grafting under general anaesthesia. Respiratory and circulatory parameters were normal except for a regular tachycardia of 130 min⁻¹. The patient was rehydrated by i.v. infusion of fluid and electrolytes and by enteral nutrition. No insulin was necessary owing to only slightly elevated blood glucose values.

Adresa pentru corespondență: Prof. dr. Peter Biro MD, DESA
Institute of Anaesthesiology
University Hospital Zürich
Raemistr. 100
CH 8091, Zürich, Switzerland
E-mail: peter.biro@usz.ch

During surgical treatments the patient had to undergo several general anaesthetics that had to be performed in a similar manner. Premedication was carried out i.v. with 5 mg morphine-hydrochloride and 50 mg ranitidine 30 min. before surgery. No benzodiazepines were used in order to avoid aggravation of the existing muscular hypotonia. Anaesthesia was performed with etomidate and atracurium for induction, oxygen and isoflurane for ventilation, and fentanyl for maintenance according to her clinical needs. We have chosen isoflurane instead of our standard volatile anaesthetic sevoflurane because the latter has been occasionally associated in case reports with pulmonary edema [4]. No suxamethonium was used owing to the burns. Monitoring included ECG, invasive arterial blood pressure, pulseoximetry, capnography and relaxography.

Exposure of the larynx was not difficult although we found a tracheal diameter which was clearly below of the corresponding age group. Thus, only a smaller tracheal tube could be inserted (ID 6.5) in the subsequent interventions. Ventilation was performed normally; after tracheo-bronchial suction and application of a moderate positive end-expiratory pressure of 6 cm H₂O (0.6 kPa = Kilopascal), blood gas analysis became normal.

Neuromuscular transmission was controlled by relaxography (Relaxograph™, Life-Tech Inc. Houston, Texas). A 50% decrease in muscular stimulus response "train of four" (TOF) was observed 5 min after application of 15 mg atracurium. After a second dose of 15 mg, a decrease in TOF to 20% was registered within another 5 min later. Only a third dose of 15 mg made TOF drop to 5%. As soon as 10 min after the last atracurium dose, TOF increased to about 66%, and within another 10 min it reached 100% of the initial value. This effect was reproducible during all anaesthetics. Upon completion of general anaesthesia, the patient could be extubated without any problem. Reversal of neuromuscular relaxation was not necessary as sufficient neuromuscular activity was shown by relaxography.

Surgical intervention was successful. After a two-month hospitalisation period, the patient was discharged in good general condition.

Discussion

Incidence and aetiology

Since the first description of PWS in 1956, the disease has been mentioned in literature over 700 times [1]. However, PWS is rarely cited in connection with anaesthesia, and if so mostly over 2 decades ago [5, 6]. The incidence of PWS is about 1 to 15,000-25,000

births; the male/female ratio is 3 to 2. The disease represents app. 1% of all cases of congenital mental retardation and is the second most frequent congenital disorder after Down's syndrome [4, 5, 7]. In 60% the illness is caused by partial deletion of the long arm of paternal chromosome 15 to q13. The type of inheritance is autosomal recessive. In another 40% uniparental disomy of the mother's chromosome 15 is postulated [8, 9]. Muscle biopsies demonstrated an infiltration of fat tissue, whereas electromyography, nerve conduction velocity and muscle enzymes remained within normal range [1, 5]. Obesity is promoted by the metabolic tendency towards lipogenesis out of carbohydrates.

Symptoms and differential diagnosis

The disease develops in two consecutive steps: during new-born age there is variable muscular hypotonia, weakness in drinking and sucking, which often results in hyporeflexia, hypothermia and the need for tube feeding [10]. Between the third and fifth year of life, there is an improvement in muscular activity, while mental retardation and behavioural derangement become more apparent. Increasing food intake with consecutive weight gain follows [3].

The main symptoms of the disease are: mental retardation (97%), hypogonadism and cryptorchism (95%), muscular hypotonia (94%), obesity (94%), acromicria (83%), and short stature (76%). Additional findings point to strabismus (48%), low bifrontal head diameter (40%), diabetes (30%), kyphoscoliosis, hip dislocation, cardiac arrhythmia, a tendency towards convulsions, carious denture, mongoloid eyelids (19%), a small triangular shaped upper lip and retarded bone age [1, 11].

In the adult, mental retardation results in an IQ between 20 to 90, mostly within the range of 55 to 65 [1]. Furthermore, the disease is associated with psychological problems, such as mental instability, sudden attacks of aggressiveness, hypersomnia and hyperphagia [3]. Of particular anaesthetic significance is the postulated incapability of vomiting, on one hand, and the disposition to regurgitation of acid gastric fluid on the other [4, 6]. There might be organic reasons for this, such as a sliding hernia or a functional disorder of the lower esophageal sphincter, but it is also interpreted as a typically PWS-related psycho-dynamic behavioural symptom. Consequences of this condition are respiratory infections and damaged teeth, typical of the disease, and not caused only by poor hygienic measures [6, 12]. PWS-patients generally have a reduced vital capacity, functional residual capacity and total lung capacity, which might be even more pronounced if kyphoscoliosis is also present [11, 13].

