Technoleg Iechyd Cymru
Health Technology Wales

HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 044 (October 2022)

Photobiomodulation for the prevention or treatment of oral mucositis in people receiving cancer treatment

HTW Guidance:

Photobiomodulation for the prevention or treatment of oral mucositis in people receiving cancer treatment shows promise, but the evidence is insufficient to support routine adoption.

The use of low-level laser photobiomodulation reduces the incidence of oral mucositis compared to sham or standard care, but there is limited evidence on the clinical effectiveness of light-emitting diode (LED) photobiomodulation.

HTW economic analyses show that laser photobiomodulation is not cost effective compared to standard care. The main driver behind the relative cost effectiveness analysis is staffing costs. Therefore, routine adoption of laser photobiomodulation cannot be supported.

Further research is recommended to establish the clinical effectiveness of LED photobiomodulation.

Why did Health Technology Wales (HTW) appraise this topic?

Oral mucositis is a common side effect of cancer treatment, and can often have a severe impact on an individual's quality of life. Symptoms can range from mild to severe and include minor discomfort, speech difficulties, ulceration, severe pain and inability to eat solid food. Current treatment options to manage oral mucositis included oral hygiene, good hydration, avoiding irritating food and drink, and painkillers. In cases of subsequent infection, antibiotics may also be used. Photobiomodulation is a non-invasive hand-held technology that aims to prevent or treat oral mucositis by stimulating healing, decreasing inflammation and increasing cellular metabolism. At the time of this guidance, there are two types of photobiomodulation: low-level laser photobiomodulation and light emitting diode (LED) photobiomodulation.

The status of HTW guidance is that NHS Wales should adopt this guidance or justify why it has not been followed. HTW will evaluate the impact of its guidance.

Evidence Summary

Refer to Evidence Appraisal Report 044 (EAR 044) for a full report of the evidence supporting this Guidance.

HTW identified and summarised evidence for the following question: What is the clinical and cost effectiveness of photobiomodulation to prevent or treat oral mucositis in people receiving cancer treatment?

One systematic review and meta-analysis was identified that included 29 randomised controlled trials (RCTs) comparing photobiomodulation with either control, sham or standard care. HTW also identified 6 additional RCTs that were published after the systematic review was undertaken, and one RCT follow-up. Most studies evaluated laser photobiomodulation; one RCT compared LED photobiomodulation with sham control. Overall, evidence showed that preventative laser photobiomodulation can reduce the risk of severe oral mucositis, reduce the overall mean grade of oral mucositis, and reduce pain (as measured using a visual analogue scale). Using laser photobiomodulation to treat existing cases of oral mucositis did not reduce the remission rates of severe oral mucositis (measured by the number of patients who still had severe oral mucositis after seven days of treatment), but it did reduce the overall duration of having severe oral mucositis.

No health economic studies were included in the Evidence Appraisal report 044, this was due to the available evidence being undertaken in a non-comparable non-OECD country. We developed a cost utility analysis, from the Welsh NHS perspective, which compared the delivery of laser photobiomodulation as a preventative intervention compared to standard care. Costs were driven by high staffing time requirements. Laser photobiomodulation was assessed as being clinically beneficial and cost incurring. The resulting incremental cost effectiveness ratio (ICER) per quality-adjusted life-year (QALY) was £33,334. This is above the commonly accepted threshold of £20,000 per QALY, indicating that the intervention is not cost effective.

LED photobiomodulation was assessed as being a cheaper option to deliver compared to laser photobiomodulation due to the shorter session duration and ease of delivery. In the absence of sufficient clinical evidence, no conclusions were arrived at for LED photobiomodulation.

The appropriate mechanism for patient engagement was determined and the patient perspective was considered where possible. For this topic, HTW received the following:

- A submission from the Swallows Charity organisation on the impact of oral mucositis on patients, and the potential impact of receiving photobiomodulation.
- Five responses to a questionnaire designed in collaboration with the North Wales Cancer Forum to gain the views, experiences and opinions of people who have had or currently have oral mucositis.

Appraisal Panel considerations

- The Appraisal Panel heard patient evidence on the debilitating impact that oral mucositis can have on people who are undergoing cancer treatment. Patient organisations and HTW public partners highlighted the severe discomfort and pain experienced by people with oral mucositis, as well as the impact on wellbeing and mental health. In severe cases, oral mucositis stops people from being able to eat, sleep and can impact on their relationships with friends and family. Patients who had experienced photobiomodulation treatment reported positive benefits and a reduction in oral mucositis symptoms.

- The Appraisal Panel considered the clinical evidence presented and heard from clinical experts about the potential benefits of low-level laser photobiomodulation and light-emitting diode (LED) photobiomodulation. The majority of randomised controlled trials (RCTs) assessed low-level laser photobiomodulation and only a single RCT was undertaken looking at LED photobiomodulation.

