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Anesthesiology Clin N Am
23 (2005) 733–743

ANESTHESIOLOGY
CLINICS OF
NORTH AMERICA

Surgery and Anesthesia for Children who have Cerebral Palsy

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Cerebral palsy (CP) is a collection of motor system disorders including choreoathetosis, hypotonia, ataxia, dystonia, spasms, or mixed forms. It originates from a non-progressive neurological insult sustained perinatally or before 2 years of age [1]. The incidence of CP is rising in the United States [2] and is currently estimated to be 2.4 per 1000 live births. The etiology of CP varies and includes any event causing cerebral injury that is non-progressive. CP predominantly affects the motor system, and the resultant spasticity and hypertonicity are progressive. A notable feature of CP is that infants generally have very low birth weight; roughly 52,000 infants are born annually with very low birth weight [2]. Long-term studies of the outcome of very premature infants have documented significant motor, cognitive, and behavioral deficits in most of these patients, especially when birth weight is ≤ 1500 g [3]. MRIs show that such infants have decreased cerebral gray and white matter volume, as well as an increased volume of cerebrospinal fluid. These infants make up more than 25% of the children diagnosed with CP. Clinically, CP can be classified into four groups according to symptoms, shown in **Box 1**.

This work was supported by NIH Grant Number P20 RR-020173-01 from the National Center for Research Resources.

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Box 1. Classification of cerebral palsy according to symptoms

Spastic: Lesion in cerebrum. Includes quadriplegia, diplegia, hemiplegia. The number of extremities affected (and the degree of spasticity) correlates with level of intelligence.

Dyskinetic: Lesion in basal ganglia. Includes dystonia (twisting position of torso), athetosis (purposeless movements of extremities), and chorea (quick, jerky proximal movements of extremities).

Ataxic: Lesion in cerebellum includes tremor, loss of balance, and speech.

Mixed: Lesion in cerebrum and cerebellum. Includes spasticity and athetoid movements.

Preoperative concerns*Gastrointestinal*

Gastroesophageal reflux is common in children who have CP, and these children often present for Nissen fundoplication [4]. Children who have CP have an impaired ability to handle pharyngeal secretions, and pooling of secretions in the oropharyngeal area is common. The etiology of increased salivation is caused by hyperactive salivary glands and impaired cranial nerve function. Some patients may have already been placed on anti-sialogogue; the most common agent used is the anticholinergic, glycopyrrolate. It is necessary to suction the oropharynx immediately following induction of anesthesia (or even before). Anticholinergics given intravenously, once this access is secured, will aid in minimizing this problem.

Respiratory

Recurrent pneumonia from chronic aspiration and lack of ability to cough effectively is often the cause of death in these patients. Reactive airway disease is prevalent and is caused by injury to the pulmonary parenchyma from chronic insults such as aspiration. Following intubation of the trachea, suctioning via an endotracheal tube is a good practice in children with increased secretions, especially if rhonchi or expiratory wheeze is present. Often, breath sounds will clear using this simple maneuver.

Neurological

Seizures are present in roughly 30% of patients who have CP. On the day of surgery, these patients are given a morning dose of anticonvulsants, and,

postoperatively, the anticonvulsants should be reinstated as soon as possible. The drugs that can be given rectally (phenytoin [Dilantin], valproic acid, carbamazepine [Tegretol]) should be administered per schedule. A gastrostomy tube can be used to administer drugs as well (within reason and based on the type of surgical procedure). Phenytoin [Dilantin], valproic acid, and phenobarbital can also be given intravenously. For more extensive procedures that involve blood loss, anticonvulsant levels should be checked postoperatively and their dose adjusted to reestablish optimal levels for the patient.

