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USING LASER THERAPY FOR URINARY AND RENAL DISEASE

PHOTOBIOMODULATION HELPS REDUCE PAIN AND INFLAMMATION IN DOGS AND CATS WITH URINARY AND RENAL DISEASE. — P. 8

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How dogs and cats with urinary and renal disease can benefit from the pain-relieving and inflammation-reducing effects of photobiomodulation or laser therapy.

LASER THERAPY

FOR LOWER URINARY TRACT AND RENAL DISEASE IN COMPANION ANIMALS

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The use of photobiomodulation, or laser therapy, as a non-invasive treatment for various injuries and conditions in veterinary medicine continues to expand and generate interest for both practitioners and the research community. Photobiomodulation (PBM) has a beneficial effect on cells and tissues, contributing to a directed modulation of cell behaviors, enhancing tissue repair and cell proliferation while simultaneously reducing inflammation and pain. This article looks at how PBM or laser therapy can help with lower urinary tract and renal disease in dogs and cats.

LOWER URINARY TRACT DISEASE

Laser devices emitting light in the visible to far-infrared spectrum have been used in humans to diagnose and/or treat various diseases of the genitourinary tract for nearly 50 years. This has included procedures on both normal and neoplastic tissues, to ablate and/or excise various lesions, and in the management of menometrorrhagia and other conditions.[15] Photobiomodulation therapy (PBMT) has been proposed by some in the human medical realm as an alternative for managing genitourinary syndrome of menopause (GSM), stress urinary incontinence (SUI), and interstitial cystitis/bladder pain syndrome (IC/BPS) in women. The biological basis, symptoms, and management of these conditions easily lend themselves to the rationale for using PBMT as a possible treatment, and devices designed for these applications in humans have demonstrated beneficial clinical and histologic changes in recent studies.[16-18] One report published on the use of a novel system for the temporary relief of pelvic muscle spasm and pain in

women showed clinically significant improvement in pelvic pain and pain with urination in 65% of participants, and follow-up data has indicated that the therapeutic effect may last several months.[18,19]

Based on the non-invasiveness of the modality, and its ease of use for feline patients in particular, PBMT may also be a possible therapeutic intervention for certain lower urinary tract disorders in cats. Feline idiopathic (or interstitial) cystitis (FIC) has also been called idiopathic feline lower urinary tract disease (FLUTD) and feline urologic syndrome.[20] While the etiology of FIC is multifactorial and not completely understood, there appears to be a complex interaction between the urinary bladder, nervous system, adrenal glands, and environmental conditions. Affected cats seem to have an excitatory sympathetic nervous system response alongside decreased adrenocortical function in response to stressful episodes or environmental changes, and an associated increase in bladder wall permeability.[19,20] This abnormal degree of urothelial permeability, also found in human IC patients, allows increased penetration of protons and potassium ions from urine to the submucosa, which causes irritation and may stimulate sensory neurons.[20-23] The positive effects noted in the aforementioned human studies are consistent with the mechanism of action of PBM, and the potential impact on multiple bladder and pelvic pain generators.[24]

As mentioned previously, studies show that PBMT results in analgesia through reduction in A-delta and C-fiber activity, modification of pro-inflammatory cytokines, growth factors and chemokines. C-fiber activation is thought to be a major contributor to the development of the allodynia responsible for the symptom of urinary frequency and bladder pain in human patients with IC/BPS.[25]

HOW PBM WORKS

Using wavelengths in the red and infrared range, PBM activates cytochrome c oxidase and increases mitochondrial electron transport, inducing a cascade of events leading to an increase in adenosine triphosphate (ATP). This produces beneficial reactive oxygen species (ROS), nitric oxide; affects healing and stimulates collagen production via the upregulation of specific substrates and cytokines (including epidermal growth factor and transforming growth factor beta); and downregulates others (e.g. interleukin [IL]-6, IL-8, and IL-1).[1-6]

Modulating the inflammatory process is a large part of the mechanism by which PBM reduces pain; however, there are other mechanisms involved as well, making it an effective analgesic modality. PBM modulates neuronal activity via the normalization of ion channels, reducing the sensitization of injured or inflamed peripheral neurons, the dorsal root ganglion (DRG) and spinal cord.[7-10] In vitro studies in rat dorsal ganglia cultures have demonstrated that PBM can disturb fast axonal transport via perturbation of microtubule arrays by reducing ATP synthesis in axonal mitochondria of small diameter neurons. An in vivo study has shown that PBM utilizing higher irradiances inhibits Aδ and C-fiber transmission, and this mechanism appears to be involved in PBM of the DRG as well.[10-13]

