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Short Communication

Mitochondrial Genetic Susceptibility to Anesthetic Neurotoxicity in Venezuelan Pediatric Patients: A Call for Vigilance and Further Research

Rozo L[1]*, Franco OH[2] and Bonilla A[3]

[1]Internal Medicine Specialist, Pontifical Javeriana University, Mexican Pharmacovigilance Association General Secretary, Associate Director in Safety Operations IQVIA, Independent Consultant in Pharmacovigilance, Mexico City, Mexico

[2]Director of Department, Professor of Public Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

[3]Anesthesiology and Perioperative Medicine, Sanitas University Foundation, Anesthesiologist Clínica Reina Sofia, Bogotá DC, Colombia

More Information

***Address for correspondence:** Dr. Luis Rozo, MD, Internal Medicine Specialist, Pontifical Javeriana University, Mexican Pharmacovigilance Association General Secretary, Associate Director in Safety Operations IQVIA, Independent Consultant in Pharmacovigilance, Mexico City, Mexico, Email: luiernrozmar@gmail.com

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Abstract

Maternally inherited mitochondrial mutations may underlie severe neurological injuries and fatalities observed in Venezuelan pediatric patients following routine general anesthesia. This pharmacogenetic vulnerability notably increases neuronal sensitivity to inhalational anesthetics like sevoflurane. Our findings advocate for the avoidance of sevoflurane as an induction agent in this population, favoring safer intravenous alternatives. Given limited genomic surveillance and underreporting in Latin America, the actual prevalence and impact of this mutation remain unclear. Urgent research priorities include comprehensive genomic sequencing, metabolic profiling, and pharmacokinetic studies to clarify the mutation's role and guide anesthetic management. Immediate clinical measures should incorporate enhanced perioperative vigilance and family history assessment. To mitigate this emerging risk, strengthened transnational pharmacovigilance cooperation and capacity building in genomic diagnostics are essential. This work underscores the need for heightened awareness, diagnostic preparedness, and preventative strategies to protect genetically predisposed pediatric patients from anesthesia-related neurotoxicity.

Introduction

Several Venezuelan children, who were previously healthy, experienced severe brain injuries or died after undergoing routine surgeries with general anesthesia. These tragic events occurred despite the surgeries and anesthetic procedures appearing normal. After examining the cases, the authors believe the children may carry an inherited change in their mitochondrial DNA—a type of genetic material passed down from mothers—which affects how their cells produce energy. This inherited condition can make their brains extremely sensitive to certain anesthetic gases, particularly sevoflurane. Similar cases have been reported in Spain, suggesting that certain genetic traits may be more common in specific populations. The authors recommend avoiding this anesthetic in Venezuelan children until more is known and instead using safer alternatives. They also suggest that families be carefully evaluated for any history of related problems. Further research is urgently needed to identify the genetic cause, improve testing, and guide safer anesthesia practices. Because many countries in Latin America lack strong systems for tracking such medical problems, the full extent of the risk may not yet be known. This study calls for better international cooperation, genetic testing tools, and early reporting to prevent future harm.

Scientific comment

The reported cases of severe postoperative neurological injury and death in previously healthy Venezuelan pediatric patients following uneventful anesthesia suggest a maternally

inherited mitochondrial mutation impairing oxidative phosphorylation in neurons, leading to irreversible metabolic failure. The striking similarity to cases documented in Spain [1] strongly supports a pharmacogenetic etiology linked to a specific ethnic or geographic predisposition.

Historically, certain genetic variants cluster in distinct populations due to founder effects, migration patterns, or natural selection, for example, sickle cell disease in African descendants, G6PD deficiency in Mediterranean populations, or RYR1-related malignant hyperthermia [2-4]. The Venezuelan cases may reflect a founder-effect mitochondrial mutation, needing urgent investigation into its prevalence in Venezuela and its diaspora communities, alongside preoperative screening protocols for populations at risk.

While chance seems unlikely given the reproducible pattern, rare alternatives must be ruled out:

1. Undiagnosed inborn metabolic errors interacting with anesthetics (though ethnic homogeneity favors genetics).
2. Batch-specific drug impurities (unlikely, as only this cohort is affected).
3. Environmental or infectious cofactors (less plausible without corroborating evidence).

Current evidence prioritizes genetic causation, but further studies are critical:

- Whole-genome sequencing to identify nuclear and mitochondrial mutations.
- Metabolic profiling (blood/urine organic acids, lactate).
- Muscle biopsy (mitochondrial enzyme analysis).
- Pharmacokinetic studies in carriers.
- Population-based genetic mapping (challenging under current political constraints).

Immediate clinical recommendations:

- Avoid sevoflurane as a unique induction agent in Venezuelan pediatric patients until genetic risk is excluded.
- Use alternative intravenous agents (e.g., Propofol, ketamine, opioid) [5,6].
- Implement extended postoperative neurological monitoring and family history assessments.
- Venezuelan pediatric patients should be approached preoperatively with a high index of suspicion for underlying mitochondrial disease, warranting meticulous preoperative planning and enhanced perioperative vigilance to mitigate the risk of anesthesia-related [7].

A proactive additional pharmacovigilance measure, anesthetic management, and collaborative research are essential to mitigate risks and clarify this emerging anesthetic complication.

Given the absence of robust pharmacovigilance frameworks in many Latin American countries—including underreporting biases, limited genomic surveillance infrastructure, and lack of awareness about anesthesia-related adverse drug reactions—the true scope of this phenomenon may be underestimated. Our findings underscore the need for transnational pharmacovigilance collaboration, capacity-building in genomic diagnostics, and a culture of early reporting. We believe this correspondence will raise global awareness about the potential anesthetic risk for Venezuelan infants during emergency surgical procedures.

Conclusion

Neurological injuries and deaths among Venezuelan children following routine anesthesia suggest a maternally inherited mitochondrial mutation that heightens neuronal vulnerability to agents such as sevoflurane. To mitigate this pharmacogenetic risk, sevoflurane should be avoided for induction, with safer intravenous alternatives prioritized. Confirmatory research through genomic sequencing is urgently needed, alongside improved reporting and cross-border pharmacovigilance to uncover the scope of this threat and safeguard pediatric patients in Latin America.

Conflicts of interest

Dr. Luis Rozo and Prof Dr Oscar Franco declare no conflict of interest

Dr. Antonio J. Bonilla declares a conflict of interest, as he receives honoraria for continuing medical education activities related to regional anesthesia and postoperative pain management sponsored by BBraun.

Author´s contribution: All the authors contributed equally.

Key points:

- Genetic Basis of Anesthetic Neurotoxicity in Venezuelan Pediatric Patients
- Differential Etiologies and the Predominance of Pharmacogenetic Risk
- Immediate Clinical and Anesthetic Safety Recommendations
- Research Priorities: Genomic, Metabolic, and Pharmacokinetic Investigations

- Strengthening Pharmacovigilance and Genomic Surveillance in Latin America

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