

# USING LIQUID VENTILATION TO IMPROVE LUNG FUNCTION IN PATIENTS WITH RESPIRATORY DISTRESS SYNDROME: A COMPREHENSIVE REVIEW OF THE LITERATURE

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*This article is a review of the research findings on the subject of liquid ventilation and how it has shown to improve lung function in patients with respiratory distress syndrome. An overview of the physiology behind the success of liquid ventilation, including current research outcomes, is presented. The literature documenting research data was obtained through an Internet search of articles published from 1962 to 2002.*

*Respiratory distress syndrome is a potential complication for any patient that has suffered damage to the lungs. It continues to carry a significantly high mortality rate, in spite of multiple conventional treatments currently in use.*

*The latest clinical research has led to the development of a new treatment for the syndrome called liquid ventilation, whereby chemicals called perfluorocarbons are used as a medium to transport vital respiratory gases into and out of the lungs. Research on animal and human subjects has shown that liquid ventilation therapy can improve lung function in certain patients with severe pulmonary dysfunction when conventional treatments have failed.*

**Key words:** Liquid ventilation, partial liquid ventilation, perfluorocarbon-assisted ventilation, total liquid ventilation, respiratory distress syndrome.

Respiration is an essential physiological function of the human body to maintain gas exchange in order to sustain life. When the respiratory muscles move air into and out of the lungs, vital processes are ongoing to ensure oxygen is delivered to the cells of the body and carbon dioxide is removed. If there has been damage to the lungs, these processes can be disrupted and respiration disturbed, leading to inadequate gas exchange. A common diagnosis for patients with inadequate gas exchange due to direct or indirect lung injury is respiratory distress syndrome (RDS), which can occur in the neonatal, pediatric, and adult population. This syndrome poses a serious threat to those affected by it, with a 50% or greater mortality rate documented in the literature.<sup>1</sup> In RDS, the respiratory membrane of the lungs is damaged and fluid is allowed to accumulate in the lung interstitium, alveolar spaces, and small airways. The fluid accumulation decreases the elasticity of the lungs, which impairs the diffusion of oxygen into the pulmonary capillary blood.<sup>2</sup>

In 1996, several hallmark symptoms of RDS including severe arterial hypoxemia despite oxygen therapy, increased intrapulmonary shunting, and decreased lung compliance and volumes were

reported in the literature. Common clinical signs are dyspnea and tachypnea, with increasing use of accessory muscles to breathe. Auscultation of the lungs will reveal bilateral rales from the fulminating pulmonary edema. Diffuse bilateral pulmonary infiltrates will be evident on the chest radiograph. As the respiratory distress worsens, mechanical ventilation is often necessary to maintain respiration. Current treatments for RDS do provide some improvement in lung function; however, harmful side effects such as barotrauma and oxygen toxicity can occur.<sup>1</sup>

Over the past few decades, researchers have embarked upon a new, somewhat unconventional strategy for treating patients with RDS. The therapy is known as liquid ventilation, which has shown promise in the treatment of the syndrome in several clinical settings across the country. The cornerstone of this method of ventilation involves using an organic liquid, perfluorocarbon, as a medium for the transport of oxygen and carbon dioxide into and out of the lungs.<sup>3</sup>

Perfluorocarbons are clear, odorless chemicals that are highly soluble for oxygen and carbon dioxide and have a low surface tension. In 1997, it was reported that 53 mL of oxygen can be carried in 100 mL of a perfluorocarbon, which is 25 times greater than for

blood alone, and 210 mL of carbon dioxide can be dissolved in 100 mL of a perfluorocarbon, which is 3 times greater than blood. There are a variety of perfluorocarbons in existence, produced by replacing the carbon-bound hydrogen atoms with fluorine atoms on organic compounds.<sup>4</sup> Perfluorocarbons can be stored at room temperature and are nonbiotransformable.<sup>5</sup>

There are 2 methods of liquid ventilation: total (or tidal) liquid ventilation and partial liquid ventilation. In total liquid ventilation, the perfluorocarbon, in an amount equal to the patient's tidal volume, is instilled slowly into the lungs through a side port on a polyvinylchloride-compatible endotracheal tube. A mechanical ventilator specifically designed for total liquid ventilation is used to move the perfluorocarbon into and out of the lungs. As the ventilator cycles the fluid through the lungs, oxygen dissolved in the perfluorocarbon is absorbed across the pulmonary capillaries into the bloodstream and carbon dioxide is removed by diffusion into the perfluorocarbon. When the fluid returns to the ventilator, oxygen is replaced in the perfluorocarbon, and carbon dioxide is removed by the ventilator's extracorporeal membrane gas exchanger, similar to a cardiopulmonary bypass circuit.<sup>3</sup>