Anesthetic management

Preoperative

In a few cases of CP, in which the child is predominantly hypotonic, it is prudent to avoid preoperative sedation. Loss of airway tone and increased risk of aspiration is greater in hypotonic children. Most children would have had sedation for radiological procedures or for other reasons in the past. Before preoperative sedation is ordered, parents should be consulted to learn how well the child previously tolerated sedation. A good, practical way to assess the need is to consider if the patient already appears sedate and looks as though he/she already received premedication, in which case premedication can be left out for that patient. However, most patients will handle premedication without incident, and reducing the dose may be more appropriate than omitting premedication altogether. If obtaining intravenous access is necessary before induction, then use of EMLA cream (lidocaine 2.5% and prilocaine 2.5%) can be helpful. Often, a combination of EMLA cream, nitrous oxide (50%–70%) with oxygen, and preoperative sedation will help in facilitating intravenous access. The extremities of these children are often cold and vasoconstricted. Use of any warming device, including warm towels and heel warmers, all aid in vasodilation and make it easier and quicker to access a peripheral vein. Some of the very profoundly affected children may have early loss of airway tone with 70% nitrous oxide. This is easily remediable with minimal airway manipulation or a decrease in the nitrous oxide concentration.

Intraoperative

Propofol for intravenous induction is a good choice, as many children with CP have reactive airway disease, and, propofol, unlike thiopental, decreases the airway tone [5]. Presence of gastroesophageal reflux and increased oropharyngeal secretions may prompt the anesthesiologist to expedite securing the airway. Studies examining the use of succinylcholine in children with CP raise concerns about the safety of its use. The first study to address the question of abnormal potassium release after succinylcholine was conducted by Dierdorf and co-workers [6]. This study concluded that there was no significant difference in

Table 1
ED50 and ED95 of succinylcholine in children who have CP [7]

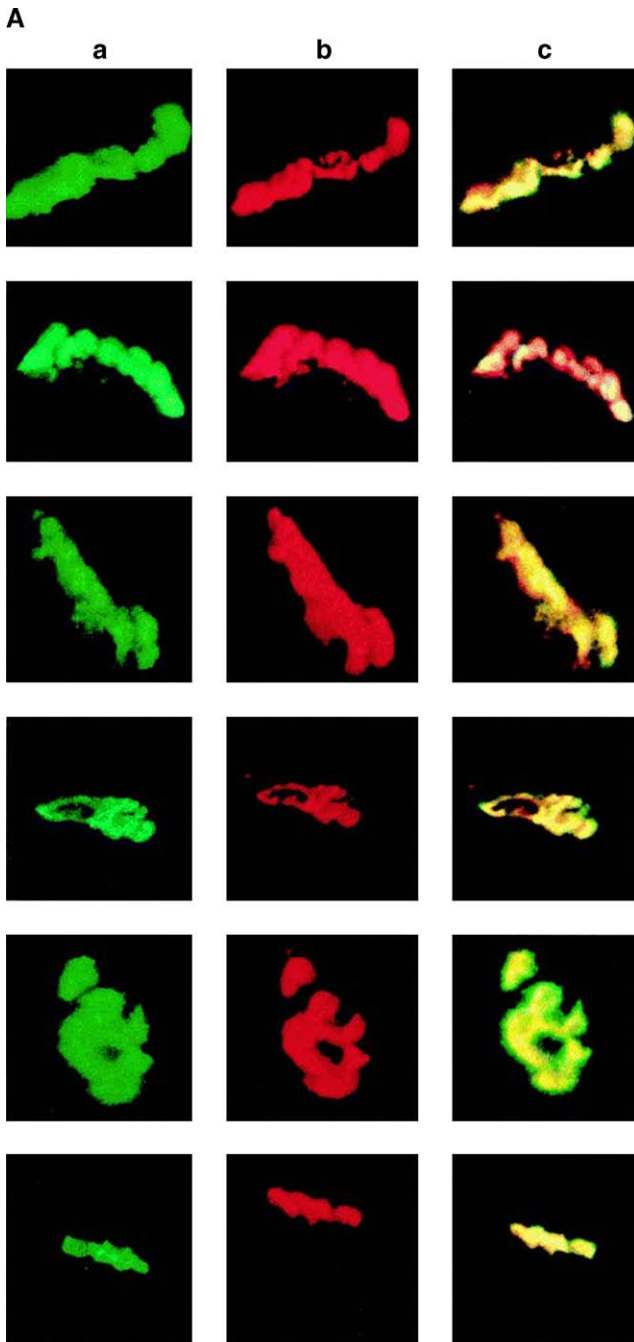
Succinylcholine ($\mu\text{g}/\text{kg}$)	CP patients*	Healthy patients**
ED50	146.8 (111.4–193.7)	228
ED95	360.5 (273.3–475.5)	445

