ORIGINAL ARTICLE

# **Propofol Sedation Dose for MRI Examination in Autistic Children Compared** with normal Children

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#### Abstract

Introduction: MRI examination is a standard procedure requested by physicians of neurologic sciences, for the patient with neurocognitive disorders. Propofol sedation was performed for this examination, and we had the suspicion that children with autism spectrum syndrome (AUT) required higher propofol dose than normal children.

Materials and methods: During a six years period, the first group of 30 autistic patients aged 3 to 10 years, received propofol infusion for brain MR, the control group of 30 normal patients with the same age, and the same mid-time of examination MR was also performed.

Results: 17 children of AUT group received 3±1 additional doses of propofol, 12 of them had to repeat MR sequences (adequate anesthesia) and the total dose of propofol 4,5 vs 3,6 compare to non-autistic children. Even and the recovery time is a little bit faster compared to the second group.

Conclusion: Autistic patients require more propofol dose to achieve a desirable level of anesthesia. All anesthesiologists should be aware in such patients with mental disorders when using propofol anesthesia.

Key words: autism, propofol dose, MR examination.

#### Introduction

Autism spectrum disorder (ASD) is a developmental disorder that affects communication and behavior. Although autism can be diagnosed at any age, it is described as a "developmental disorder" because symptoms generally appear in the first two years of life. [1] According to a report by Centers for Disease Control and Prevention that was released in March 30th 2012, referring to 2008 surveillance year, the prevalence of ASD among 8 years

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old children in 14 Autism and Developmental Disabilities Monitoring (ADDM) sites in the United States is more than 1% (11.3 per 1000 or one per 88 children) and that male/ female ratio is approximately 4/1 (ASD is more seen among boys, 18.4 per 1000, that is one in 54 boys while in girls the prevalence was 4.0 per 1000, that is one per 252 girls) [2] The pathophysiology of ASD remains hotly debated, but a leading hypothesis in the field is that inhibitory  $\gamma$ aminobutyric acid (GABA) signaling develops abnormally in the disorder. [3] Magnetic resonance (MR) examination allows researchers and clinicians to noninvasively examine brain anatomy in vivo. Structural MR examination is widely used to investigate brain morphology because of its high-contrast sensitivity and spatial resolution and because it entails no radiation exposure; the last feature is particularly important for children and adolescents [4] MR requires complete immobility for accurate imaging during examination. Deep sedation with anesthetic drugs is required to achieve this goal especially for children with ASD.

Propofol (2,6-diisoprovl-phenol) is commonly used for anesthesia and sedation. Propofol is discussed to be the best of all i.v. drugs for pediatric sedation. [5] However, its narrow therapeutic window and the vulnerability of children



to the sedative effects may lead quickly to unintended deep anesthesia with loss of protective reflexes even after small dosage increases. (6] Thus, an appropriate low dosage of propofol, which nevertheless ensures sufficient sleep for successful MRI completion, would probably minimize these adverse events. Since propofol is reported to act via gamma aminobutyric acid (GABA)A receptors [7-8] and autistic patients have a neurodevelopmental disorder that may involve the GABA inhibitory system. GABAA receptor sensitivity to propofol in autistic patients may differ from that in other cortically disabled. Our hypothesis was that children with AUT need more propofol to achieve desirable level of anesthesia as normal patients. We compared two groups of patients performing MR with propofol IV anesthesia.

#### Materials and method

During a period from may February 2015 to February 2020, 30 children with ASD and 30 others without any cerebral disorders aged from 3 to 10 years performed MRI in our institution. For all the patient we used the same anesthesia protocol. Early in the morning approximately at 8 o clock AM without feeding. After insertion of venous access with 22 or 24 G cannula the children were transferred to MR room with parents without crying. Mix propofol 1% and lidocaine 2% -2 mg/ml was administered slowly for 20 to continuous 25 sec. The initial propofol loading dose in protocol was 2,0 mg/kg but in different children the dose was higher. IV. An anesthesiologist blinded to the study protocol assessed the sedation level using a University of Michigan Sedation Scale (UMSS) (Table 1).