Partial liquid ventilation uses the conventional method of gas ventilation combined with perfluorocarbon. The fluid, in an amount equal to the patient's functional residual capacity, is slowly poured down the endotracheal tube side port. The perfluorocarbon is instilled until a sustained meniscus of the liquid is seen in the endotracheal tube at end-expiration at the level of the patient's sternum with the patient supine. The patient continues to receive traditional mechanical gas ventilation to move the perfluorocarbon in and out of the airway divisions. This type of ventilation allows oxygen to be thoroughly dispersed in the alveoli. As the lung compliance changes and the liquid evaporates, additional perfluorocarbon is instilled to maintain a meniscus in the endotracheal tube. Gas exchange occurs as oxygen travels to the alveolar units and forms bubbles in the perfluorocarbon.<sup>4</sup> Oxygen and carbon dioxide are exchanged based on their partial pressure gradient.<sup>6</sup>

Research on human subjects has shown that liquid ventilation therapy can improve lung function in patients with RDS where conventional treatment modalities have failed. Due to their higher density, as compared to water, perfluorocarbons have the ability to reach areas of lung tissue and may help to open atelectatic areas and improve gas exchange. As the fluid reaches the dependent areas of the lungs, more alveoli are recruited to participate in gas exchange and functional residual capacity is increased. The density

of the liquid also redistributes pulmonary blood flow to nondependent lung regions.<sup>3</sup> The liquid acts as a lavage medium to engulf mucous plugs and facilitate suctioning of debris out of the lungs.<sup>7</sup> Perfluorocarbons also reduce the surface tension in the lining of the alveoli to improve lung compliance.<sup>1</sup>

## **Literature related to conventional treatments for RDS**

Treatment for RDS focuses on correcting the causative factor and maintaining adequate oxygenation to the tissues. In 1996, the findings from multiple research studies that evaluated several respiratory support modalities were reported. These treatments included volume and pressure-controlled ventilation, prone positioning, surfactant therapy, inhalation of nitric oxide, and extracorporeal membrane oxygenation. Volume and pressure-controlled ventilation with positive end-expiratory pressures are the most widely used treatment methods, but injury to the lungs can occur from barotrauma and if high inspired oxygen concentrations are required, oxygen toxicity may result.<sup>1</sup>

Surfactant therapy has been shown to improve oxygenation in pediatric patients with RDS, but the success is short-lived in adult patients if pulmonary edema is present. Pulmonary edema can manifest in patients with acute respiratory distress syndrome (ARDS) due to the damaged respiratory membrane of the lungs, which allows fluid to accumulate in the interstitium and alveolar spaces. The surfactant is unable to reach these areas of the lungs, thereby diminishing its efficacy.<sup>1</sup> Nitric oxide, a potent pulmonary vasodilator, is a relatively new therapy used in the treatment of RDS. It is an endogenous gas that activates guanylate cyclase inside cells, which, in turn, increases the cyclic guanosine monophosphate (cGMP) concentration. The increase in intracellular cGMP produces vascular smooth muscle relaxation, thereby decreasing pulmonary vascular resistance.<sup>8</sup> Nitric oxide can improve arterial oxygenation and reduce pulmonary hypertension in neonates and adults, but more research is needed for long-term effects. Extracorporeal membrane oxygenation and carbon dioxide removal, where a membrane oxygenator takes over the work of the lungs, has shown some success in pediatric and adult populations; however, such intervention is invasive, requires significant anticoagulation, and is not appropriate for an extended period of time.<sup>1</sup>

The findings of several research studies on treatments for RDS were described in 1998. The therapies included positive pressure ventilation, extracorporeal

membrane oxygenation, surfactant replacement therapy, high-frequency ventilation, and inhaled nitric oxide. Multiple damaging side effects of these treatments were listed including inflammation and infection of the airways, hemodynamic instability, and mechanical injury to the lungs.<sup>3</sup>

### **Literature related to liquid ventilation in animals**

The research on liquid ventilation began in 1962 when researchers wanted to investigate the notion that land dwelling animals could survive by breathing fluid, as it was believed that all land dwelling vertebrates evolved from fluid-breathing fish. The researchers submerged adult unanesthetized mice in Sterofundin (a balanced salt solution), Sterofundin with 0.1% hydroxymethyl aminomethane, tap water, and water from the North Sea. The mice were placed in tanks partially filled with the fluids, and a valve allowed compressed gases to flow into the tanks. The tanks were then placed under pressure.<sup>9</sup>

Multiple pressure ranges and temperatures were tested to evaluate the mice and their respiratory movements. The study found that the longest survival time of mice in a balanced salt solution under oxygen at 8 atmospheres was observed to be 18 hours at a temperature of 20°C.<sup>9</sup> This hallmark research finding prompted the continued investigation of the use of liquids as a medium for respiratory gas exchange.

