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SUMMARY WITH CRITICAL APPRAISAL

Video-Oculography for the Diagnosis of Ocular Myasthenia Gravis: A Review of Diagnostic Accuracy, Cost-Effectiveness, and Guidelines

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Context and Policy Issues

Myasthenia gravis is an autoimmune disorder characterized by muscle weakness, as a result of neuromuscular transmission impairment;[1] the fluctuating muscle weakness generally occurs in voluntary skeletal muscles, and varies in severity between patients.[2] The prevalence is estimated to be 77.7 per million persons according to a meta-analysis of epidemiologic studies published between 1950 and 2017 worldwide.[1] This makes myasthenia gravis the most common neuromuscular transmission disorder.[2]

Ocular myasthenia gravis occurs when the extrinsic ocular muscles are involved.[2] Ocular muscle weakness can cause symptoms such as ptosis (dropping of the upper eyelid) or binocular diplopia (double vision).[3] Ocular symptoms are common in those with myasthenia gravis.[2] Some patients with myasthenia gravis have only ocular symptoms.[2] However, for more than 80% of the those with ocular symptoms only at the onset of myasthenia gravis, weakness spreads to other muscle groups at some point.[2] One retrospective cohort study has indicated that early intervention for ocular myasthenia gravis was associated with the decrease in the frequencies of ocular symptoms and the delay or potential prevention of the occurrence of generalized myasthenia gravis.[4]

The diagnosis of ocular myasthenia gravis is not an easy task when ptosis is the only ophthalmic symptom.[3] A series of tests can be used to diagnose ocular myasthenia gravis, such as serum antibodies, the tensilon test, and electromyography (EMG).[5] These exams are not always able to identify the patients with ocular myasthenia gravis. The detection of antibodies to muscle acetylcholine receptors or the muscle-specific receptor tyrosine kinase in the serum can be useful in identifying cases,[1] but antibodies do not present in all patients, rendering the antibody test ineffective for some.[3] The tensilon test has a sensitivity around 80% and uses edrophonium, a drug that blocks acetylcholinesterase and reverse muscle weakness temporarily.[3] However, edrophonium can cause life-threatening side effects, such as hypotension and bradycardia.[3] EMG uses repetitive nerve stimulations to detect decreasing amplitude with repetitive stimulation.[3] Single-fibre EMG is used to detect variability between individual muscle fibres within a motor unit.[3] By measuring the jitter of the muscle fibres, single-fibre EMG can determine whether acetylcholine release is within normal ranges and the neuromuscular transmission functions well.[6] One major disadvantage of EMG is that it requires electrodes inserted in the target muscles.[3] The invasive nature of this test can prevent patients from being examined.[3]

Recently, video-oculography, a non-invasive test that tracks eye movements using video cameras, has been used in medicine for a few indications.[7] There is some evidence showing that eye-tracking technology, such as video-oculography, can be used for the diagnosis of ocular myasthenia gravis.[8] With the potential to avoid side effects of invasive procedures and prevent generalized myasthenia gravis, there is a need to review the diagnostic accuracy and cost-effectiveness of video-oculography for the detection of ocular myasthenia gravis, as well as the clinical guidelines regarding the use of eye-movement analysis (video-oculography) for suspected myasthenia gravis.

Research Questions

1. What is the comparative diagnostic accuracy of eye-movement analysis using video-oculography versus single fibre electromyography (EMG) for detection of ocular myasthenia gravis?

2. What is the comparative cost-effectiveness of eye-movement analysis using video-oculography versus single fibre EMG for detection of ocular myasthenia gravis?
3. What are the evidence based guidelines regarding the use of eye-movement analysis using video-oculography for suspected ocular myasthenia gravis?

Key Findings

No relevant evidence regarding the comparative diagnostic accuracy or cost-effectiveness of video-oculography versus single fibre electromyography for the detection of ocular myasthenia gravis was identified. There were no evidence-based guidelines providing recommendations on the use of video-oculography for the detection of ocular myasthenia gravis. Further research on the use of video-oculography for the diagnosis of ocular myasthenia gravis, compared with current methods, such as electromyography, may help to reduce the uncertainty regarding its use in clinical practice.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE via Ovid, EMBASE via Ovid, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were video-oculography and myasthenia gravis. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and May 27, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with suspected ocular myasthenia gravis
Intervention	Eye-movement analysis using video-oculography
Comparator	Single fibre electromyography (EMG)
Outcomes	RQ1: Diagnostic accuracy (e.g., velocity, amplitude, sustained gaze, ptosis, diplopia in primary and downward gaze) RQ2: Cost-effectiveness RQ3: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, and guidelines

EMG = electromyography; RQ = research question

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2009. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

No relevant evidence regarding the video-oculography for the detection of ocular myasthenia gravis was identified; therefore, critical appraisal was not conducted.

Summary of Evidence

Quantity of Research Available

A total of 323 citations were identified in the literature search. Following screening of titles and abstracts, 296 citations were excluded and 27 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publications were retrieved from the grey literature search for full text review. Of these potentially relevant articles, 27 publications were excluded for various reasons, and no publications met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA[9] flowchart of the study selection.

References of potential interest are provided in Appendix 2.

Summary of Findings

Diagnostic accuracy of video-oculography

No relevant evidence regarding the comparative diagnostic accuracy of video-oculography compared with EMG for the detection of ocular myasthenia gravis was identified; therefore, no summary can be provided.

Cost-Effectiveness of video-oculography

No relevant economic evaluations regarding the use of video-oculography for the detection of ocular myasthenia gravis compared with EMG were identified; therefore, no summary can be provided.

Guidelines

No relevant evidence-based guidelines regarding the use of video-oculography for the detection of ocular myasthenia gravis were identified; therefore, no summary can be provided.