* The 95% confidence intervals are given for the CP patients; ** Data from Brown TC, Meretoja OA, Bell B, et al. Suxamethonium: electromyographic studies in children. *Anaesth Intensive Care* 1990;18:473–6.

potassium release after succinylcholine in children with CP when compared with normal children. Unfortunately, events such as hyperkalemia following succinylcholine administration are rare enough that a study design like the one used by these investigators will not be expected to capture it. However, a study by Theroux and colleagues [7] that examined the potency of succinylcholine, demonstrated increased sensitivity toward succinylcholine in children with CP. This study showed that the effective dose (ED) of succinylcholine to depress 50% of baseline twitch (ED50) is less in children who have cerebral palsy when compared with healthy children. The same relationship is true for the effective dose of succinylcholine to depress 95% (ED95) of baseline twitch (Table 1).

In a more recent study, the same investigators examined the abnormal distribution of acetylcholine receptors in muscle biopsies obtained from children who have CP [8]. Theroux and coworkers used a double-staining method in which acetylcholinesterase stained the limits of neuromuscular junction, which was followed by a second stain in which alpha-bungarotoxin stained the acetylcholine receptors. This methodology made it possible to examine the spread of acetylcholine receptors (AChRs) in relationship to the boundaries of neuromuscular junction (Figs. 1A, B). Up to 30% of the children [8] had AChRs over and beyond the boundary of neuromuscular junction. This direct evidence compounded by indirect evidence from clinical studies renders the routine use of succinylcholine in children who have CP questionable at best.

Fig. 1. (A) Histologic examination of neuromuscular junctions (NMJs) for children who have idiopathic scoliosis. NMJs from six children are shown. These represent typical staining patterns for NMJs in children with a diagnosis of idiopathic scoliosis. Column A shows the staining pattern for acetylcholine esterase (AChE), column B shows the staining pattern for acetylcholine receptor (AChR), and column C shows the combined fluorescence images. In all cases, the NMJs in these children showed AChR staining that was contained within the limits of the acetylcholinesterase staining. (B) Histologic examination of neuromuscular junctions (NMJs) from children with cerebral palsy (CP). Neuromuscular junctions from six children who have a diagnosis of scoliosis associated with CP are shown. Column A shows the staining pattern for acetylcholinesterase (AChE), column B shows the staining pattern for acetylcholine receptor (AChR), and column C shows the combined fluorescence images. Each of the six NMJs shown was scored positive for the presence of extrajunctional AChR receptors. Arrows point toward the staining (AChRs) beyond the limits of neuromuscular junction. (From Theroux MC, Akins RE, Barone C. Neuromuscular junctions in cerebral palsy. Presence of extrajunctional acetylcholine receptors. *Anesthesiology* 2002;96:330–5; with permission.)