In addition to effects mediated primarily via the biologically active chromophore mentioned above, there are also light-sensitive ion channels within the cell membrane. These ion channels are gated by light and include "transient receptor potential" (TRP) channels[14] which are activated by specific factors, such as heat or cold, noxious chemicals, and mechanical forces, among others. When activated, TRP channels open, allowing ions such as sodium to flow into the cell. This results in an action potential, which is realized as a nerve impulse. Mounting evidence suggests that light mediated activation of TRP is responsible for some of PBM's mechanisms of action as well, particularly regarding histamine-dependent wound healing effects and antinociceptive effects.[14]

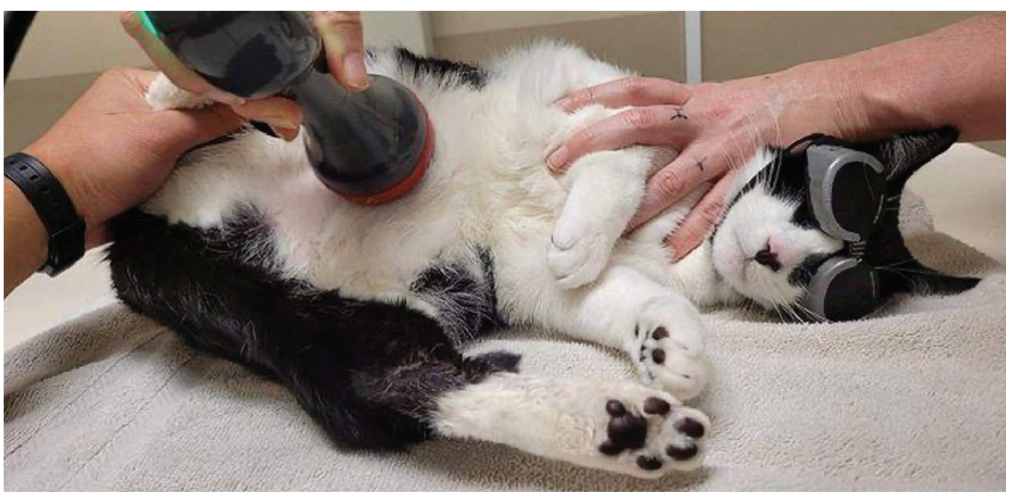

Figure 1. Photobiomodulation being applied to the caudal abdomen of a feline patient.

Photo courtesy of Black Mountain Animal Hospital, Henderson, NV.

C-fiber sensory neurons in the bladder are more sensitive in cats with FIC than in normal cats, contributing to altered activation of neural pathways. Research has also indicated that abnormal transient receptor potential (TRP) vanilloid receptor 1 responses of afferent neurons may contribute to this enhanced bladder sensitivity in FIC.[26] The ability to potentially mediate the activation of TRP[14] and/or reduce the sensitivity of C-fiber sensory neurons in the bladder of these patients could be a potential target for PBMT to exert antinociceptive effects.

Cats with FIC may have a wide range of presentations, including frequent recurrent episodes, chronic persistent signs, or even urethral obstruction.[27] PBMT may be of potential benefit in all these situations as part of the multimodal management, decreasing the severity of clinical signs via providing analgesia, and decreasing urethral spasm during episodes of acute pain. When urethral obstruction does occur, many veterinarians, including the author, have also found PBMT helpful for decreasing swelling, spasm, and pain prior to and/or during the placement of a urinary catheter to alleviate any obstruction, and in providing pain management for cats that have been unblocked and/or remain in hospital with indwelling urinary catheters.[28]

In each of these scenarios, treating the area(s) of the urinary bladder (Figure 1) and the perineum (to target the urethra [and the penis when applicable]) is recommended. Additionally, treating the lumbar and sacral spine could be of added benefit, targeting the sensory neurons innervating the bladder via the pelvic and hypogastric nerves, which originate from the dorsal horn of the sacral and lumbar spinal cord, respectively. A deep tissue dosage of 6-10 J/cm^2 is recommended, treating ON contact to minimize light loss(es) from reflection.[28] The treatment head/handpiece utilized (and therefore the spot size of the laser beam), and treatment power (in watts) for administering therapy, will determine the irradiance at the skin surface, and subsequently at the level of the urinary bladder.