Limitations

One major limitation was that there was no relevant evidence regarding the video-oculography for the detection of ocular myasthenia gravis identified. Video oculography remains infrequently used in the diagnosis of medical conditions.[7] There was one clinical study and one case series that were identified to use eye-tracking technology in patients with myasthenia gravis, but studies did not compare with EMG.[8]

Conclusions and Implications for Decision or Policy Making

No relevant evidence regarding the use of video-oculography for the detection of ocular myasthenia gravis compared with EMG was identified. Based on the search, eye-tracking technology was studied only in two primary studies that recruited seven and two patients with myasthenia gravis[8,10] In these studies, EMG was not used as comparison.[8,10] No relevant evidence-based guidelines providing recommendations on the use of video-oculography for the detection of ocular myasthenia gravis were identified.

The diagnostic accuracy and cost-effectiveness of video-oculography for the detection of ocular myasthenia gravis remains unclear. Further clinical trials on the use of video-oculography for the diagnosis of ocular myasthenia gravis, compared with current methods, such as electromyography, may help to decrease the uncertainty in clinical practice.

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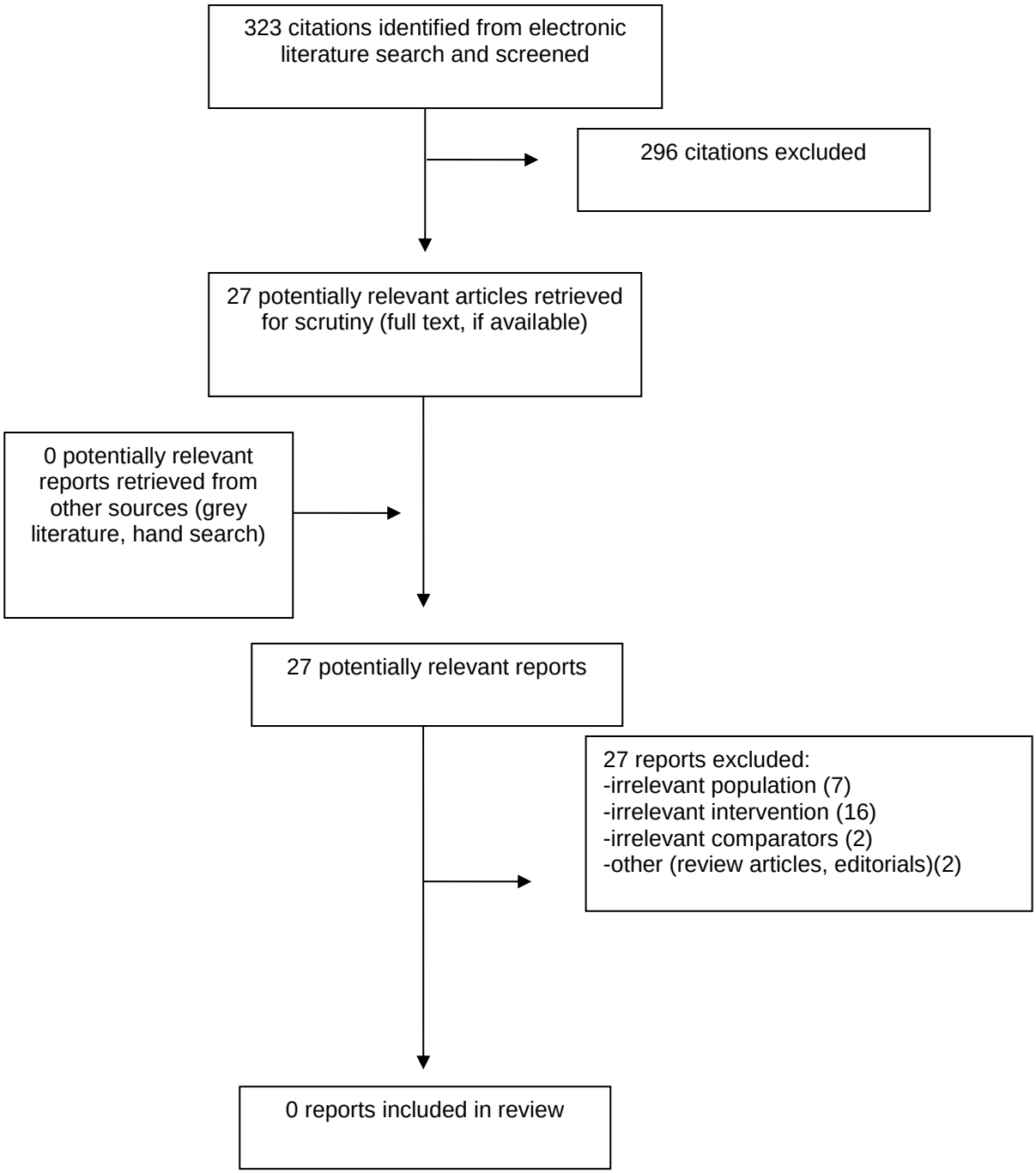
Appendix 1: Selection of Included Studies



Appendix 2: Additional References of Potential Interest

Recommendations without Systematic Methodology

Evoli A, Antonini G, Antozzi C, et al. Italian recommendations for the diagnosis and treatment of myasthenia gravis. *Neurol Sci.* 2019;40(6):1111-1124.

Reviews without systematic literature searches

Azri M, Young S, Lin H, Tan C, Yang Z. Diagnosis of Ocular Myasthenia Gravis by means of tracking eye parameters. *Conference Proceedings: Annual International Conference of the IEEE Engineering in Medicine & Biology Society.* 2014;2014:1460-1464.