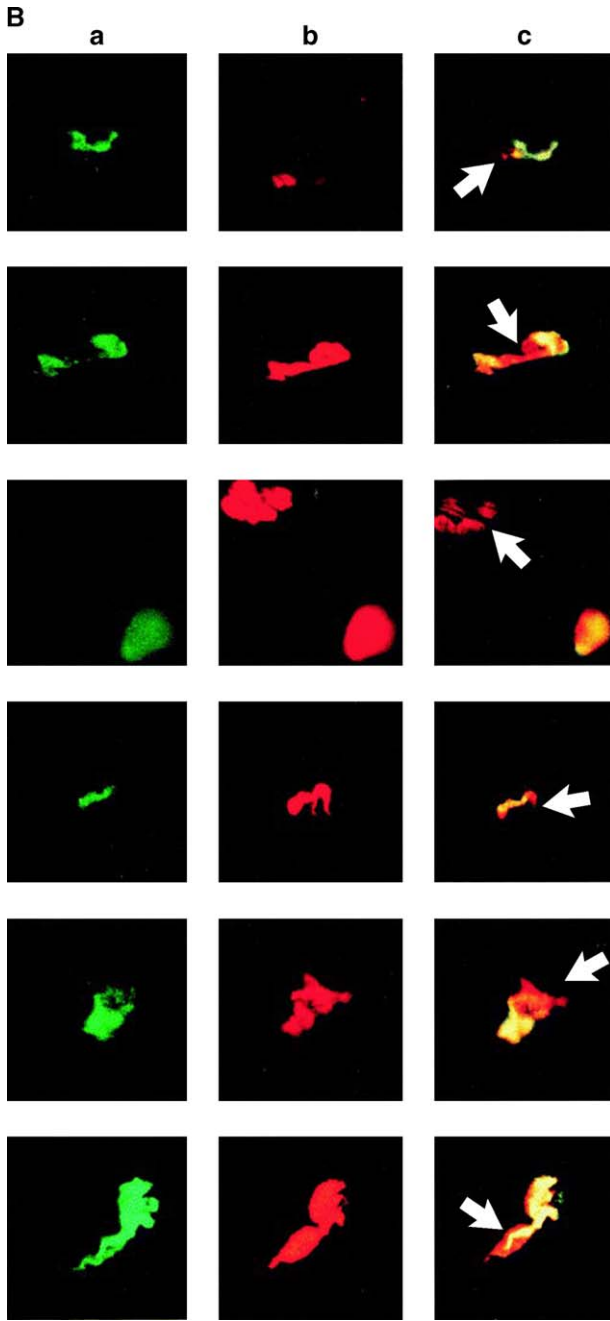


Fig. 1 (continued).

Non-depolarizing muscle relaxants demonstrate less potency in children with CP [9]. In other words, a non-depolarizing muscle relaxant will have greater dosing requirement and, possibly, shorter duration when compared with normal children. This finding agrees with other studies examining up-regulation of AchRs [10–12]. In order to maintain neuromuscular blockade during surgery in children with CP, greater than expected doses of muscle relaxants are needed.

Mean alveolar concentrations (MAC) of halothane are lower in children with CP when compared with normal children [13]. The MAC of halothane is 0.9 in healthy children; in children who have CP, it is 0.71. It is interesting to note that children who have CP and who were receiving anticonvulsants had an even lower MAC: 0.63. Similarly, anesthetic agents lead to a greater hypnotic state in these children as evidenced by lower bispectral index score (BIS) when exposed to similar concentrations of sevoflurane and compared with patients who are otherwise normal [14]. In this comparative study, children with spastic quadriplegic CP and similarly aged healthy children were exposed to similar concentrations of sevoflurane. The children who have CP had baseline BIS values that were lower than the healthy children and that continued to remain significantly lower at varying anesthetic concentrations. In clinical practice, narcotics appear to have greater potency in children who have CP. Doses need to be reduced, and greater vigilance is necessary to ensure maintenance of a patent airway post extubation.

Regional techniques

Use of regional techniques for postoperative pain management makes postoperative care of these patients easier [15]. Patients can be monitored for epidural management of pain in much the same way as normal patients having similar surgery. Use of clonidine along with bupivacaine and hydromorphone (or fentanyl) is becoming common, and it is believed that clonidine helps reduce the spasticity as well. Postoperative hypotension is more likely in some patients when all three agents are used.

In 1993, Ohta and coworkers [16] studied the safety and efficacy of three different opioids via the epidural route for management of pain during the postoperative period. Eighty-five children between 5 and 15 years of age who had CP and underwent surgery were studied [16]. These patients received, in addition to general anesthesia, one of four agents caudally at the end of the operation: (1) no agent; (2) morphine, 40 $\mu\text{g}/\text{kg}$; (3) buprenorphine, 3 $\mu\text{g}/\text{kg}$; or (4) butorphanol, 30 $\mu\text{g}/\text{kg}$. The investigators concluded that epidural opioids achieve safe and useful postoperative pain control in children with cerebral palsy.

