

# Asperger Syndrome: An Anesthetic Point of View: Review

## Asperger Sendromu: Anestezik Açından Bakış

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**ABSTRACT** Asperger Syndrome (AS) is an 'autistic spectrum disorder' characterized by significant difficulties in social interaction, non-verbal communication problems, and restricted, repetitive behavior. Individuals with AS differ from classic autism patients by relatively normal speech development and normal or superior intellectual abilities. A number of diseases like Fragile X syndrome, Tuberos Sclerosis, Sotos syndrome may associate this psychiatric disease. These associated problems, the medications they may be using and the features of the disease itself may be important in anesthetic procedure. A careful disease and medication history and a detailed physical examination looking for the signs of possible additional problems are the paramount principals of evaluation. Hospitalization experience and surgical procedure may be more traumatic to an AS child than their peers. We must consider their adherence to their daily schedule. It is very difficult for them to adjust to changes in their routine. We should change our routine anesthesia practice, discuss and perform the anesthetic management most appropriate for their different and delicate personalities. This will prevent us from adding difficulty to their future lives with an unpleasant hospital experience. A good communication with family and involving parents before induction and at recovery, minimizing waiting time before surgery, providing quiet areas before surgery and during recovery, and discharge home as early as possible are the most important principles of care.

**Key Words:** Autistic disorder; Asperger syndrome; anesthesia

**ÖZET** Asperger Sendromu (AS), otistik spektrum bozukluğu yelpazesinde yer alır. Sosyal etkileşimde belirgin zorluk, sözel olmayan iletişim problemleri ve kısıtlı, tekrar eden hareketlerle karakterize bir hastalıktır. AS tanısı almış hastaların klasik otizm hastalarından en belirgin farkı bu hastaların dil gelişiminin rölatif olarak korunmuş olması ve normal hatta üstün entelektüel beceriye sahip olmalarıdır. Bu psikiyatrik hastalığa Frajil X sendromu, tuberoz skleroz ve Sotos sendromu gibi bazı yandaş hastalıklar eşlik edebilir. Anestezik yaklaşımda hastaların kullandıkları ilaçlar ve yandaş hastalıkların özellikleri önem arz edebilir. Hastalık hikayesi ve kullandığı ilaçları içeren ayrıntılı bir anamnez alınması ve muhtemel eşlik eden hastalıkların özelliklerini de göz önüne alan ayrıntılı bir fizik muayene yapılması önemlidir. Bu hastaların yapılacak cerrahi işlem için yaşadıkları hastane deneyimleri yaşıtalarına göre çok daha travmatik olabilmektedir. AS tanısı almış çocuklar, günlük aktivitelerine çok sıkı bağlıdırlar ve rutin hayatlarında meydana gelen değişikliklerde ciddi adaptasyon zorluğu yaşayabilirler. Rutin anestezi pratiğimizde bu hastaların özel ve narin tabiatlarına uygun değişikliklerin yapılması ve en uygun anestezik yaklaşımların seçilmesi, hastaların ileriki hayatlarında geçirdikleri işleme bağlı ek sıkıntılar yaşamalarına engel olacaktır. Aile ile sıkı bir iletişim, induksiyon öncesi ve derlenme sırasında çocuğun ailesiyle beraber kalmasını sağlamak, ameliyat öncesi hastanede kalış süresini mümkün olduğunca kısaltmak, operasyona hazırlık aşamasında ve derlenmede çocuğu sakin ve sessiz alanlarda tutmak ve olabilecek en erken sürede taburcu etmek öne çıkan önlemler olarak sayılabilir.

**Anahtar Kelimeler:** Otistik bozukluk; Asperger sendromu; anestezi

Asperger Syndrome (AS) is first described by Hans Asperger, a Viennese pediatrician, in 1944.<sup>1</sup> 'Asperger's disorder' is the synonym for the syndrome.<sup>2</sup>

## CHARACTERISTICS

Patients diagnosed as AS, have marked difficulties in social interaction, restricted and repetitive behavior and non-verbal communication problems.<sup>2,3</sup> The main difference from other autism spectrum disorders is that individuals with Asperger syndrome have relative preservation of linguistic and cognitive development. Affected children may be normally intelligent and usually IQ is over 70.<sup>2-4</sup>

Asperger Syndrome falls under the topic of "pervasive developmental disorder" in DSM-IV-TR (The Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> edition-Text Revision).<sup>3</sup> In the very recently released DSM-5 Asperger syndrome is replaced by 'Autistic Spectrum Disorder'. This single diagnostic label now serves for all subcategories of autism.<sup>5</sup>