In 1966, researchers performed the first study using organic liquid as a medium for respiratory gas exchange. They believed that organic liquids, such as silicone and perfluorochemicals, might be capable of supporting respiration based on the findings of the 1962 original study and the idea that oxygen solubility was greater in these fluids than in plasma or saline. The researchers tested mice and cats by submerging each in oxygen-saturated silicone oils at different viscosities, time intervals, and temperatures.<sup>10</sup>

The researchers found that mice breathing the liquid perfluorocarbon for 1 hour lived for several weeks after removal from the fluid. Oxygen diffusion through the perfluorocarbon was measured by an oxygen electrode and liquid-soaked filter paper and found to be 4 times as fast as through saline. The study could not determine if the pulmonary damage observed upon the death of the animals was due to solvent activity, toxic impurities, a chemical reaction of the perfluorocarbon structure with the lungs, or some other factor. This finding sparked another topic for research. However, the study did confirm that perfluorocarbon liquid was a superior medium to silicone oils for liquid respiratory gas exchange.<sup>10</sup>

As more experimental studies on liquid ventilation were undertaken in the 1970s, the research focused on the ability to reconvert a fluid-ventilated animal back to gas ventilation. In 1971, 30 mongrel dogs were used to determine if the animals could survive after being ventilated with oxygenated perfluorocarbon liquid and then converted back to ventilation with gaseous oxygen. Each dog was anesthetized and endotracheally intubated. Blood sampling and cardiac pressure catheters were inserted for continual measurements of arterial pH, PaCO<sub>2</sub>, PaO<sub>2</sub>, and hemodynamics. The dogs were allowed to spontaneously breathe 100% oxygen via a reservoir bag/valve system for 15 to 20 minutes. Blood samples were obtained before 15 dogs were chemically paralyzed and ventilated with a reservoir chamber containing 1,200 mL of perfluorocarbon liquid, the specific chemical being FX-80. FX-80 is a mixture of perfluorobutyltetrahydrofuran and isomeric compounds. The remaining 15 dogs also underwent the liquid ventilation, without receiving the muscle relaxant.<sup>11</sup>

One hour later, the perfluorocarbon was drained from the lungs by gravity, and the dogs were allowed to breathe 100% oxygen for 3 hours. The paralyzed group received mechanical gas ventilation, while the other group continued spontaneous ventilation. To explore the possibility of pulmonary damage to the lungs after perfluorocarbon ventilation (as suggested in previous studies), 10 of the dogs, including 5 from each group, were chemically sacrificed after 3 hours to allow histologic examination of the lung tissue. Another group of dogs was sacrificed at 72 hours followed by yet another group 7 to 10 days later to examine their lung tissue.<sup>11</sup>

All of the animals in the study survived ventilation with oxygenated perfluorocarbon liquid and reversion to breathing gaseous oxygen. After conversion to breathing 100% oxygen, no differences were noted in the arterial blood gases of both groups of dogs. Microscopic examination of the lung tissue did show an early acute inflammatory reaction with the later appearance of macrophages engulfing the perfluorocarbon, with the largest number apparent at 72 hours postliquid ventilation. This reaction was believed to be from the trauma of distending the alveoli of the lungs with liquid or an irritant effect of the perfluorocarbon liquid used in the study, FX-80. The researchers concluded that mammals could successfully breathe perfluorocarbon liquid for 1 hour and reconvert to gas breathing without severe deleterious effects.<sup>11</sup>

The presence of the inflammatory reaction found on histologic examination of the lung tissue from the animals ventilated with the perfluorocarbon FX-80 in

the previous study and in other studies left an unanswered question in the minds of the researchers. If humans were to ever successfully breathe perfluorocarbon liquid, a chemical that caused no permanent alteration in lung structure had to be found.<sup>12</sup>

In 1973, researchers set out to eliminate the possibility that changes in lung structure in previous studies on animals ventilated with perfluorocarbon liquid might be caused by an impurity or isomer in the liquid. The methods used in this study paralleled the format of the 1971 study with the perfluorocarbon FX-80, with the exception of the liquid selected for ventilation. Thirty-two mongrel dogs were anesthetized and then ventilated with Caroxin-D perfluorocarbon liquid for 1 hour.<sup>12</sup>