Temperature

The more affected the child, the greater the likelihood that they are unable to regulate their temperature [17,18]. Often, these children will come to the operating room with borderline hypothermia (<35.0). Measures to conserve

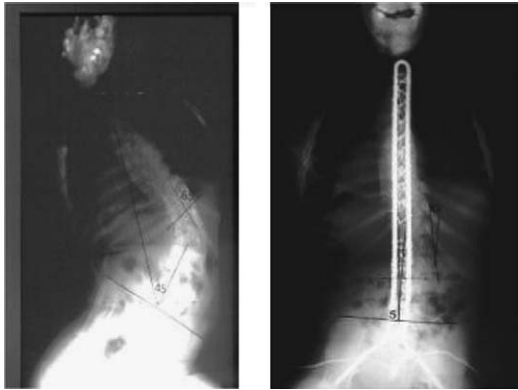


Fig. 2. Radiographic evidence of severe scoliosis in a child with cerebral palsy: curvature of spine before and after correction with a unit rod. (From Theroux MC. Anesthesia for pediatric orthopaedics. In: Litman RS, editor. Pediatric anesthesia: the requisites of anesthesiology. Philadelphia: Elsevier; 2004. p. 275–82; with permission.)

temperature should be used from the start of the anesthetic, or it is likely that 1–2°C heat could be lost before the patient is prepped and draped.

Intraoperative bleeding

It is worth mentioning that the spinal fusion surgery performed in CP, along with other types of neuromuscular scoliosis, is often a much more extensive procedure than spinal fusion performed for idiopathic scoliosis in normal children. The spine is surgically fused from T1 to sacrum [19] and is associated with bleeding that amounts to one or two blood volumes of the patient (Fig. 2).

Monitoring of evoked potentials to ascertain spinal cord integrity, although routinely performed during spinal fusion for otherwise healthy children, is often thought to be somewhat meaningless as the baseline evoked response is diminished or even absent in children who have CP. However, the monitoring capability is evolving, and children who have CP are being monitored with

Table 2

Percentage of patients with neuromuscular scoliosis who were monitored successfully with somatosensory evoked potentials (SSEP) and/or transcranial motor evoked potentials (TceMEP)

Type of neuromuscular scoliosis	SSEP	TceMEP
CP–Mild	4/4 (100%)	3/3 (100%)
CP–Moderate	12/12 (100%)	7/7 (100%)
CP–Severe	16/23 (70%)	9/10 (90%)
Non–CP (Other)	25/29 (86%)	25/29 (86%)

From Dicindio S, Theroux M, Shah S, et al. Multimodality monitoring of transcranial electric motor and somatosensory-evoked potentials during surgical correction of spinal deformity in patients with cerebral palsy and other neuromuscular disorders. *Spine* 2003;28:1851–5; with permission.

Table 3

Prothrombin time (PT), Partial thromboplastin time (PTT), and factor levels measured at baseline (Base) and again at blood loss of 25% of patient's blood volume (BL₂₅)**

Patient	Base PT	BL ₂₅ PT	Base PTT	BL ₂₅ PTT	Base II	BL ₂₅ II	Base VII	BL ₂₅ VII	Base IX	BL ₂₅ IX	Base X	BL ₂₅ X
1	10	*12	29	*38	90	*68	*43	*49	70	*74	58	*45
2	10	*15	34	*67	100	*46	110	*30	100	*37	100	*57
3	*12	*15	28	*43	85	*48	64	*12	100	*52	100	*22
4	*13	*14	*39	*48	90	*55	70	*70	37	*52	60	*39
5	*13	*16	30	*46	100	*46	80	*64	74	*29	57	*57

* Subnormal values as per the laboratory where the tests were performed; ** Normal range for PT, 9–11 min; for PTT, 23–38 min; for normal factor levels, 50%–150% of normal.

increasing frequency. A study by Dicindio and coworkers [20], which examined the feasibility of spinal cord monitoring using both sensory and evoked potentials, has shown that a greater than anticipated number of children who have CP can be monitored using currently available technology (Table 2).

