Pulsed electromagnetic field changes protein expression in urothelial cells in culture: A pilot study

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INTRODUCTION

Pulsed electromagnetic field (PEMF) therapy has been found to be an effective treatment for multiple chronic pain conditions and *in vitro* studies have found it modulates the inflammatory cytokine profile in immune cells. Recently, it has been found that PEMF may be an effective symptomatic treatment in interstitial cystitis/bladder pain syndrome (IC/BPS), a condition wherein bladder urothelial cell function is abnormal, resulting in a compromised urothelium. The effect of PEMF on urothelial cells is unknown. Therefore, our objective was to evaluate changes in inflammatory protein expression in urothelial cells following exposure to PEMF.

MATERIAL & METHODS

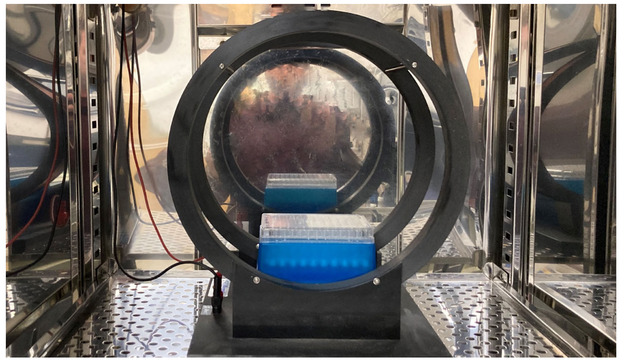
- 3 wells of urothelial cells from a single healthy donor (Sciencell Research Laboratories) were cultured in urothelial cell specific growth media under identical conditions (37°C, 5% CO_2)
- One plate was exposed to PEMF (33Hz, 0.5mT, 10 minutes, twice daily) every other day Monday, Wednesday, and Friday for one week
- The other (control) plate was incubated under identical conditions in a separate incubator sans PEMF exposure
- Two wells of growth media alone (sans cells) were assessed to control for background
- 100 µL of growth media was taken from each well, frozen at -20°C and sent for analysis with a multiplex protein expression array (measures 48 cytokines and chemokines; Eve Technologies)
- Baseline (media) cytokine/chemokine levels were subtracted from cultured cell supernatant
- Mean expression levels were compared between exposed (treatment group) and unexposed (control) cells utilizing student's t-test ($p<0.05$ considered significant)

.:TABLE 1:.

Cytokine/ Chemokine/ Growth Factor	PEMF exposed Mean ± SD (pg/ml)	Controls Mean ± SD (pg/ml)	Difference; P-value
EGF	4.07 ± 0.38	5.2 ± 0.35	-1.13; p=0.019
FGF-2	1850.5 ± 63.47	2333.46 ± 132.47	-482.96; p=0.012
FLT-3L	2.59 ± 0.56	1.21 ± 0.58	1.38; p=0.041
G-CSF	226.58 ± 70.05	66.60 ± 33.58	159.98; p=0.04
GROα	404.89 ± 89.52	171.91 ± 106.37	232.98; p=0.046
IL-15	2.42 ± 0.67	1.01 ± 0.34	1.41; p=0.048
MCP-1	3.63 ± 0.64	1.71 ± 0.247	1.92; p=0.023
MIG	6.94 ± 2.78	1.56 ± 0.64	5.38; p=0.031
PDGF-AA	826.39 ± 149.37	480.91 ± 111.03	345.48; p=0.036

Cytokines, chemokines, and growth factors that are significantly altered by exposure to PEMF

.:FIGURE 1:.



Cell culture plate in place with Helmholtz coil to administer PEMF

RESULTS

- PEMF exposure did not significantly alter baseline cytokine, chemokine, and growth factor levels in growth media alone (Exception: Eotaxin [1.065 vs 1.905 pg/mL; p=0.049]
- Out of 48 proteins analyzed, 9 were found to be significantly altered via PEMF exposure ($p<0.05$; Table 1)
  - Downregulated
    - Epidermal growth factor (EGF)
    - Fibroblast growth factor 2 (FGF-2)
  - Upregulated
    - Fms-related tyrosine kinase 3 ligand (FLT-3L)
    - Granulocyte colony stimulating factor (G-CSF)
    - Growth related oncogene alpha (GROα)
    - Interleukin 15 (IL-15)
    - Monocyte chemoattractant protein-1 (MCP-1)
    - Monokine induced by gamma (MIG)
    - Platelet derived growth factor-AA (PDGF-AA)

CONCLUSION

This pilot study has revealed that even a relatively brief exposure to PEMF significantly alters the expression of growth factors and cytokines in cultured urothelial cells. Further characterization is needed, specifically in urothelial cells from patients with IC/BPS, to begin to describe the molecular basis for patient benefit/improvement following PEMF treatment.

Next steps

Repeated and larger scale studies on healthy urothelial cells to investigate inflammatory and with concomitant urothelial permeability changes. Extension of this treatment model to urothelial cells cultured from patients with IC/BPS