Surveillance of Cardiac Arrhythmias in Paediatric Patients with Myotonic Dystrophy Type 1

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Objectives

- To determine the prevalence of cardiac arrhythmias within the population of DM1 patients that received care at Children's Hospital of Eastern Ontario during a 24 year time period (1990-2014).
- The occurrence and type of cardiac arrhythmia will be identified and compared with the severity of disease, indicated by the number of cytosine-thymine-guanine (CTG) triplet repeats in the patient and first degree relatives who have undergone genetic testing.

Background Information

- Myotonic dystrophy type 1 is a autosomal dominant neuromuscular disorder caused by a trinucleotide CTG repeat expansion mutation in 19q13 involving skeletal muscle, respiratory and cardiac systems.[1]
- The development of cardiac arrhythmia in the younger subset of these patients is thought to be uncommon and their relationship to the manifestation of other disease findings is unclear.[1,4,5]
- Patients with DM1 are at an increased risk of sudden cardiac death primarily from atrioventricular block.[8]
- Sinus bradycardia, tachyarrhythmias such as atrial flutter, ventricular tachycardia and atrial fibrillation, and atrio-ventricular and intraventricular conduction blocks have been reported in paediatric patients and in neonates with DM1. [1,4,5,6,7]

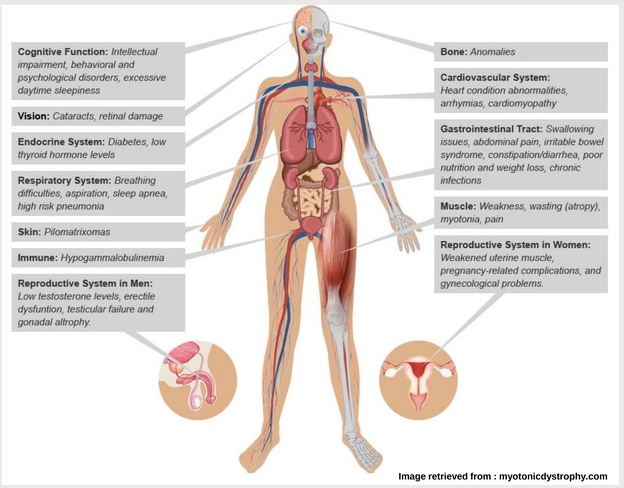

Image retrieved from : myotonicdystrophy.com

- The prevalence of DM1 ranges from 2.1-14.3 per 100 000 worldwide, but reaches 189 per 100 000 in Saguenay-Lac-Saint-Jean region in eastern Quebec.[9,10]
- The Children's Hospital of Eastern Ontario is a tertiary referral center for a geographical area which has a higher prevalence of myotonic dystrophy type 1 than the general population.

Methods: Retrospective Cohort Study

**This protocol was approved by the Research Ethics Board of the Children's Hospital of Eastern Ontario (No: 14/100X; 20140283)*

- **Population:** Paediatric patients diagnosed with DM1 between (January 1990 – May 2014) at the Children's Hospital of Eastern Ontario will be eligible for entry into the study.

Inclusion Criteria	Exclusion Criteria
1) Age 0-18 years at time of diagnosis 2) Myotonic dystrophy diagnosed via genetic testing indicating ≥ 50 CTG repeats at CHEO Jan 1990 – May 2014. 3) Patient must have underwent ECG, Holter monitor, echocardiogram or exercise stress test.	1) Incomplete medical records and/or unavailable genetic diagnosis 2) Cardiac disease not associated with a diagnosis of myotonic dystrophy type 1

- **Primary Indicators of disease:** Evidence of cardiac arrhythmia documented at least once on electrocardiogram (ECG) or Holter monitor (24h ECG).
- **Secondary Indicators of disease :** Evidence of anatomical abnormalities in the heart seen on echocardiogram.