In general, children who have CP bleed more per segment of spine fused when compared with idiopathic scoliosis patients [21]. Reasons are unclear and often attributed to their poor nutritional status or a lifelong non-ambulatory status [22]. Studies are emerging on this subject. A pilot study that examined clotting factors, found subnormal factor levels are frequently prevalent in children who have CP (Table 2). Of five patients who have severe, spastic CP in this study, two patients had subnormal factor levels measured before the beginning of surgery. All five

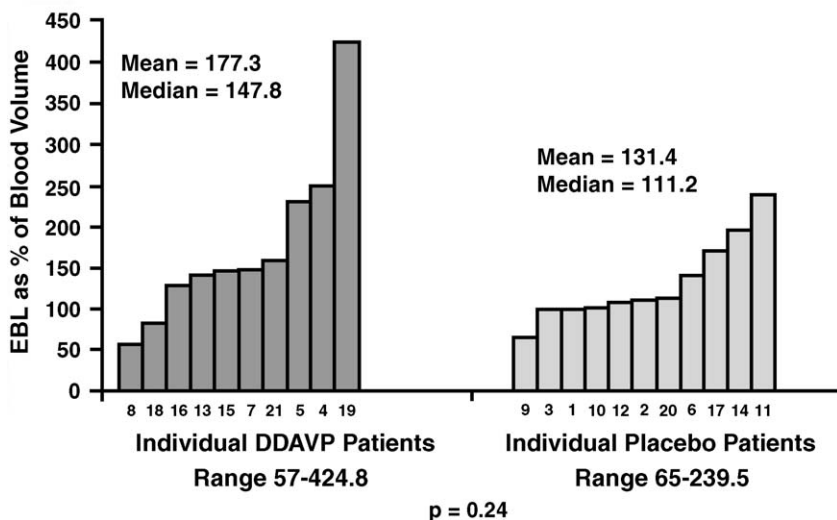


Fig. 3. Blood loss during spinal fusion: 1–desamino-8-D-arginine vasopressin (DDAVP) versus placebo. (From Theroux MC, Corddry DH, Tietz AE, et al. A study of desmopressin and blood loss during spinal fusion for neuromuscular scoliosis. Anesthesiology 1997;87:260–7; with permission.)

patients had at least one factor below normal level by the time they lost 25% of their estimated blood volume (Table 3). Therefore, early use of fresh frozen plasma is often practiced in surgical procedures involving significant blood loss.

Platelets are often borderline low in these children because of prolonged use of anticonvulsants. Platelet function is also affected by anticonvulsants [23,24]. Procoagulants have been studied to examine their potential benefit in reducing operative blood loss in these patients. The procoagulant 1-desamino-8-D-arginine vasopressin was found to have no effect in a randomized controlled study [25] (Fig. 3). Aprotinin may be more promising, but definitive studies in children who have CP are lacking.