Differential diagnosis of PWS includes Pickwick syndrome, sleep apnoea syndrome, diabetes, hypothyreosis, hypothalamic obesity, Laurence-Moon-Biedl-Bardet syndrome, Down syndrome, Angelman syndrome, and Cushing syndrome [7, 8].

Therapy and prognosis

Causal therapy is not available. However, several symptoms may be treated by means of prophylactic measures against regurgitation and aspiration, and antibiotic treatment of respiratory infections. Psychosocial support and dietary measures are part of the lifelong care. Often associated with the disease are ophthalmological, maxillo-facial, orthopaedic, and urological problems, which require surgical interventions in early age [11].

There are a few reports of death during the first two decades of life, mostly due to cardio-respiratory complications. Life expectancy may reach the fifth decade if marked obesity is avoided [5, 7, 14].

Preoperative tests

Preoperative tests should exclude other diseases, especially those listed in the differential diagnosis. A variety of tests helps us recognise anaesthetically relevant organ malfunctions, as well as evaluate and optimise ongoing therapies. Important tests concern lung function, respiration (chest X-ray), circulatory values, metabolic values (blood glucose), and serum electrolytes.

Anaesthesia in Prader-Willi syndrome

Most of the typical findings in patients with PWS have a significant impact on anaesthesia (Table 1). Benzodiazepines for premedication should be used carefully with regard to the prevalent muscular hypotonia and hypersomnia. In consideration of the tendency to gastro-esophageal regurgitation H₂-receptor blockers and metoclopramide should be administered 30 minutes prior to general anaesthesia. Additionally, up to 30 ml of sodium citrate can be given orally for neutralisation of gastric acid [6].

In choosing the type of anaesthesia to be applied, the degree of mental retardation of the patient is decisive. Regional anaesthesia is not contraindicated, but its application can be very difficult in the case of a patient's lack of cooperation, or in the presence of scoliosis or obesity. General anaesthesia may be performed with the usual anaesthetics. Owing to reduced swallowing and coughing reflex, increased intra-abdominal pressure and a higher risk of aspiration, general anaesthesia should be performed only with a secured airway after induction in the sense of a "rapid sequence" [6, 12].

Table 1. Anaesthesia-related problems associated with Prader-Willi syndrome

- chronic respiratory infections
- risk of perioperative pulmonary complications
- difficult airway and difficult intubation
- disturbed thermoregulation
- tendency to hypoventilation and sleep apnoea
- immature and inappropriately narrow airways
- mental retardation (reduced patient compliance)
- muscular hypotonia
- risk of aspiration
- unforeseeable effects of relaxants
- unstable glucose metabolism

Intubation often presents difficulties owing to the obesity of the patient or anomalies in the face and neck area, such as micrognathia, hypoplasia of the mandible, a "gothic" palate, carious denture, or difficult access to the airway [14]. In our patient laryngoscopy revealed an unusually small tracheal diameter, corresponding to that of an 8-year-old child, but intubation was performed easily with a matching tracheal tube.

With regard to the muscular hypotonia and the reduced muscle mass in relation to the weight, one might have expected a lower demand for muscle relaxants. Our patient, however, needed unexpectedly high doses of a non-depolarising muscle relaxant. With a body weight of 52 kg, she required a total of 45 mg atracurium over a period of 15 min, corresponding to 1.5-2 times the usual amount. A paravenous injection or a loss of drug efficiency was excluded. The higher requirement of non depolarising relaxants can be explained by the major burn injuries exceeding 35% of body surface. This feature based upon up-regulation of acetylcholine receptors has been widely reported by various authors [15, 16]. In spite of the low sensitivity to relaxants related to the burns, we recommend a titrating procedure under relaxographic control for every PWS-patient.

Stress can result in pronounced hyperglycaemia, even in patients without manifest diabetes. On the other hand, PWS patients are prone to hypoglycaemia after long periods of fasting [3]. Thus, repeated perioperative tests of blood glucose, and early intravenous application of an infusion containing glucose are mandatory. The persistent slight hyperglycaemia in our patient could be managed with a balanced and continuous supply of carbohydrates.

Owing to disturbed thermoregulation (tendency towards poikilothermia), hyper and hypothermia – occasionally associated with metabolic acidosis – were repeatedly observed in PWS-patients during general anaesthesia [10]. No reference to malignant hyper-

thermia (MH) has been made so far. Therefore, no contraindication is given for MH-triggering substances. Nonetheless, continuous monitoring of the body temperature is anyway indicated. Blood-gas and acid-base status should be regularly checked.

