Effective dose delivery: The key component joining two growing technologies

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For the Education Center

New treatments are providing safer and more effective ways to manage common conditions, including soft tissue injuries and osteoarthritis.

Two examples of continuously evolving therapeutic modalities include photobiomodulation therapy (PBMT), also commonly referred to as laser therapy, and regenerative therapies, which include platelet rich plasma (PRP) and stem cell therapies. In recent years, these therapies have experienced a renaissance both in the evolution of their clinical applications and in our understanding of their role in a multimodal approach to conservative management of our patients.

Through this time of expanded awareness and learning, the single most important advancement in these therapies has been a better understanding of what is required to provide an effective "dose" to treat common conditions. As with medications, delivering a therapeutic dose of laser therapy or regenerative medicine is a critical component to delivering successful treatments.

Photobiomodulation therapy

PBMT provides an important tool to facilitate healing and pain management for a wide variety of conditions, including arthritis, postsurgical wound closure, otitis, and many others. You already may be using PBMT in your practice and seeing results, but are you getting optimal and consistent results?

Like any other treatment modality, it is important that the therapy dosage is appropriate for the species, condition, area, and depth of target tissue being treated. For PBMT, this equates to delivering the appropriate dosage of light energy calculated as joules/cm^2 to a given area of affected tissue at the proper irradiance (W/cm^2) to achieve therapeutic efficacy. As our understanding of treating numerous conditions has advanced, we now know there are several factors that must be taken into account when calculating an appropriate dosage that will result in optimal treatment response. Some of these key factors include:

- Condition being treated
- Acute or chronic
- Superficial versus deep tissue
- Size of area being treated
- Characteristics of intervening tissue layers
- Patient size and body type
- Patient hair coat (amount and pigmentation)
- Patient skin (thickness and pigmentation)
- Mechanism of light delivery
- On versus off contact

Recent technology innovations include the development of comprehensive species and condition-specific protocols that when properly used can ensure you are delivering the right dose for a variety of conditions and patients. However, a thorough understanding of laser dosimetry will assist the astute laser operator in "double checking" the recommended parameters. All laser software should list all parameters delivered for the medical record and for the laser operator's use should adjustments to further treatment protocols need to be made.

The fields of PBMT and regenerative medicine continue to grow every year. The combination of these treatment modalities as tools in a multimodal approach to pain management continues to evolve.

The new textbook, *Laser Therapy in Veterinary Medicine: Photobiomodulation* (Wiley, 2017) contains the most current, and comprehensive information on PBMT worldwide. The publication includes specific information about the most effective way to combine PBMT with other treatment techniques and modalities. This book is also a good resource to learn about the fundamental evidence behind effectively dosing tissue.

Regenerative medicine

Regenerative medicine, which includes PRP and stem cell therapies, uses the body's own cells to promote healing and damaged tissue regeneration. These therapies can be effective when used as part of the multimodal approach to treating osteoarthritis, and soft tissue injuries including tendon, ligament, and spinal injuries.

Regenerative therapies have recently made an appearance in the veterinary market as systems originally designed for use in human patients were placed into veterinary practices for the treatment of our four-legged patients.

However, it became quickly apparent the needs of canine patients were unique and species-specific design and validation needed to take place to yield an optimal product. For example, when regenerative therapy systems were tested using canine blood to produce PRP, it was found many of the commercially available systems did not provide the same consistent output as when processing human blood.[1] Based on the inconsistent results of these early tests, it was obvious a system engineered and validated for the canine patient was necessary. Several studies have been performed to compare popular regenerative therapies systems to determine which systems are producing the most effective final product for administration to the patient.[2,3] What constitutes the "ideal" PRP sample to produce an optimal therapeutic outcome?

For PRP, there are three main parameters that should be considered for delivering an effective treatment.

Platelet concentration

Platelets contain beneficial growth factors that act as messengers in the body, communicating to promote healing and repair of the damaged tissue. To have a significant effect on the healing cascade, an increase in concentration of growth factors is needed; therefore, an increase in platelets is needed in the sample. It is generally accepted that a three- to seven-fold concentration of platelets provides an effective dose for treating common conditions such as osteoarthritis.[4]

In order to obtain a three- to seven-fold concentration of platelets in a volume appropriate for the joint space/tissue being treated, a higher volume of blood is typically needed to harvest the platelets, which make up less than 1 percent of total blood volume. For example, to obtain 4 mL of PRP with a three- to seven-fold concentration, it is necessary to draw upwards of 40 to 50 mL of whole blood to capture the appropriate amount of platelets.[2]

Red blood cell concentration

It is generally accepted that red blood cells (RBC) must be eliminated from the sample as much as possible. When RBCs are exposed directly to any tissue without the barrier provided by a vessel, they produce harmful reactive oxygen species and also increase the concentration of unwanted inflammatory mediators including IL-1 and TGF-α.[5] Injection of RBCs directly into a tissue would result in further tissue damage and could lead to increased pain for the patient.

Neutrophils

Like RBCs, it is also generally recommended that neutrophils be eliminated from the PRP sample as much as possible. Although these cells are beneficial for the control of infections, neutrophils are detrimental to cartilage and synovium as observed in autoimmune diseases, including rheumatoid arthritis, and common tick-borne diseases, including Lyme disease. Neutrophils increase the concentrations of unwanted inflammatory mediators, which include IL-1β, TNF-α, IL-6 and IL-8. It has also been observed that neutrophils, when included in a PRP sample, correlate with an increased concentration of MMP-9, which degrades collagen and other extracellular material.[5]

Now that we know what an ideal PRP sample contains, you may be wondering how you know whether the system you currently have or considering provides an optimal dose of platelets while eliminating the harmful cell types.

If you currently have a regenerative medicine system, perform a simple pre- and post-complete blood count on the blood sample and final PRP product to see what was concentrated and eliminated from the sample. If your system is not providing an adequate increase in platelets or a reduction in RBCs or neutrophils, contact the manufacturer and ask them how you can modify the processing to provide the ideal PRP sample.

If you are looking at available systems and want to know what you should expect in your final sample, ask the manufacturer for its validation paper/research that shows what the system will produce.

Technologies here to stay

PBMT, when dosed and administered correctly, has proven its effectiveness and ability to stand the test of time as it has become standard of care over the past 10 years. Regenerative medicine is just beginning its climb to popularity in veterinary medicine, but with the promising results seen from the canine-validated systems. As with all emerging technologies, it is important that we understand the science behind why it works and employ correct administration techniques and dosages. ●

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