## INCIDENCE AND EPIDEMIOLOGY

The rate of AS in children is 7.1 in 1000 and represents a male predominance, M/F ratio is 2.3/1.<sup>6</sup> During the last decades an apparent increase in the incidence of patients diagnosed as AS has been reported.<sup>6-8</sup> It is unclear whether this is a real increase or an increased recognition and interest focused on the condition.<sup>8,9</sup> Although the pathophysiology of the disease is unknown, there may be a genetic component as the incidence of disease in first-degree relatives of AS patients is significantly greater.<sup>9,10</sup>

## ASSOCIATED MEDICAL CONDITIONS

There is a wide variety of associated clinically important diseases. The features and signs of these associated diseases may also bring the patients to the operating rooms and be important for anesthetic management.<sup>2,7-9,11</sup>

Fragile X syndrome, Tuberous Sclerosis, Sotos syndrome are some of the comorbid disorders

associated with AS.<sup>2,7</sup> Patients with Fragile X syndrome have a high incidence of mitral valve prolapse (MVP) and antibiotic prophylaxis must be considered for subacute bacterial endocarditis. Preoperative echocardiography must be considered. A more complex monitoring such as 12-lead ECG will be better to diagnose possible cardiac arrhythmias. Abnormal palate and elongated face are other important features of Fragile X syndrome that may cause difficult mask ventilation and intubation.

In patients diagnosed with Tuberous Sclerosis as a co-morbid disease hypertension, cardiac (rhabdomyomas), neurogenic tumors and bilateral polycystic renal disease must be expected and they are more prone to seizure disorder and hypertension.

Sotos syndrome is characterized with macrocrania and prominent jaw that make difficulty in mask ventilation and intubation.

Steinert's Myothonic Dystrophy, Hypomelanosis of Ito, Marfan like syndrome, Fetal Alcohol Syndrome, Neurofibromatosis, Aminoaciduria, Duchenne muscular dystrophy, Congenital nistagmus, Ligamentous laxity, Colobomas of the eye, Thyroid disease, Motor dyscontrol problems are other co-morbid diseases seen in patients with AS.<sup>2,7,12-17</sup> Iron deficiency anemia is not common.<sup>18</sup> Latif et al. reported that only two of the 44 patients with AS, had iron deficiency anemia and, among the 22 children who had their serum ferritin measured in the same group, only three were iron deficient.<sup>18</sup>

In addition to the problems listed above, many psychiatric disorders including depression.<sup>4</sup> Tics and Tourette's syndrome, attention deficit/hyperactivity disorder (ADHD), developmental coordination disorder (DCD), obsessive compulsive disorder, bipolar disorder, aggression, self injury and abnormal sensory responses may associate AS.<sup>2,7,11,19</sup> Epilepsy is also more common compared to the general population.<sup>2,7</sup>

## PREANESTHETIC EVALUATION

Patients with AS need a neuropsychological evaluation and medical work-up consisting of a

detailed history and physical examination looking for signs of possible additional problems and particular physical phenotypes of associated syndromes. Chromosomal analysis can be made for screening the possible genetic diseases. Radiological imaging, cardiac and other consultations should be considered where appropriate.<sup>2,11</sup> A careful medication history is particularly relevant since these patients may be taking medications such as SSRI, lithium and other antipsychotic, antidepressant, antiepileptic medications.<sup>19-21</sup> Some individuals with AS have severe attention problems, so it is possible that these are under central stimulant treatment.<sup>7,22,23</sup> Antipsychotics and anxiolytic/hypnotics are the other common prescribed drugs.<sup>20</sup>

## DRUG INTERACTIONS

Central stimulants eg: Methylphenidate (Ritalin®) has the potential to cause seizures and altered drug metabolism.<sup>22,23</sup> Concomitant administration of extended release methylphenidate and clonidine, which has gained popularity in anesthesia practice in a number of indications including premedication of children, is reported to have adverse cardiovascular events and/or death.<sup>22,24</sup>

Methylphenidate appears to increase central and peripheral anticholinergic effects of atropine.<sup>22,23</sup> It may be appropriate to eliminate the use of central acting anticholinergic drugs as a preoperative medication in patients being treated with anticholinergic psychoactive drugs as these patients are at greater risk of developing central anticholinergic syndrome postoperatively. AS patients may be also be using Antipsychotics and anxiolytic/hypnotics.

