CASE STUDY

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Spinal Cord Injury: Respiratory Assessment of Targeted Nanoconjugate Treatment Using Conscious Respiratory Plethysmography and EMG in Rats

Introduction

Throughout the world, between 250,000 - 500,000 people suffer a spinal cord injury (SCI) every year. Most SCIs are due to preventable causes, such as motor vehicle accidents, violence, falls, and contact sports injuries. While the healthcare field has advanced over the past 30 years, outcomes for individuals with SCI have not. In fact, they are twice as likely to die prematurely, with the rate of mortality being the highest during the first year post injury.[1] Many of these patients will experience acute and chronic health difficulties, particularly respiratory complications which occur in 80% of cases and are most prevalent during the acute phase.[2] Due to the physical and financial burden SCIs put on patients and their families, research must continue to find solutions that increase quality of life and are conducted in translatable environments to ensure the best patient outcomes.

The Background

Researchers previously studied the effects of an A_1 adenosine receptor antagonist called DPCPX, a targeted nanoconjugate, on anesthetized male Sprague-Dawley rats. Rats are the most commonly used species, making up 75% of the animal models used in SCI research.[3] Results showed DPCPX induced recovery of diaphragm function following cervical 2 (C2) SCI without causing unwanted side effects typically seen with systemic administration of A_1 and A_2 receptor antagonists. With the promising outcome of DPCPX, the next step was for researchers to conduct the same study on a more translatable model. Due to known depressive qualities of anesthesia on the respiratory system, the researchers needed to better quantify the respiratory effects in conscious, unanesthetized rats.

The Study

To monitor the respiratory system in unanesthetized subjects, researchers brought in a DSI Buxco® Whole Body Plethysmograph (WBP) solution to assess the same targeted treatment in awake and unrestrained male Sprague-Dawley rats. Prior to respiratory assessment, rats were given SCI at the C2 vertebral segment by cutting just caudal to the dorsal roots to induce left hemidiaphragm paralysis. The rats were then split into control ($n=7$) and treatment ($n = 8$) groups. To ensure unresponsiveness, diaphragmatic electromyography (EMG) was used to verify termination of muscle contractility under anesthesia. After verification of paralysis and with the diaphragm being exposed, the DPCPX nanoconjugate or vehicle control (distilled water) were injected along the entire length of the left hemidiaphragm. After recovery and a period of chamber acclimation, the rats were placed inside the WBP chambers which are connected to pressure transducers that measure small pressure changes inside each chamber. These pressure changes were acquired and analyzed using Ponemah software and translated to respiratory flow tracings (Figure 1). Respiratory data was collected for 30 minutes, starting on day 3 post paralysis, and continued weeks 1, 2, 3, and 4. Ambulatory data was excluded from analysis.

The Results

Using diaphragmatic EMG, results showed early efficacy with only one dose of nanoconjugate DPCPX. Muscle and phrenic nerve activity were restored in as early as 3 days after administration. Ventilation improvements were not detected until day 14 post injury using WBP. Increases in respiratory frequency occurred at day 14, while tidal volume saw a return to pre-injury levels by day 14 and continued to rise through study termination (Figure 2). Minute volume started to show improvement at day 21.

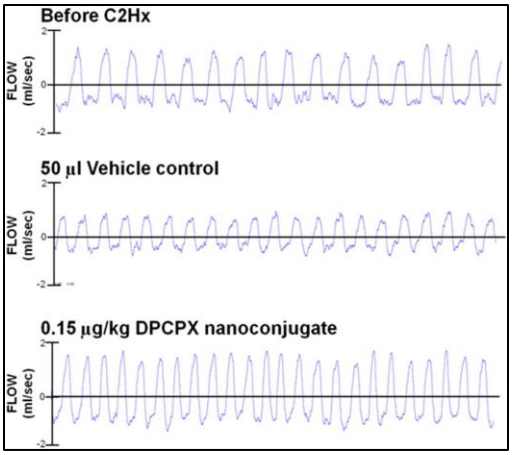

Figure 1: Respiratory flow (ml/sec) measured using WBP in awake and freely moving animals breathing room air. X-axis, 10-s time intervals

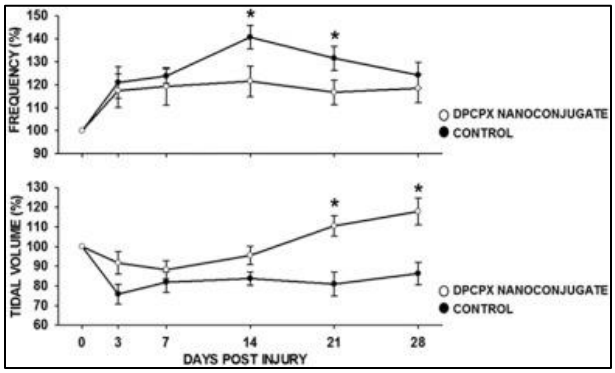

Figure 2: Frequency (F, %) and total volume (%) of control vs treatment

The Successes

This study was a first-time evaluation of a targeted nanoconjugate treatment on respiratory recovery post SCI. The WBP system allowed researchers to collect respiratory data from unanesthetized, freely moving, and spontaneously breathing rats. Increases in respiratory volume and rate throughout the study were observed, validating the treatment effect on strengthening respiratory and ventilation performance following SCI. The decreased stress from minimal handling, along with continuous acute or chronic data collection benefits researchers and science to acquire translatable animal to human data, resulting in more clinically relevant research results.

DSI

Data Sciences International (DSI) offers complete systems that sense, transmit, acquire, and report physiologic data. In order to create a more robust study design, scientists rely on DSI technology to study specific targets as well as obtain a holistic view; allowing them to look at side effects that are upstream or downstream of the main pathology.

The DSI team ensures that researchers are equipped and prepared from the first minute of their study to the last; because your research is everything.

References:

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