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Background

Musculoskeletal diseases comprise of several conditions characterized by pain, limitation in mobility and functional ability, with substantial impact on quality of life, mental well-being, and impose considerable cost on individual, health system as well as disability insurance. Worldwide burden of musculoskeletal disorders increased from 2000 to 2015 as quantified using daily adjusted life years (DALYs), with median proportion of years lived with disability (YLDs) due to musculoskeletal disorders was 11.8% in 2000 to 13.5% in 2015. The largest contribution to the YLDs among the musculoskeletal disorders is due to back and neck pain, followed by osteoarthritis. Back pain is the most common presentation of spinal pathologies, affecting patient health and quality of life. It is expected between 60 and 80% of the world population will experience LBP during lifetime, with 65% being recurrent and longstanding episodes. Approximately one in five patients with back pain will require intervention, commonly spinal fusion, with annual estimated cost of nine billion USD.

Pharmaceutical options in musculoskeletal disorders are often associated with adverse effects, whereas some interventions were invasive associated with complication such as migration (for implanted device) and infection. Though intervention such as spinal fusion following spinal pathologies can improve quality of life, outcomes may be negatively impacted by complication such as non-union and hardware failure. Hence, there is a demand for intervention free of side effects and less invasive. Pulsed electromagnetic field (PEMF) therapy provided an alternative approach to treating bone and joint diseases since 1970s, especially for elderly or those who are unable to undergo surgery or take medications. Pulsed electromagnetic fields devices are usually applied directly on the targeted body or using full body therapy system. The PEMF was reported as a non-invasive and non-thermal approach to accelerate the repair of delayed and non-union fractures and chronic wounds, reduced pain and inflammation. There is increasing interest in the application of magnetic and electromagnetic fields for therapeutic purposes. The largest interest is in its potential in the alleviation of pain. The National Institutes of Health estimated that more than 48 million Americans suffer chronic pain that resulted in a $65 billion loss of productivity and over $100 billion spent on pain care.

Despite the inconsistencies in effectiveness and safety of this procedure, it is being used as a modality of treatment for a wide range of applications including to heal damaged tissue and bone, to relieve injury related pain, to stimulate organs, to treat depression, diabetes, as well as used for skin lifting and skin rejuvenation, as advertised by one of a wellness center in Sibu, Sarawak. This technology review was conducted following a request from the Private Medical Practice Control Unit, Sarawak State Health Department to provide the current best scientific evidence on effectiveness, safety and cost-effectiveness of PEMF to heal damaged tissue and bone, to relieve pain, to stimulate organs, to treat depression, to treat diabetes, as well as for skin lifting and skin rejuvenation.

Objective

The objective of this technology review is to assess the effectiveness, safety and cost-effectiveness of PEMF to heal damaged tissue and bone, to relieve pain, to stimulate organs, to treat depression, to treat

diabetes, as well as for skin lifting and skin rejuvenation.

Methods

A systematic review was conducted. Studies were identified by searching electronic databases. Search strategy was developed by the main author and *Information Specialist*. The following databases were searched through the Ovid interface: MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to present. EBM Reviews-Cochrane Database of Systematic Reviews (2005 to March 2021), EBM Reviews-Cochrane Central Register of Controlled Trials (March 2021), EBM Reviews – Database of Abstracts of Review of Effects (1st Quarter 2021), EBM Reviews-Health Technology Assessment (1st Quarter 2021), EBM Reviews-NHS Economic Evaluation Database (1st Quarter 2021). Parallel searches were run in PubMed. No limits were applied to the search. The last search was run on 1 March 2021. Additional articles were identified from reviewing the references of retrieved articles. Among the tools used to assess the risk of bias and methodological quality of the included studies are the Cochrane Risk of Bias (ROB)2 and Critical Appraisal Skills Programme (CASP) checklist. Level of evidence of included articles were based on guidelines from the US/Canadian Preventive Services Task Force.

Results and conclusion:

The review included sixteen studies which consisted of systematic reviews with or without meta-analysis (seven), RCT (eight) and cost-effectiveness analysis (one). The included articles were published between 2016 and 2020. The studies were conducted in countries such as US, Germany, Italy, Poland, Egypt and the Netherland. This review included a total of 3,529 participants enrolled from all the studies. Sample size for each of the included studies ranged from 27 to 914 participants. The longest follow-up of the included study was up to 12 months. There is wide variation in the study population of this review, in which mostly were osteoarthritis, low back pain, and post-operative spinal surgery patients as well as patients with mild to moderate metabolic disorder, benign prostatic hyperplasia and female patients with primary dysmenorrhea. The intervention, PEMF therapy, varies widely in duration of application (ranged from five days to three weeks) and frequency of application from four times a day to twice a week).