All these psychoactive drugs may both interfere with cardiovascular medications and interact with drugs used in anesthesia causing alterations in anesthetic requirements and they may delay recovery. Significant respiratory depression, prolonged apnea and hypotension can occur during sedation and anesthesia of patients who are concurrently receiving psychoactive

drugs. Concerns about interaction of antiepileptics with medications used in anesthesia are necessary in children having autism spectrum disorders associated with epilepsy. In this group of patients caution is also indicated if the patient is also being treated with psychoactive drugs for behavior as these drugs may also lower the convulsive seizure threshold.<sup>21,25</sup>

## SURGERY

The most frequent surgeries are adenotonsillectomy, ear tube placement and dental procedures. Need for monitored anesthesia care and sedation for radio imaging techniques are also at rise in this patient population. An unusually high incidence of surgery to the genitals of children with AS has been reported according to personal experience.<sup>11</sup> Wu et al. reported a high-incidence of developmental disabilities in hypospadias patients.<sup>26</sup> The writer of this review has met only one child diagnosed with Asperger Syndrome and this child had inverted nipples, buried penis and was undergoing grommet insertion.

## ANESTHETIC MANAGEMENT

### IN THE WAITING AREA, PATIENT PREPARATION

It may be difficult to cooperate with these patients as the disorder is characterized with a paucity of empathy, inappropriate expression, poor non-verbal communication and pedantic speech.<sup>2,3,4,9,11</sup> We must realize that the lack of communication does not mean lack of understanding. A good communication with parents and learning what the AS child likes and dislikes are the best way to understand the patient. It may be helpful to speak clearly and to make eye contact if possible. We must avoid talking with complex words and sentences, using jargon, metaphors, abbreviations, acronyms, sarcasm or imaginary vocabulary and we must avoid shouting. It may be wise to keep parents with children until they sleep, especially those without premedication, and in the recovery room.<sup>27</sup>

The most important measure to be taken is to minimize disruption to their normal daily routine. We must always consider their adherence to their daily routine. A change in their daily schedule may cause extreme anxiety and panic and the severity can be more compared to their peers. So to minimize the waiting time, surgical team may be warned to operate the patient as the first patient in the surgical list.<sup>28</sup>

During patient preparation, we must consider that these patients may have tactile sensitivity.<sup>7</sup> We must take the patients' permission for any physical contact. A particular intensity of touch, for example, the unpleasant sense of an unfamiliar dress may cause extreme sensitivity and disturbed behavior. It may be more comfortable for them to keep their own dresses on until they sleep and we better start monitoring after the patient fall to sleep.<sup>28,29</sup>

### THE CHOICE OF ANESTHESIA

The care strategy must focus on faster discharge and shorter hospital stay. We must build our plan aiming hemodynamic stability, optimal delivery of anesthetic agents, minimal adverse effects, and maximum safety to facilitate early and easy recovery. Total Intravenous Anesthesia (TIVA) can be considered as a good alternative to inhalation anesthesia both to decrease postoperative emesis and to shorten recovery and hospital stay. Bispectral index system (BIS) monitoring and Bispectral Index System-guided Total Intravenous Anesthesia optimizes the delivery of anesthetic agents providing some advantages such as earlier extubation, hemodynamic stability, early and easy recovery, faster discharge and less adverse effects.<sup>30,31</sup>

Use of regional blocks may be preferred in regard of their contribution to less postoperative pain and shorter hospital stay.<sup>32</sup> Antiemetic prophylaxis and more liberal use of antiemetics should be considered as postoperative nausea and vomiting may prolong hospital stay.

Bolus doses of preoperative crystalloid fluid may also help to minimize the risk of postoperative nausea and vomiting.<sup>33</sup>

### RECOVERY ROOM

The place the child will recover is also a matter of consideration as these patients are sensitive to sounds. Some noises may cause intense anxiety and panic.<sup>11</sup> To separate the child in the recovery or at least to put the child in a relatively quieter place covered with curtains and accompaniment of parents may help. We must carefully secure all the lines, canulas, tubes and all those should be removed as soon as possible after surgery not to cause additional distress.<sup>28,29,34,35</sup>

### PAIN MANAGEMENT

In the whole autistic spectrum patients sensory/perceptual abnormalities are most frequent in Asperger subgroup. They may show over reactivity to sound and light and under reactivity to pain. An AS child may (seem to) lack sensitivity to low levels of pain. Reduced pain sensitivity and high threshold for pain are some of the explanations for their altered pain sensation.<sup>3,36</sup> Insensitivity to pain may result from deficient mean of expression of pain and internal bodily feelings. Nevertheless, in a study assessing pain reactions to venipuncture, it was reported that patients having autism were as reactive to pain as age matched control patients.<sup>37</sup> Pain of a patient with special needs may be very difficult to assess and distinguish from the other causes of postoperative distress. Other potential causes of postoperative distress that we must consider are nausea, an unfamiliar environment and persons.