References

- [1] Dabney KW, Lipton GE, Miller F. Cerebral palsy. *Curr Opin Pediatr* 1997;9:81–8.
- [2] Kuban KC, Leviton A. Cerebral palsy. *N Engl J Med* 1994;330:188–95.
- [3] Inder TE, Warfield SK, Wang H, et al. Abnormal cerebral structure is present at term in premature infants. *Pediatrics* 2005;115:286–94.
- [4] Spiroglou K, Xinias I, Karatzas N, et al. Gastric emptying in children with cerebral palsy and gastroesophageal reflux. *Pediatr Neurol* 2004;31:177–82.
- [5] Shapiro JM. Management of respiratory failure in status asthmaticus. *Am J Respir Med* 2002;1:409–16.
- [6] Dierdorf SF, McNiece WL, Rao CC, et al. Effect of succinylcholine on plasma potassium in children with cerebral palsy. *Anesthesiology* 1985;62:88–90.
- [7] Theroux MC, Brandom BW, Zagnoev M, et al. Dose response of succinylcholine at the adductor pollicis of children with cerebral palsy during propofol and nitrous oxide anesthesia. *Anesth Analg* 1994;79:761–5.
- [8] Theroux MC, Akins RE, Barone C. Neuromuscular junctions in cerebral palsy. Presence of extrajunctional acetylcholine receptors. *Anesthesiology* 2002;96:330–5.
- [9] Hepaguslar H, Ozzybek D, Elar Z. The effect of cerebral palsy on the action of vecuronium with or without anticonvulsants. *Anaesthesia* 1999;54:593–6.
- [10] Martyn JA, White DA, Gronert GA, et al. Up- and down-regulation of skeletal muscle acetylcholine receptors. Effects on neuromuscular blockers. *Anesthesiology* 1992;76:822–43.
- [11] Hogue Jr CW, Itani MS, Martyn JA. Resistance to d-tubocurarine in lower motor neuron injury is related to increased acetylcholine receptors at the neuromuscular junction. *Anesthesiology* 1990;73:703–9.
- [12] Hogue Jr CW, Ward JM, Itani MS, et al. Tolerance and upregulation of acetylcholine receptors follow chronic infusion of d-tubocurarine. *J Appl Physiol* 1992;72:1326–31.
- [13] Frei FJ, Haemmerle MH, Brunner R, et al. Minimum alveolar concentration for halothane in children with cerebral palsy and severe mental retardation. *Anaesthesia* 1997;52:1056–60.
- [14] Choudhry DK, Brenn BR. Bispectral index monitoring: a comparison between normal children and children with quadriplegic cerebral palsy. *Anesth Analg* 2002;95:1582–5.
- [15] Brenn BR, Rose JB. Epidural analgesia in children with cerebral palsy. *Can J Anaesth* 1998;45:1156–61.
- [16] Ohta K, Katsuno M, Kawana S, et al. Epidural opioids for post-operative pain control in pediatric patients with cerebral palsy. *Masui* 1993;42:664–8.
- [17] Dickerson RN, Brown RO, Hanna DL, et al. Energy requirements of non-ambulatory, tube-fed adult patients with cerebral palsy and chronic hypothermia. *Nutrition* 2003;19:741–6.
- [18] Mitchell D, Laburn HP. Pathophysiology of temperature regulation. *Physiologist* 1985;28:507–17.

- [19] Dabney KW, Miller F, Lipton GE, et al. Correction of sagittal plane spinal deformities with unit rod instrumentation in children with cerebral palsy. *J Bone Joint Surg Am* 2004; 86(Suppl 1):156–68.
- [20] DiCindio S, Theroux M, Shah S, et al. Multimodality monitoring of transcranial electric motor and somatosensory-evoked potentials during surgical correction of spinal deformity in patients with cerebral palsy and other neuromuscular disorders. *Spine* 2003;28:1851–5.
- [21] Bobechko WP. Blood loss in scoliosis surgery. *Spine* 1991;5:75–82.
- [22] Brenn BR, Theroux MC, Dabney KW, et al. Clotting parameters and thromboelastography in children with neuromuscular and idiopathic scoliosis undergoing posterior spinal fusion. *Spine* 2004;29:310–4.
- [23] Sherard Jr ES, Couri D. Treatment of childhood epilepsy with valproic acid: results of the first 100 patients in a six-month trial. *Neurology* 1980;30:31–5.
- [24] Kreuz W, Funk M, Meyer-Schrod R, et al. Valproate therapy induces von Willebrand disease type 1. *Epilepsia* 1992;33:178–84.
- [25] Theroux MC, Corddry DH, Tietz AE, et al. A study of desmopressin and blood loss during spinal fusion for neuromuscular scoliosis: a randomized, controlled, double-blinded study. *Anesthesiology* 1997;87:260–7.