Effectiveness

Based on the above review, there was sufficient good level of evidence retrieved on PEMF to be used in the treatment of patients with osteoarthritis, LBP and post-operative (spinal surgery). However, there was limited evidence retrieved on PEMF to be used in the treatment of patients with mild to moderate metabolic disorder, benign prostatic hyperplasia and patients with primary dysmenorrhoea. No evidence retrieved on PEMF use in the treatment of patients with depression, diabetes, as well as in its use for skin lifting and skin rejuvenation.

The PEMF appeared beneficial in reducing pain and improving physical function in patients with knee and hand OA, but not in patients with cervical OA, compared with placebo or sham.

- Reduction in pain score was observed after treatment with PEMF in patients affected by knee OA compared to placebo or sham group (SMD -0.54, 95%CI -1.04 to -0.04) and hand OA (SMD -2.85,

95%CI -3.65 to -2.04), at short term (longest follow-up 24 weeks), but not in cervical OA.

- Significant improvement in function was observed following PEMF in patients with knee (SMD -0.34, 95%CI -0.53 to -0.14), and hand OA (SMD -1.49, 95%CI -2.12 to -0.86), compared with the sham group, but not in patients with cervical OA.
- No improvement in WOMAC stiffness score (WMD -0.50, 95%CI –1.09 to 0.09) (five studies, n=301), was observed following PEMF in patients with knee OA, compared to placebo.

Good level of evidence retrieved, demonstrating benefits of PEMF to relieve pain and improve functionality in patients with LBP until 12 weeks of follow-up, compared to sham treatment.

- In patients with LBP, reduction in pain intensity following PEMF was observed, from baseline to the endpoint, with Cohen effect size ranged from 0.21 (95%CI -0.78 to1.18) to 1.01(95%CI 0.33 to 1.64). Improvement in disability using Oswestry Disability Index, has been demonstrated following PEMF, from baseline to week six however the effect size was small [ranged d= 0.10 (95%CI -0.52 to 0.72) to d=0.15 (95%CI -0.49 to 0.78)], compared to sham group. This difference is persisted at week-12 of follow-up.

Limited fair level of evidence retrieved on PEMF in the treatment of patients post spinal surgery, fracture with cast immobilisation, mild to moderate metabolic syndrome, benign prostate hyperplasia and primary dysmenorrhoea.

- For post-operative spinal fusion patients, PEMF increased the odds of a successful fusion by 2.5 times relative to control.
- In patients with fracture (distal radius) on cast immobilisation, PEMF appeared beneficial in reducing pain, improving mobility, touch (exteroceptive) sensation and reducing disability of the upper limb (the arm, shoulder, and hand).
- In patients with mild to moderate metabolic disorder, PEMF may improve blood pressure (BP) at rest and during exercise, and increase plasma circulating Nitric Oxide (NO) level
  - Significant increase in NO was observed following PEMF (16.5 ± 5.6 µmol/L to 22.2 ± 12.5 µmol/L, p=0.04), compared to the sham group.
  - Significant reduction in SBP (reduce by 11.3 ± 13.4mmHg), DBP (reduce by 6.4 ± 7.9 mmHg) and MAP (reduce by 8.0 ± 9.0 mmHg) in participants with underlying hypertension (at rest) (SBP≥140 mmHg) has been demonstrated following PEMF, compared to sham with hypertension.
  - Evaluation of BP at peak exercise showed the PEMF reduced peak SBP by 14.4 ± 20.3 mmHg (p=0.04), compared to increase in SBP in the sham group by 6.0 ± 20.9 mmHg. No difference between groups for peak DBP and peak MAP showed.
- In patients with benign prostatic hyperplasia aged 55 to 65 years, PEMF combined with pelvic floor and aerobic exercises improved Residual Urine, Flow Rate, Prostate Specific Antigen and International Prostate Symptom Score, compared with PEMF alone or placebo
- In patients with primary dysmenorrhea aged between 18 to 24 years, PEMF is beneficial in alleviating pain and decreasing prostaglandin level in blood

Safety

The PEMF therapy appeared safe and well tolerated in the study population with mild adverse events reported. The electro-magnetic field devices were approved by the USFDA (Class III) within the category of bone growth simulation/osteogenesis stimulation. Peripheral electromagnetic field was approved by USFDA (Class III) device to aid wound healing. The wearable ActiPatch PEMF Device was FDA 510k cleared as adjunctive treatment of musculoskeletal pain related to plantar fasciitis of the heel and osteoarthritis of the knee, and the wearable RecoveryRx PEMF Device was FDA cleared for adjunctive treatment of postoperative pain. The use of this device is well tolerated. However, it's use is contraindicated in patients with implanted electrical devices like pacemakers or intrathecal pumps and should be used with caution in certain conditions such as Grave's disease or active bleeding.

Cost-effectiveness

There was limited evidence retrieved on cost-effectiveness of PEMF. Based on cost utility analysis from societal perspective done in Netherland, the PEMF cannot be considered as a cost-effective treatment for acute fractures of the scaphoid bone, when comparing the effects of PEMF to standard health care in terms of QALY's.