AS children as their peers may be referred to as 'less than ideal candidates' for patient controlled analgesia. Pain killer protocols with background infusion and nurse-controlled bolus doses may be a better option than PCA.<sup>34</sup>

Ketamine is a prominent drug that can be administered through almost any route and be used in the perioperative period for different purposes.<sup>34,38,39</sup> Paracetamol and NSAID can also be used for postoperative pain control.<sup>29</sup>

In conclusion, perioperative anesthetic management of a child with Asperger's syndrome may be very challenging. We specially want to

mention that Asperger syndrome is, in fact, a very severe psychiatric disease. It is very difficult for them to adjust to changes in their routine and they are very adherent to their daily schedule. Hospitalization experience and surgical procedure may be more traumatic to an AS child than their peers. AS child should be approached as a child with a severe medical condition. In addition, they should be treated with respect to their emotional state. In this point of view, AS

patients, require the greatest flexibility to the usual pattern of care. A good communication with family and involving parents and providing quiet areas before induction and during recovery, minimizing the waiting time before surgery and discharge home as early as possible are the most important principles of therapy. The adaptation of these measures to our daily practice will furnish minimum emotional trauma to both the child and the parents.

## REFERENCES

- Asperger H. Die "autistischen Psychopathen" im Kindersalter. *Arch Psychiatr Nervenkrank* 1944;117:76-136.
- Christopher G, Mary C. Asperger syndrome. *The Biology of the Autistic Syndromes*. 3<sup>rd</sup> ed. New York: Cambridge University Press; 2000. p.39-52.
- American Psychiatric Association. *Pervasive Developmental Disorders. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)*. 4<sup>th</sup> ed. Text Revision. Washington, DC: American Psychiatric Publishing; 2000. p.69-84.
- Volkmar FR, Klin A, Schultz RT, Rubin E, Bronnen R. Asperger's disorder. *Am J Psychiatry* 2000;157 (2):262-7.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Health Disorders (DSM-V)*. 5<sup>th</sup> ed. Washington, DC: American Psychiatric Publishing; 2013. p.1-991.
- Ehlers S, Gillberg C. The epidemiology of Asperger syndrome. A total population study. *J Child Psychol Psychiatry* 1993;34(8):1327-50.
- Gillberg C, Billstedt E. Autism and Asperger syndrome: coexistence with other clinical disorders. *Acta Psychiatr Scand* 2000;102(5): 321-30.
- Prior M. Is there an increase in the prevalence of autism spectrum disorders? *J Paediatr Child Health* 2003;39(2):81-2.
- Gillberg C. Asperger syndrome and high-functioning autism. *Br J Psychiatry* 1998;172:200-9.
- Volkmar FR, Klin A, Pauls D. Nosological and genetic aspects of Asperger syndrome. *J Autism Dev Disord* 1998;28(5):457-63.
- Klin A, Volkmar FR, Sparrow SS. *Asperger Syndrome*. 1<sup>st</sup> ed. New York: The Guilford Press; 2000. p.25-394.
- Blondis TA, Cook E Jr, Koza-Taylor P, Finn T. Asperger syndrome associated with Steinert's myotonic dystrophy. *Dev Med Child Neurol* 1996;38(9):840-7.
- Gillberg C. Asperger syndrome in 23 Swedish children. *Dev Med Child Neurol* 1989;31(4): 520-31.
- Gürkan CK, Hagerman RJ. Targeted treatments in autism and fragile X syndrome. *Res Autism Spectr Disord* 2012;6(4):1311-20.
- Tantam D, Evered C, Hersov L. Asperger's syndrome and ligamentous laxity. *J Am Acad Child Adolesc Psychiatry* 1990;29(6):892-6.
- Gillberg IC, Gillberg C, Kopp S. Hypothyroidism and autism spectrum disorders. *J Child Psychol Psychiatry* 1992;33(3):531-42.