- The Appraisal Panel sought input from experts on the differences in the use of low-level laser and LED photobiomodulation and their implementation. The clinical experts reported that LED photobiomodulation does not require the same level of staff and safety requirements, making this option more feasible to implement in practice. The Appraisal Panel asked experts whether it would be appropriate to extrapolate the evidence on laser photobiomodulation to LED photobiomodulation. The experts advised that this would not be appropriate, due to the differences in the devices, such as wavelength emission and delivery. The Appraisal Panel concluded, therefore, that it would not be appropriate to apply the more substantial evidence for laser photobiomodulation to the use of LED photobiomodulation.

- The Appraisal Panel noted that there is a lack of evidence of positive long-term outcomes associated with treatment with photobiomodulation in preventing or treating mucositis following cancer treatment.

- The Appraisal Panel concluded that the clinical evidence demonstrates a clear benefit of laser photobiomodulation, but that the effectiveness of LED photobiomodulation is less certain due to a lack of RCTs comparing LED photobiomodulation with standard care.

- Regarding cost effectiveness, the Appraisal Panel considered a de novo cost-effectiveness analysis that was undertaken by HTW that compared preventative laser photobiomodulation to standard care. The results showed that laser photobiomodulation is more effective, but more costly than standard care. The Panel noted that staff resource was the primary driver behind these results, due to the additional expertise and safety requirements needed to implement a laser provision. The Panel noted that the most plausible estimated ICER is £33,334 and therefore concluded that laser photobiomodulation is not cost effective.

- The Panel also considered de novo cost effectiveness evidence comparing preventative LED photobiomodulation to standard care. Applying outcome clinical evidence from the use of laser photobiomodulation, the analysis showed that LED has the potential to be cost effective. This is largely due to the reduced staffing and safety implications of using LED compared with laser. The Appraisal Panel concluded, however, that the clinical effectiveness evidence for low level laser was not generalisable to LED and therefore drawing cost-effectiveness conclusions for LED was inappropriate.

- Overall, the Appraisal Panel concluded that while laser photobiomodulation is clinically effective, it is not cost effective. In addition, while there are practical benefits associated with using LED photobiomodulation rather than laser photobiomodulation, there is a lack of clinical evidence to support LED photobiomodulation.

- The HTW Appraisal Panel recommends further research to:

    - establish the relative clinical and cost effectiveness of LED photobiomodulation for the prevention or treatment of mucositis following cancer treatment.
    - to determine the optimal treatment protocols for the use of photobiomodulation.
    - to explore the usability of LED probes in clinical practice both for extra-oral and intra-oral usage.
    - establish the staffing and implementation requirements of using laser or LED photobiomodulation in clinical practice in Wales.

Responsibilities for consideration of this Guidance

Health Technology Wales (HTW) was established by Ministerial recommendation[1,2] to support a strategic, national approach to the identification, appraisal and adoption of non-medicine health technologies into health and care settings. The HTW Appraisal Panel comprises senior representation from all Welsh boards with delegated authority to produce guidance 'from NHS Wales, for NHS Wales'. The status of HTW guidance is 'adopt or justify'. There is an expectation from Welsh Government that HTW guidance is implemented with adoption regularly audited by HTW.[3]

The guidance in this document is intended to assist Welsh care system decision makers to make evidence-informed decisions when determining the place of health technologies and thereby improve the quality of care services.

The content of this HTW guidance was based upon the evidence and factors available at the time of publication. An international evidence base was reviewed and external topic experts and HTW committee members consulted to contextualise available evidence to Wales. Readers are asked to consider the generalisability of the evidence reviewed to NHS Wales and that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. It is acknowledged that evidence constitutes only one of the sources needed for decision making and planning.

This guidance does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

No part of this guidance may be used without the whole of the guidance being quoted in full. This guidance represents the view of HTW at the date noted. HTW guidance is not routinely updated. It may, however, be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the guidance given.

Standard operating procedures outlining HTW's evidence review methods and framework for producing its guidance are available from the HTW website.

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Declarations of interest were sought from all reviewers. All contributions from reviewers were considered by HTW's Assessment Group. However, reviewers had no role in authorship or editorial control and the views expressed are those of Health Technology Wales.

Chair, Health Technology Wales Appraisal Panel

1. National Assembly for Wales, Health and Social Care Committee. Access to medical technologies in Wales. December 2014.
2. Response to Recommendations from the Health & Social Care Committee: Inquiry into Access to Medical Technologies in Wales. February 2015.
3. Gething, V. Letter to all Health Board Chairs re Funding for Sacral Nerve Stimulation in Wales. VG_01655_17. September 2017.