Table1. The University of Michigan Sedation Scale (UMSS)

| Value | Patientstate  |
|-------|---|
| 0.    | Awake andalert  |
| 1.    | Minimallysedated:tired/sleepy,<br>appropriateresponsetoverbalconversation, and/or sound                         |
| 2.    | Moderately sedated: somnolent/sleeping, easily aroused with light tactile stimulation or a simple verbalcommand |
| 3.    | Deeply sedated: deep sleep, aroused only with significant physical stimulation                                  |
| 4.    | Unarousable   |

The propofol titration is to achieve UMSS score between 2-3. After sedation, patients lay down on the MRI bed, earphones were placed in head to exclude any noises, and supplemental oxygen was given by a transparent face mask at a flow rate of 3 L/min. A soft roll was placed under the patient's shoulder to slightly extend the neck.

ECG, peripheral oxygen saturation (SpO2), were monitored continuously. Glucose 5 % solution was placed in iv access in amount 100 ml/hour. Additional propofol in dose 0,5 mg/kg was administered intermittently, in 3-minute interval. For depth of sedation, heart rate and chest movement were observed. Propofol was stopped 4 minutes before the end of the examination. After the MR examination was completed, the patients were transferred from the MR suite to the induction room, where they rejoined their parents. After full recovery, 30 minutes later the patients were discharge from hospital.

#### Results

From all autistic children 3 of them had taken sodium valproate and 2 others carbamazepine. In the control group 3 of them had taken anticonvulsant for epilepsy seizure. All the patient s characteristics and outcomes are in table 2

 Table 2. Characteristics of patients receiving intravenous general anesthesia and measure outcomes

| GroupAUT<br>(n=30) | Group II<br>(n=30)   |
|--------------------|--|
| 6.5 ±3,5           | 6,3 ±3,6   |
| 20.3 ±9,4          | $22.5\pm\!\!10$  |
| 24:6               | 22:8   |
|                    | 3  |
| $17 \pm 4.0$       | 15± 4.7  |
| 12                 | 2  |
| $7.5 \pm 4,3$      | 9 ±5,5   |
| 2,8                | 2.0  |
| 17                 | 3  |
| 3±1                | 1  |
| 4,5±0,8            | 3,6±0,7  |
|                    | GroupAUT $(n=30)$ $6.5 \pm 3,5$ $20.3 \pm 9,4$ $24:6$ $17 \pm 4.0$ $12$ $7.5 \pm 4,3$ $2,8$ $17$ $3\pm 1$ $4,5\pm 0,8$ |

Immediately after propofol injection, respiratory

events (desaturation <95% and partial airway obstruction) occurred in normal children (SpO2<95%) and no one in autistic patient patients with successful sedation. The successful sedation with UMSS  $\geq$ 2 were 2.0 mg/kg for normal children and 2,8 for AUT children. The second dose for AUT patients was after 1 minute because of movement in MR bed (in 17 of them). Between one or two additional doses of 0,5 mg/ kg were injected in 17 AUT patients and one dose for 3 normal children. No adverse events such as hypotension, bradycardia, or arrhythmia were observed during the MR examination. All scheduled MR examinations were successfully completed within 20 minutes.



# Discussion

During diagnostic procedures with sedation like anesthesia there are these goals to follow: (1) guard their patients' safety, vital signs like heart rate, respiration watching chest movement (2) no body movements, (3) return the patient to a state in which safe discharge from medical super- vision. [9]

To achieve this goal the anesthesiologist will start sedation with the lowest anesthetic dose.

The comparison between two groups showed that autistic patients require more propofol than intellectually impaired children (4,5 > 3,6). Even and number of bolus of propofol was higher in the first group. Recovery time was higher in normal children  $(7.5 \pm 4,3 < 9 \pm 5,5 \text{ min})$ .

The difference need for propofol between groups may have some relation with the change of GABAA receptor subunit distribution during brain maturation [10] because autistic patients have been reported to have abnormal GABAA receptors [11]. The serum levels of glutamate, an excitatory neurotransmitter, are increased in adult autistic patients [12] The differing response of autistic patients may also correlate with their hypersensitivity to acoustic stimuli and increased serum levels of glutamate. Autistic patients are more sensitive to noise [13] including uncomfortable sound of MR machine.

### **Conclusion**

Autistic patients require more propofol dose to achieve the desirable level of anesthesia. All anesthesiologist should be aware, in such patients with mental disorders, when using propofol anesthesia.

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