- Aronson M, Hagberg B, Gillberg C. Attention deficits and autistic spectrum problems in children exposed to alcohol during gestation: a follow-up study. *Dev Med Child Neurol* 1997;39(9):583-7.
- Latif A, Heinz P, Cook R. Iron deficiency in autism and Asperger syndrome. *Autism* 2002;6(1):103-14.
- Frazier JA, Doyle R, Chiu S, Coyle JT. Treating a child with Asperger's disorder and comorbid bipolar disorder. *Am J Psychiatry* 2002;159(1):13-21.
- Langworthy-Lam KS, Aman MG, Van Bourgondien ME. Prevalence and patterns of use of psychoactive medicines in individuals with autism in the Autism Society of North Carolina. *J Child Adolesc Psychopharmacol* 2002;12(4): 311-21.
- Martin A, Scahill L, Klin A, Volkmar FR. Higher-functioning pervasive developmental disorders: rates and patterns of psychotropic drug use. *J Am Acad Child Adolesc Psychiatry* 1999;38(7):923-31.
- Lyseng-Williamson KA, Keating GM. Extended-release methylphenidate (Ritalin LA). *Drugs* 2002;62(15):2251-9; discussion 2260-1.
- Novartis Pharmaceuticals Corp. *Ritalin LA (methylphenidate HCL) product monograph*. East Hanover (NJ): Novartis Pharmaceuticals Corp; 2002. p.1-22.
- Maze M, Tranquilli W. Alpha-2 adrenoceptor agonists: defining the role in clinical anesthesia. *Anesthesiology* 1991;74(3):581-605.
- Pisani F, Oteri G, Costa C, Di Raimondo G, Di Perri R. Effects of psychotropic drugs on seizure threshold. *Drug Saf* 2002;25(2):91-110.
- Wu WH, Chuang JH, Ting YC, Lee SY, Hsieh CS. Developmental anomalies and disabilities associated with hypospadias. *J Urol* 2002; 168(1):229-32.
- Schwartz AJ. Daddy was there! *Anesthesiology* 2011;115(3):650-2.
- van der Walt JH, Moran C. An audit of perioperative management of autistic children. *Paediatr Anaesth* 2001;11(4):401-8.
- Short JA, Calder A. Anaesthesia for children with special needs, including autistic spectrum disorder. *Continuing Education in Anaesthesia, Critical Care & Pain* 2013;13(4):107-12.
- Okur S, Arıkan M, Temel G, Temel V. BIS-guided total intravenous anesthesia for orchiopexy and circumcision in a child with severe autism: A case report. *Case Rep Anesthesiol* 2012;2012:718594. doi: 10.1155/2012/718594.
- Messieha ZS, Ananda RC, Hoffman WE, Punwani IC, Koenig HM. Bispectral index system (BIS) monitoring reduces time to extubation and discharge in children requiring oral premedication and general anesthesia for outpatient dental rehabilitation. *Pediatr Dent* 2005;27(6): 500-4.

32. Petersen PL, Stjernholm P, Kristiansen VB, Torup H, Hansen EG, Mitchell AU, et al. The beneficial effect of transversus abdominis plane block after laparoscopic cholecystectomy in day-case surgery: a randomized clinical trial. *Anesth Analg* 2012;115(3):527-33.
33. Maharaj CH, Kallam SR, Malik A, Hassett P, Grady D, Laffey JG. Preoperative intravenous fluid therapy decreases postoperative nausea and pain in high risk patients. *Anesth Analg* 2005;100 (3):675-82, table of contents.
34. Rainey L, van der Walt JH. The anaesthetic management of autistic children. *Anaesth Intensive Care* 1998;26(6):682-6.
35. Karam VY, Barakat H. Perioperative management of the child with behavioral disorders. *Middle East J Anesthesiol* 2011;21(2): 191-7.
36. Gillberg C, Terenius L, Lönnerholm G. Endorphin activity in childhood psychosis. Spinal fluid levels in 24 cases. *Arch Gen Psychiatry* 1985;42(8):780-3.
37. Nader R, Oberlander TF, Chambers CT, Craig KD. Expression of pain in children with autism. *Clin J Pain* 2004;20(2):88-97.
38. Dahmani S, Michelet D, Abback PS, Wood C, Brasher C, Nivoche Y, et al. Ketamine for perioperative pain management in children: a meta-analysis of published studies. *Paediatr Anaesth* 2011;21(6):636-52.
39. Roelofse JA. The evolution of ketamine applications in children. *Paediatr Anaesth* 2010; 20(3): 240-5.