EVOKE Letter

The EVOKE trial[1] comes at an interesting time with a 2020 systematic review[2] reporting that spinal cord stimulation typically provides 1 point greater pain reduction on a 0-10 pain scale than placebo. By any measure a treatment benefit of 1 point is quite modest, and the benefit is also uncertain as the systematic review only found 8 trials with a total of 185 participants.

EVOKE is therefore a significant trial as it enrolled 134 patients; but unfortunately the current publication leaves important questions unanswered. While the title suggests answers to questions about long term safety and efficacy it answers neither question sufficiently. As there was no placebo group it cannot establish efficacy and because outcomes were confined to 12 months it is unclear if this treatment is effective and safe in the long term. Some caution with spinal cord stimulators is wise given a recent report from Australia's Therapeutic Goods Administration.[3] The report catalogues over 500 incidents associated with spinal cord stimulators in Australia. These include health problems such as infection, wound breakdown, seizure and pulmonary embolus as well hardware issues such as lead and device failure. In a number of cases devices needed to be revised or replaced and sometimes removed completely due to lack of efficacy. So understanding how the participants in EVOKE fared in the long term is an important issue not addressed in the current publication.

There are also some concerns about aspects of the conduct and reporting of EVOKE. The claim for blinding of participants is questionable because the instructions given to participants during consent clearly outlined the nature of the two different stimulation modes and the results on page 8 and Figure S4 show that participants in the two groups behaved differently in adjusting the stimulation. It is important to recognise this because Duarte et al[2], in their systematic review, suggest that the magnitude of treatment effect varies across trials and, in part, depends on the quality of patient blinding. There is also some concern about the accuracy of the reporting of the results. For example, the authors report that for secondary outcomes the improvements were generally greater in the closed loop group but if you check the online appendix that benefit was only statistically significant for the minority (4 of 16 – derived from Table S1).

EVOKE is a welcome trial but it does not tell us sufficiently about efficacy, in the short or long term and safety in the long term of evoked compound action potential (ECAP) controlled closed-loop spinal cord stimulation. A further important factor is that of cost-effectiveness which is not reported in the publication. So, as the authors conclude, further investigation is warranted but conclusions about efficacy and long term safety should not be drawn at this stage.

References

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2. Duarte RV, Nevitt S, McNicol E, et al. Systematic review and meta-analysis of placebo/sham controlled randomised trials of spinal cord stimulation for neuropathic pain. *Pain* 2020; **161**(1): 24-35.

3. Therapeutic Goods Administration (Australia). A document relating to the registration and adverse events for spinal cord stimulators https://www.tga.gov.au/documents-released-under-section-11c-freedom-information-act-1982-jul-2018-jun-2019. 2019.

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