Antibiotic neuromuscular junction myasthenic mimetics

Maartje G Huijbers and colleagues[1] are to be commended for their instructive and comprehensive Review of autoimmune neuromuscular junction disease. However, they do not discuss antibiotics that mimic some of the mechanisms of autoimmune neuromuscular junction disease and can therefore exacerbate the clinical features of neuromuscular myasthenic syndromes. International consensus guidance on the management of myasthenia gravis[2] advises against the use of aminoglycosides, macrolides, and fluoroquinolones in people with myasthenia gravis and advocates for raising awareness of the potentially serious adverse reactions of these antibiotics in patients with this autoimmune neuromuscular myasthenic syndrome. However, there is little guidance on antibiotic contraindications in Lambert-Eaton myasthenic syndrome. Aminoglycoside-mediated blockade of voltage-gated calcium channels essentially mimics the pathological mechanism of Lambert-Eaton myasthenic syndrome. Hence, aminoglycosides should, at least theoretically, be avoided in patients with this condition.

The aminoglycoside gentamicin is routinely used in common operations, such as joint arthroplasty or any trauma surgery when metalware is implanted.[3] For lower limb arthroplasty, in particular for total hip and knee replacements, gentamicin-loaded bone cement is used to fix a prosthesis to the bone. This cement elutes gentamicin into the surrounding tissues and systemic circulation. There is no explicit guidance on the use of antibiotic-laden prosthetics in people with myasthenia gravis or Lambert-Eaton myasthenic syndrome. However, bone cement manufacturers do advise caution when using their products in patients with various neuromuscular conditions, with myasthenia gravis specifically mentioned.[4] Patients with myasthenia gravis could account for up to 0·1% of all patients undergoing knee or hip arthroplasty.[5] Given that more than 1·5 million arthroplasty procedures are done annually in the USA,[5] the number of patients in whom there is potential for exacerbation of clinical symptoms is not negligible.

β blockers are another drug class that is strongly linked to exacerbation of myasthenic symptoms.[2] Because of the range of drug classes associated with exacerbation of clinical features of autoimmune neuromuscular myasthenic syndromes, antibiotic and drug interactions with myasthenia gravis and Lambert-Eaton myasthenic syndrome are relevant and can be important considerations at the time of medical and surgical treatment of patients with autoimmune myasthenic syndromes.

We declare no competing interests.

*Chika Edward Uzoigwe, Frederick Campbell-Jones
chika@doctors.org.uk

Medicine and Surgery, Harcourt House, Sheffield S10 1DG, UK (CEU); Department of Anaesthesia, Glenfield Hospital, University Hospitals of Leicester NHS Trust, Leicester, UK (FC-J)

1 Huijbers MG, Marx A, Plomp JJ, Le Panse R, Phillips WD. Advances in the understanding of disease mechanisms of autoimmune neuromuscular junction disorders. *Lancet Neurol* 2022; **21:** 163–75.
2 Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology* 2021; **96:** 114–22.
3 NICE. Antibacterials, use for prophylaxis. https://bnf.nice.org.uk/treatment-summaries/antibacterials-use-for-prophylaxis/#orthopaedic-surgery-antibacterial-prophylaxis (accessed June 11, 2022).
4 Heraeus Medical. High-viscosity, radiopaque ready to mix bone cement containing gentamicin. Wehrheim: Heraeus Medical, 2020. https://www.heraeus.com/media/media/hme/doc_hme/products_us/PALACOS_RG_pro_IFU_US.pdf (accessed June 11, 2022).
5 Sherman WF, Wu VJ, Ofa SA, Ross BJ, Savage-Elliott ID, Sanchez FL. Increased rate of complications in myasthenia gravis patients following hip and knee arthroplasty: a nationwide database study in the PearlDiver Database on 257 707 patients. *Acta Orthop* 2021; **92:** 176–81.

Authors' reply

Chika E Uzoigwe and Frederick Campbell-Jones[1] highlight an important issue in medical practice for managing patients with neuromuscular autoimmune disease, and their remarks are a useful addition to our Review in the Series. Indeed, the use of particular antibiotics, muscle relaxants, and other drugs are known to worsen the disease in patients with myasthenia gravis or Lambert-Eaton myasthenic syndrome. Uzoigwe and Campbell-Jones mention gentamycin-loaded bone cement as a possible under-recognised source among these aggravating drugs.

Many drugs are associated with worsening of signs and symptoms in patients with myasthenia gravis or Lambert-Eaton myasthenic syndrome. However, reported associations do not necessarily mean these drugs should never be prescribed for patients with these conditions. Reports of disease worsening are often rare or might represent a coincidental association. Clinical judgment and the cost-benefit ratio of a drug should be considered when that drug is deemed important for the treatment of a patient with myasthenia gravis or Lambert-Eaton myasthenic syndrome.[2]

See appendix for declarations of interest.

Maartje G Huijbers, Anna Punga, Jan J Verschuuren

1 Uzoigwe CE, Campbell-Jones F. Antibiotic neuromuscular junction myasthenic mimetics. *Lancet Neurol* 2022; **21:** 681.
2 Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology* 2021; **96:** 114–22.

Exercise training and neuroprotection in multiple sclerosis

We read with interest the Correspondence by Brian M Sandroff and colleagues[1] on exercise training in multiple sclerosis, but believe that the rationale behind this

See **Online** for appendix