Variables of Interest		
Demographics	**Disease Markers**	**Clinical Findings**
• Gender • Gestational Age at birth • Place of residence at birth	• Age at diagnosis / onset of disease of the patient • Number of CTG repeats in patient • Age at diagnosis in first degree relatives	• Presence of contractures • Perinatal events (intubation, perinatal resuscitation) • Skeletal Muscle Involvement (myotonia, dysphagia) • Sleep study assessment • Psycho-educational assessment

Results

Characteristics of patients with Myotonic Dystrophy (Type 1) in the CHEO cohort

Distribution of DM1 Subtypes (n=38)	
Mild DM1	1
Congenital / Infantile DM1	37

- Between 1990-2014, **38 patients** were followed at CHEO for DM1
- Genetic testing confirmed CTG repeat expansion in **35/38 (92%)**
- Median age at diagnosis was 30.5 months old
- 26 of the patients had a mother that was diagnosed with DM1
- 2 of the patients had a father diagnosed with DM1 (4 unknown)
- 10 patients had siblings that had been diagnosed with DM1

Cardiac Abnormalities

- 12 patients were found to have abnormal results on electrocardiogram (ECG)
- 14 patients were found to have an abnormal cardiac ECHO
- No patients were started on prophylactic medications during the retrospective review period

Median number of trinucleotide repeats in affected alleles	
Maternal Allele (n = 33)	1000
Paternal Allele (n=2)	500
***In two cases the paternal allele (500 repeats) had more repeats than the maternal allele.**	

Abnormalities found on ECHO cardiogram	
Atrial Septal Defect (Patent Foramen Ovale)	9
Patent Ductus Arteriosus	4
Tricuspid Regurgitation (mild)	2
Ventricular Septal defect	1
Asymmetric thickening of intraventricular septum	1
Myxomatous Mitral Valve (asymptomatic)	1

Abnormalities found through serial ECG testing	
Left Ventricular Hypertrophy +/- L-axis deviation	5
Right Ventricular Hypertrophy +/- R-axis deviation	7
1st Degree AV block	2
2nd Degree Heart Block Type 1 (WenkeBach)	1
Non specific Q wave changes	2
Non-specific T wave changes	2
Non-specifc intraventricular conduction delay (LBBB)	5
Wolff-Parkinson White	1
Supraventricular Tachycardia	1

Respiratory Disease

- 13 patients were found to have respiratory disease:
- 10 patients were reported to have an abnormal sleep study

Respiratory Disease present in the CHEO Myotonic Dystrophy Cohort	
Obstructive sleep apnea	6
Central Sleep Apnea	4
Apneic spells	5
Obstructive Airway Disease and asthma	3
Nocturnal hypoventilation	3
Other (bronchopulmonary dysplasia)	1

Developmental Milestones

- 34 of 38 patients were found to have a developmental delay and subsequent intellectual disability or learning impairment

Median Age to meeting Developmental Milestones (months)	
Sitting Independently (n=17)	10 (4-36)
Walking Independently (n=28)	18 (12-90)
First Words (n=18)	17 (9-42)
Construction of 2 word phrase (n=18)	34.5 (14-82)

Discussion and Conclusion

- Children with myotonic dystrophy have significant global developmental delay.
- Two cases of paternally-inherited of DM1 were found.
- DM1 is typically inherited from the maternal allele.
- Two significant cardiac arrhythmias were identified in 2 of 38 patients in our study (Wolf-Parkinson-White and second degree heart block)
- The occurrence of cardiac arrhythmias is less common in children and adolescents with DM1. Only 5% of our population had significant cardiac arrhythmias.
- Adult patients with myotonic dystrophy are much more likely to demonstrate cardiac arrhythmia (20-40%). 30% of mortality in adults with DM1 are due to a cardiac cause.[11]
- Current surveillance for cardiac arrhythmia in this population closely follows the standard of practice in adult patients, but no such standard has been established in paediatric care.

Key Findings on Myotonic Dystrophy Type 1 in Paediatric Patients

- Clinicians should be aware of an increased prevalence of conduction abnormalities in children with DM1. Cardiac complaints should illicit increased awareness. (Level C)
- Children with DM1 are more likely to have intellectual disability. Increased support for education and development should be initiated (level C)

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