In the postoperative period, there is a certain propensity towards chronic hypoventilation [7], similarly to many diseases associated with obesity and hypersomnia. These findings are directly connected to the fact that respiratory arrest secondary to hypotonia and hypoventilation is a leading cause of mortality in PWS [3]. Accordingly, an overhang of anaesthetics and relaxants has strictly to be avoided. Prolonged supervision of the respiratory function, blood glucose level, and body temperature is recommended.

References

- Butler MG. Prader-Willi syndrome: current understanding of cause and diagnosis. *Am J Med Genet* 1990; 35: 319-332
- Jacob SS, Jacob JJ, Paul TV. Foreign body aspiration in a boy with Prader-Willi Syndrome. *Singapore Med J* 2008; 49: e12-14
- Meco BC, Alanoglu Z, Cengiz OS, Alkis N. Anesthesia for a 16-month-old patient with Prader-Willi syndrome. *J Anesth* 2010; 24: 949-950
- Mantadakis E, Spanaki AM, Geromarkaki E, Vassilaki E, Briassoulis G. Near demise of a child with Prader-Willi syndrome during elective orchidopexy. *Pediatr Anesth* 2006; 16: 790-793
- Mackenzie JW. Anesthesia and the Prader-Willi syndrome. *J R Soc Med* 1991; 84: 239
- Sloan TB, Kaye CI. Ruminant risk of aspiration of gastric contents in the Prader-Willi syndrome. *Anesth Analg* 1991; 73: 492-495
- Kaplan J, Fredrickson PA, Richardson JW. Sleep and breathing in patients with the Prader-Willi syndrome. *Mayo Clin Proc* 1991; 66: 1124-1126
- Nicholls RD, Knoll JH, Butler MG, Karam S, Lalande M. Genetic imprinting suggested by maternal heterodisomy in nondeletion Prader-Willi syndrome. *Nature* 1989; 342: 281-285
- Robinson WP, Bottani A, Xie YG, et al. Molecular, cytogenetic, and clinical investigations of Prader-Willi syndrome patients. *Am J Hum Genet* 1991; 49: 1219-1234
- Ince E, Ciftçi E, Tekin M, et al. Characteristics of hyperthermia and its complications in patients with Prader Willi syndrome. *Pediatr Int* 2005; 47: 550-553
- Bray GA, Dahms WT, Swerdloff RS, Fiser RH, Atkinson RL, Carrel RE. The Prader-Willi syndrome: a study of 40 patients and a review of the literature. *Medicine (Baltimore)* 1983; 62: 59-80
- Alexander RC, Greenswag LR, Nowak AJ. Ruminant and vomiting in Prader-Willi syndrome. *Am J Med Genet* 1987; 28: 889-895
- Hákonarson H, Moskovitz J, Daigle KL, Cassidy SB, Cloutier MM. Pulmonary function abnormalities in Prader-Willi syndrome. *J Pediatr* 1995; 126: 565-570
- Greenswag LR. Adults with Prader-Willi syndrome: a survey of 232 cases. *Dev Med Child Neurol* 1987; 29: 145-152
- Marathe PH, Dwersteg JF, Pavlin EG, Haschke RH, Heimbach DM, Slattey JT. Effect of thermal injury on the pharmacokinetics and pharmacodynamics of atracurium in humans. *Anesthesiology* 1989; 70: 752-755
- Martyn J. Clinical pharmacology and drug therapy in the burned patient. *Anesthesiology* 1986; 65: 67-75

Anestezia la un pacient cu sindrom Prader-Willi și arsuri severe: prezentare de caz

Rezumat

Sindromul Prader-Willi (SPW) este o tulburare de dezvoltare congenitală care pune probleme serioase în cursul anesteziei. De interes particular sunt alterările morfologice și fiziopatologice care pot produce complicații respiratorii considerabile, inclusiv un risc crescut de regurgitare și aspirație și tendința la hiperventilație postoperatorie. Alte dificultăți pot apărea din cauza retardului mental, tulburărilor de termoreglare și un metabolism glucidic instabil.

La pacientul prezentat, aceste caracteristici au fost agravate de o arsură tegumentară de peste 35% din suprafața corpului. A fost necesară o îngrijire deosebită a funcțiilor circulatorie și respiratorie și urmărirea nivelului glicemiei și a temperaturii corporale timp de câteva săptămâni, fiind necesare numeroase intervenții chirurgicale pentru evitarea altor complicații. În plus, la pacientul nostru s-au pus în evidență căile aeriene îngustate necorespunzând vârstei și o rezistență semnificativă la relaxantele musculare nedepolarizante care putea fi pusă pe seama leziunilor prin arsură.

Pentru anesteziști, importanța SPW poate fi apreciată de circumstanța că este considerat aproape la fel de frecvent ca și trisomia-21. Un SPW în contextul unor arsuri extinse încă nu a fost comunicat. Sunt discutate pe larg cazul clinic și literatura recentă privind conduita anestezicologică a sindromului Prader-Willi.

Cuvinte cheie: anestezie, boli coexistente: sindromul Prader-Willi, arsuri; complicații: intubație dificilă, risc de aspirație, rezistență la miorelaxante