

Does Noonan Syndrome Increase Malignant Hyperthermia Susceptibility?

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Recommendations

- Review of the medical literature does not support a correlation between Noonan syndrome and malignant hyperthermia (MH) susceptibility.
- There are no known contraindications to the use of volatile anesthetics and/or triggering agents in Noonan syndrome patients.

Supporting Evidence

Literature Review:

Searches of the National Library of Medicine were completed using keywords: “malignant hyperthermia”, “Noonan syndrome”, “pediatric anesthesia complications”, “King-Denborough syndrome”. All articles pertaining to anesthetic management and perioperative complications in patients with Noonan syndrome were reviewed. Articles that delineated between Noonan syndrome and King-Denborough syndrome were also reviewed.

Background:

Noonan syndrome is often described as a “Male Turner syndrome” presenting with pterygium colli, short stature, pectus excavatum, webbed neck, down-slanting palpebral fissures and eyelid ptosis, and congenital heart disease (most commonly, pulmonary artery valvular stenosis). King-Denborough syndrome presents with a very similar phenotypic appearance and has a known link to MH susceptibility. There is a commonly held belief that patients with Noonan syndrome also have increased susceptibility to MH (Benca and Hogan, 2009).

Evidence Thus Far:

Hunter et al. (1975) reported an evaluation of the association between MH and Noonan syndrome using creatine phosphokinase (CPK) levels. King and Denborough (1972) had previously described a subgroup of King-Denborough syndrome patients with elevated CPK levels. Hunter et al. described an 11 year old boy with Noonan syndrome and consistently elevated serum CPK levels. This patient underwent 4 uneventful surgical procedures with a total of 190 minutes exposure to halothane and 1 exposure to succinylcholine. Even with the use of these triggering agents, there was no MH in this child.

Lee et al. (2001) reported a case series of 60 Noonan syndrome patients who underwent surgery to fix spinal deformities. The author describes one case of MH in the 60 patients included in the study. In this report, the diagnostic criteria for Noonan syndrome were not described, nor were any details about the purported MH event. One of the coauthors wrote in a letter to the *Lancet* (Pinsky, 1972) that “it can be argued that most patients with the syndrome are not at risk.”

Author Commentary:

The “evidence” supporting increased susceptibility to MH in patients with Noonan syndrome is extremely weak. We believe there is only one purported case (Lee, 2001), for which the details are unknown. Since the physical characteristics of Noonan syndrome are similar to King-Denborough syndrome (known to be at increased risk of MH susceptibility), we believe that it is possible that a King-Denborough syndrome child could be mislabeled as Noonan syndrome. This assumption preceded the identification of the genetic basis of these disorders. King-Denborough syndrome has been linked to a mutation on chromosome

19 located near the gene that encodes the ryanodine receptor whereas Noonan syndrome is associated with a mutation on chromosome 12.

We recently reviewed the anesthetic records (at the Children's Hospital of Philadelphia) of patients with Noonan syndrome that received triggering anesthetic agents. In 34 patients, there were no incidents of MH in 113 anesthetics. Taking this evidence into account, along with the absence of proof of a Noonan syndrome -MH link in the literature, we conclude that there is no need for MH precautions in Noonan syndrome patients.

References

1. Hunter A, Pinsky L. An evaluation of the possible association of malignant hyperpyrexia with the Noonan syndrome using serum creatine phosphokinase levels. *J Pediatr.* 1975 Mar;86(3):412-415.
2. King JO, Denborough MA, Zapf PW. Inheritance of malignant hyperpyrexia. *Lancet* 1972;1:365-370.
3. Lee CK, Chang BS, Hong YM, et al. Spinal deformities in Noonan syndrome: a clinical review of sixty cases. *J Bone Joint Surg* 2001;83-A:1495-1502.
4. Pinsky, L. The XX-XY Turner phenotype and malignant hyperthermia. *Lancet* 2: 383, 1972.
5. Benca J, Hogan K. Malignant hyperthermia, coexisting disorders, and enzymopathies: risks and management options. *Anesth Analg.* 2009 Oct;109(4):1049-53.