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Case report

Unexpected neurological sequelae following propofol anesthesia in infants: Three case reports

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Abstract

Propofol is a widely used hypnotic agent for induction and maintenance of pediatric anesthesia with a well known safety profile. Experimental *in vitro* studies suggest that propofol may be toxic to developing neurons. We report the cases of three infants who underwent surgery before 2 months of age for different benign pathologies. Propofol was used for induction and maintenance of anesthesia in all cases. The three patients developed convulsions with similar clinical characteristics (cluster of recurrent clinical and subclinical seizures) between the 23th and 30th hours following anesthesia. Clinical and electroencephalographic improvement was obtained between the third and fourth day of management in pediatric intensive care unit. The seizures never recurred, and the three patients underwent further uneventful general anesthesia without propofol. Follow-up of the three patients disclosed unexpected neurological dysfunction: progressive microcephaly (head circumferences were normal at birth), developmental impairment with cognitive and behavioural disturbances in two cases, and bilateral symmetrical white-matter abnormalities on cerebral magnetic resonance imaging. *Conclusion:* The causal relationship between propofol anesthesia and the neurological symptoms of our patients remains difficult to ascertain, but we believe that pediatricians, anesthetists and intensive care-givers should be aware of this possible adverse reaction that has never been described before.

Keywords: Anesthesia; Developmental disabilities; Microcephaly; Propofol; Seizures

1. Introduction

Propofol is an intravenous hypnotic who acts as a γ-aminobutyric acid. Its rapid onset of action with dose-related hypnotic effect and rapid recovery make it widely used in induction and maintenance of pediatric anesthesia. Despite its remarkable safety profile, there is growing interest concerning side effects of propofol in pediatric population [1], especially the propofol infusion syndrome [2] which led to its contraindication in pediatric intensive care sedation [3]. We report the case of three infants born between 2003 and 2004 who presented a cluster of recurrent seizures following propofol anesthesia, and who developed progressive unexpected neurological impairment with microcephaly.

2. Case report

Clinical data and further details regarding the surgical procedure are summarized in Table 1.

Abbreviations: EEG, electroencephalogram; MRI, magnetic resonance imaging; PICU, pediatric intensive care unit; CSF, cortico-spinal fluid; T2W, T2-weighted.

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Table 1
Main clinical data of our three patients.

	Case 1	Case 2	Case 3
Birth head circumference (cm)/percentile	35/57th	32.5/34th	34/38th
Surgery indication	Left leucocoria	Piriform sinuses hypoplasia	Left ovarian inguinal hernia
Age at anesthesia (days)	34	54	55
Weight at anesthesia (g)	3900	3600	4500
Anesthesia duration (minutes)	150	180	60
Anesthetic drugs total dose used:			
Propofol (mg kg^{-1})	20	27	4.4
Fentanyl (μg kg^{-1})	1.95	–	–
Sufentanyl (μg kg^{-1})	–	6	0.4
Sevoflurane (%)	3.1–8	3.1–8	3.1–5
Time between anesthesia and seizures onset (h)	29	30	23
Seizure type	Partial, clinical and subclinical	Partial secondary generalized, clinical and subclinical	Partial secondary generalized, clinical and subclinical
Drugs used in the PICU to obtain seizure control	Intravenous Clonazepam Fosphenytoin	Intravenous Diazepam Fosphenytoin Phenobarbital	Intravenous Diazepam Fosphenytoin Thiopental
Intubation	No	No	3 days
Cardiovascular monitoring and investigations	Normal	Normal	Normal
Biological investigations[a]	Normal	Normal	Normal
Anesthetic drugs used for subsequent anesthesia for MRI	Sevoflurane Midazolam	Sevoflurane Midazolam	Sevoflurane Midazolam
Age at last follow-up	3 years 9 months	5 years 2 months	4 years 8 months
Head circumference at last follow-up (cm)/percentile	46.6/3.4	45/<0.1	45/<0.1
Neurological outcome at last follow-up	Normal psychomotor achievements, mild hyperkinesia	Discrete lower limb pyramidal tract signs, mental deficiency with hyperkinesia	Normal neurological examination, global developmental delay of 2 years with hyperkinesia

PICU, pediatric intensive care unit; CSF, cerebrospinal fluid.

[a] All patients underwent CSF and blood screening, including infectious, toxicological and metabolic investigations. Patient 2 underwent skin fibroblast study and genetic investigations (karyotype, 22q11, 15q11q12, MECP2).