The study showed that adequate arterial oxygen tensions were maintained during Caroxin-D ventilation. Blood gas values for PaCO<sub>2</sub> and pH returned to normal immediately after return to conventional gas ventilation. The PaO<sub>2</sub> values were significantly higher 24 hours after Caroxin-D ventilation than in FX-80 ventilation. Decreased lung compliance was evident 24 hours after the liquid ventilation but returned to normal by 1 week. One year after the Caroxin-D ventilation, significant amounts of perfluorocarbon were still found in the animals' lungs after they were sacrificed. The notion of possible scarring of lung tissues from the residual perfluorocarbon was left open for further study. Conclusions from this study confirmed that dogs could be ventilated with Caroxin-D perfluorocarbon liquid with return to normal lung function for at least 20 months, despite residual perfluorocarbon remaining in the lungs.<sup>12</sup>

The early research involving liquid ventilation evaluated perfluorocarbons as a medium for gas exchange by using a total liquid ventilation technique. The animals used in these studies received the perfluorocarbon liquid in place of normal gas ventilation by way of a reservoir or gravity dependent system. The need for an easier method to use the promising therapeutic effects of perfluorocarbons in treating pulmonary dysfunction prompted researchers to explore a partial liquid ventilation technique. In 1993, researchers tested the effects of different doses of perfluorocarbon on lung mechanics and gas exchange in adult rabbits with respiratory failure to assess whether perfluorocarbons combined with conventional mechanical ventilation would provide any benefit.<sup>13</sup>

Thirty rabbits were anesthetized and mechanically ventilated via an endotracheal tube for this study. Acute respiratory failure was induced in the rabbits by lavaging the lungs with warm saline until an arterial oxygen pressure less than 100 mm Hg was achieved

under standard ventilator settings. The animals were placed into 5 groups of 6 each, and 4 groups received varying doses of an intratracheal perfluorocarbon known as perflubron. The control group did not receive the perflubron, and their lungs were ventilated with gas. After the perflubron was instilled down the endotracheal tube, a mechanical gas ventilator was reconnected at the standard settings set by the researchers. The animals were ventilated for 6 hours, during which arterial blood gases, hemodynamic parameters, lung mechanics, and carbon dioxide exchange data were collected.<sup>13</sup>

The data from the study showed that arterial oxygen pressure increased significantly in a dose-dependent manner, and peak airway pressures decreased significantly from pretreatment values in the perflubron-ventilated animals. However, the improved pulmonary parameters could be extended to 6 hours only in the animals treated with high doses (9 mL/kg to 12 mL/kg) of perflubron. The researchers concluded that perfluorocarbon administration with mechanical gas ventilation offered a simplified alternative treatment for RDS, without the added complexity of total liquid ventilation equipment. Partial liquid ventilation can provide adequate respiratory gas exchange at lower airway pressures with high perfluorocarbon doses, thereby avoiding the barotrauma often seen with traditional mechanical ventilation in RDS.<sup>13</sup>

Another variable of partial liquid ventilation that has yet to be determined is the optimal dose of perfluorocarbon needed to produce maximum ventilatory improvement in RDS. The lungs of patients with RDS are pathologically heterogeneous, with the dependent lung suffering more airway collapse and disease than the nondependent lung. This finding has led researchers to believe that the optimal dose of perfluorocarbon in partial liquid ventilation should be less than the patient's functional residual capacity, if indeed the nondependent lung has normal function. In 2000, researchers tested this hypothesis in an animal study including 12 rabbits with dependent lung-dominant pulmonary injury.<sup>14</sup>

Twelve rabbits were anesthetized, and tracheostomy was performed for passage of an endotracheal tube into the trachea. Mechanical ventilation with standard settings was instituted. The animals received a warm saline solution via their endotracheal tube to induce lung injury, and they were kept in a supine position to spare the nondependent lung from injury. Partial liquid ventilation was initiated with the rabbits in positions to assure even distribution of the perfluorocarbon. Varying dosages of perfluorocarbon ranging from 3 mL/kg to 18 mL/kg were administered at 15-minute intervals.<sup>14</sup>

Peak airway pressures and inspiratory pause pressures with partial liquid ventilation were lower at doses of 3 mL/kg to 15 mL/kg, but not different at 18 mL/kg, in comparison to gas ventilation. The researchers concluded that the optimal dose of perfluorocarbon for respiratory mechanics during partial liquid ventilation was found to be less than the liquid functional residual capacity dose in a setting of acute dependent lung injury. Excess perfluorocarbon did not improve the compliance factors of the lung.<sup>14</sup>

