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Recommendations of an expert group for cardiac assessment of non-dystrophic myotonic adult patients treated with mexiletine

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Introduction

- Mexiletine (NaMuscla™) is indicated for the symptomatic treatment of myotonia in adults with non-dystrophic myotonia (NDM).[1]
- A cardiac assessment is required, as mexiletine may have a pro-arrhythmic effect.[2]
- Long-term safety data supporting use of mexiletine in patients with NDM, combined with the extensive clinical experience of an expert group, resulted in creation of an algorithm for cardiac monitoring of NDM patients treated with mexiletine.[1,2]

Methods

- To define the treatment algorithm, several workshops were set up with experts including 3 neurologists and 5 cardiologists from different French neuromuscular reference centres.
- These workshops aimed to define the screening and surveillance tools required to avoid cardiac events in mexiletine-treated patients.
- The recommendations are based on the summary of product characteristics (SmPC), a review of the literature on the safety of mexiletine-treated NDM patients, and the combined expertise of the authors.

Results

- The expert group concluded that the cardiac safety profile of mexiletine in NDM patients appears similar to that of the general population.
- Therefore, NDM patients treated with mexiletine should be monitored as any patient treated with a class 1b anti-arrhythmic.
- Cardiac assessment should be performed before initiation of mexiletine and at least every 2 years under treatment (see graphic).

Conclusions

- An algorithm for cardiac safety monitoring in patients with NDM treated with mexiletine has been developed to assist the neurologists and cardiologists managing these patients.
- We hope that this algorithm will provide a clear guide for healthcare teams who are managing patients with myotonia using mexiletine.

References

1. NaMuscla™ Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/namuscla-epar-product-information_en.pdf.
2. Singh S, et al. Mexiletine. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. https://pubmed.ncbi.nlm.nih.gov/30085587/

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Mexiletine prescription algorithm in patients with non-dystrophic myotonia, NDM

1. Before initiation: Evaluation by a cardiologist
Screening for cardiac contraindications to mexiletine prescription according to the summary of product characteristics, SmPC

Systematic investigations
- ✓ ECG
- ✓ Echocardiography

Optional investigations
Depending on medical history (similar to general population without genetic disease) and at the physician's discretion

Medical history
- Myocardial infarction (acute/past)
- Angina/non-revascularized coronary artery disease[a]
- High-grade atrioventricular block without permanent pacing[b]
- Cardiac disease-modifying therapy[c]: drugs that may cause torsades de pointes
- Ventricular tachycardia (VT)[d]
- Atrial fibrillation*, atrial flutter

NO

Electrocardiogram (ECG)
- Sinus bradycardia (heart rate <50 beats per min)
- First-degree atrioventricular block with PR duration ≥240 ms
- Bundle branch block (QRS duration ≥120 ms)
- Bifascicular/trifascicular block
- High-degree atrioventricular block (Mobitz II or complete block)
- Necrosis Q wave, repolarization abnormalities

≥1 present → NO MEXILETINE

NO

Echocardiography
- Left ventricular ejection fraction <50%
- Segmental wall motion abnormality

NO

START MEXILETINE

Control after treatment initiation (Private practice or hospital)
ECG at the maximum effective dose, usually 3 weeks after first dose

CONTINUE MEXILETINE

2. Long-term follow-up

New cardiac symptom
(e.g. chest pain, unusual palpitations, syncope)

YES → If modifications observed, seek cardiologist's opinion (possible contraindication)

NO

ECG control by neurologist or cardiologist every 2 years or more frequently,[e] at physician's discretion

Abnormalities or modified → If modifications observed, seek cardiologist's opinion (possible contraindication)

CONTINUE MEXILETINE → Systematic cardiology consultation every 5 years
Cardiovascular risk assessment
Screening for coronary artery disease[f]

[a] Revascularized coronary disease without sequelae of infarction is not an absolute contraindication
[b] For patients with high-grade atrioventricular block with a device, concomitant presence of ventricular rhythm disorders must be checked
[c] Mexiletine SmPC: http://www.medicines.org.uk/emc/product/13304/smpc
[d] Sustained VT is an absolute contraindication. For non-sustained VT, the decision can take into account the mode of diagnosis (pacemaker or Holter), symptom presence and favouring factors (hydroelectrolytic disturbances to be normalized if possible)
[e] Mexiletine SmPC recommends ECG + echocardiography every year in cases with known cardiac abnormality, or more frequently if deemed necessary
[f] According to 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: https://doi.org/10.1093/eurheartj/ehz425

*Original indication for mexiletine as an anti-arrhythmic but contraindicated in NaMuscla SmPC

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