Extrapolating from computational modeling (COMSOL Multiphysics, Burlington, MA) and previous cadaver work in dogs,[29] a treatment spot size of 5 cm^2, and a power setting of 5-8 W (1-1.6 W/cm^2) at the skin surface means the irradiance at the target tissue should be approximately 155-250 mW/cm^2.

The author recommends scanning the entire caudal abdomen to treat the urinary bladder, utilizing a similar technique to scanning the area for a diagnostic ultrasound, trying to aim for all aspects of the bladder where it is positioned in the abdomen. Due to the perineum often being contaminated with urine and/or prepped for catheterization, an off-contact treatment technique should be used in this particular area, treating around the entire perineal area and never hovering over one spot, to allow tissues to appropriately thermally relax.

Though this discussion has focused primarily on feline patients, the same technique of treating the urinary bladder might also be applied to canine patients experiencing discomfort from cystitis. For acute situations or hospitalized patients, PBMT sessions may be performed daily for pain management, weaning the frequency of treatment sessions as the patient improves, until resolution. For more chronic situations, weaning out to a maintenance schedule of treatments that aid in keeping a patient's symptoms to a minimum (typically once every two to four weeks) is recommended after initial improvement(s) are clinically noted.

CHRONIC KIDNEY DISEASE

Mitochondrial dysfunction, reactive oxidative stress, inflammation, and renal tissue fibrosis are inherent components in chronic kidney disease (CKD), depending on etiology. Studies have investigated PBMT for its potential to aid in the treatment of these patients due to its ability to stimulate repair and attenuate the sequelae of inflammation and fibrosis.

Studies examining the mechanisms of PBMT on CKD have described beneficial findings with regards to decreasing inflammatory cytokines,[30] decreasing renal hypertension, preserving glomerular filtration rate,[31] and decreasing renal fibrosis particularly through affecting TGFβ1 signaling.[31,32] One study looking at the effects of PBM in a streptozotocin-induced diabetic kidney model showed that the therapy lowered the values of serum BUN, serum creatinine, and BUN/creatinine ratio in diabetic rats.[33] Veterinary colleagues as well as the author have noted anecdotal subjective improvements in their own CKD-PBM treated patients with regards to decreasing azotemia and stimulating appetite and overall well-being.[34]

To attempt to treat the kidneys, the recommendation is to use a deep tissue dose of 6-10 J/cm^2 on contact (scaling up with the size of the patient/depth of the target tissues) and focus on the cranial abdomen, including the area of the kidneys (as though performing a diagnostic ultrasound scan of that area). Approaching from both the ventral aspect of the abdomen and the lateral walls of the abdomen, the left kidney should be easier to localize than the right kidney because of its lateral location along the mid-abdomen, and may even be palpable. The right kidney, due to its craniodorsal location, may have to be treated based on aiming the treatment beam in that orientation under the rib cage of the abdomen on that side, or even utilizing a lateral approach in large deep-chested dogs through the 11th or 12th intercostal space, making sure to keep the beam scanning and moving at all times.

This author as well as other veterinary colleagues[34] recommend an initial treatment session frequency of two to three times per week, weaning the frequency of treatment sessions after two weeks, until a maintenance phase treatment session of typically once every two to three weeks is established based on the patient's response and any improvements noted in labwork. It should be noted that the author is not advocating that PBMT be used in place of traditional CKD management, including nutritional modifications, renoprotective treatments, phosphorus reduction, or the identification and correction of any existing prerenal or postrenal disorders and/or primary disease processes or complicating disorders. As with most complex disease management, a multimodal approach, taking into consideration therapeutic priorities based on the patient's stage of CKD, is best.

In conclusion, a large amount of research has been done over the last 60 years to elucidate the mechanisms behind PBM. Ongoing research is exploring additional molecular mechanisms, biological context, and optimal dosing parameters for various conditions; however, great progress has been made. While further studies in dogs and cats should be performed, this unique, non-invasive modality has the potential to make a significant impact on the overall prognosis and outcome of many veterinary patients being treated for urinary or renal conditions, although this therapy may not always be top of mind when evaluating these cases. PBM should be considered for these patients, as well as to reduce their pain and hasten recovery where possible; and in chronic conditions, to possibly ameliorate other long-term consequences of the dog or cat's disease.

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