### **Literature related to total liquid ventilation in humans**

The only reported human study using total liquid ventilation was published in 1990. The researchers in this study hoped to improve pulmonary gas exchange and mechanics in preterm neonates with severe respiratory compromise. Three immature neonates that had separately received high frequency ventilation and exogenous pulmonary surfactant for their severe lung disease were selected for the study.<sup>15</sup>

The liquid ventilation was initiated after sedation, and skeletal muscle paralysis was induced in the neonates. Conventional gas mechanical ventilation was stopped, and a gravity-driven reservoir system instilled a functional residual capacity dose (30 mL/kg) of heated, oxygenated perfluorocarbon into their lungs via the endotracheal tube. The neonates received the liquid ventilation in 2 (3- to 5-minute) cycles separated by 15 minutes of conventional ventilation. Each tidal volume of the perfluorocarbon was held in the patient's lungs for 10 seconds and then allowed to drain by gravity into another reservoir.<sup>15</sup>

Despite worsening acidosis in all 3 neonates during total liquid ventilation, each showed a marked increase in total respiratory compliance after the therapy. Peak airway pressures decreased by 30% after liquid ventilation in 2 of the neonates, and the third neonate had a 12% greater tidal volume with each breath after liquid ventilation. The patients did not survive after the liquid ventilation therapy due to the severity of their illness and their extreme prematurity; however, the researchers concluded that the observed physiological responses in the neonates to the liquid ventilation expressed the potential for the therapy to treat neonatal respiratory failure.<sup>15</sup>

### **Literature related to partial liquid ventilation in humans**

After the initial total liquid ventilation human study in 1990 was published, researchers began to realize the potential of perfluorocarbon-assisted ventilation in critically ill patients with RDS. In 1995, a team of

researchers enrolled 19 adults, children, and neonates with respiratory failure requiring extracorporeal life support (ECLS) in a study designed to measure the alveolar to arterial oxygen tension difference ((A-a)D<sub>O<sub>2</sub></sub>). The partial liquid ventilation was started 1 to 11 days after the patients were placed on ECLS. The patients each received perflubron via their endotracheal tube at 2.5 to 10 mL/kg over 5 to 15 minutes. The dose was repeated every half hour until a sustained meniscus in the endotracheal tube at the sternal level was noted. The perflubron was redosed daily for 1 to 7 days. Conventional mechanical gas ventilation with standard settings was continued throughout the study.<sup>16</sup>

The outcome measurement in this study was (A-a)D<sub>O<sub>2</sub></sub> during 10-minute periods of discontinuation of ECLS. A decrease in (A-a)D<sub>O<sub>2</sub></sub> from 590 to 471 occurred during temporary removal of ECLS during the first 3 days of partial liquid ventilation. Pulmonary compliance increased by an average of 0.18 to 0.29 mL/cm H<sub>2</sub>O per kilogram. Of the original 19 patients in the study, 14 were removed from ECLS and 11 survived to discharge from the hospital. Gas exchange and pulmonary compliance were improved during the partial liquid ventilation therapy. The data collected during partial liquid ventilation without ECLS showed that gas exchange could be sustained during partial liquid ventilation in patients with respiratory failure. The researchers did not have a control group in the study, so they could not verify that the lung function improvement was totally due to the partial liquid ventilation. The success in this initial study prompted more randomized, controlled research on partial liquid ventilation.<sup>16</sup>

Surfactant therapy also has been used to improve lung function in patients with severe RDS, but with limited success. In 1996, researchers evaluated the effectiveness of partial liquid ventilation in patients with RDS unresponsive to exogenous pulmonary surfactant. Ten premature infants with severe RDS unresponsive to surfactant who were less than 5 days old and required maximum ventilatory support were selected for this study. The infants, while receiving continual mechanical gas ventilation, had perflubron instilled via their endotracheal tubes at a rate of 1 mL/kg per minute. Perflubron was replaced as needed to maintain a meniscus in the endotracheal tube.<sup>17</sup>

Pulmonary mechanics and gas exchange values were significantly improved in the infants during the partial liquid ventilation. The arterial oxygen tension increased by 138% and the dynamic compliance by 61% during the first hour of partial liquid ventilation therapy. Eight of the infants survived to 36 weeks' gestational age. This study did not include a control

group; therefore, any generalizations are limited. However, the pulmonary function of these infants did improve with the initiation of partial liquid ventilation therapy. The researchers concluded that partial liquid ventilation can produce clinical improvement and survival in moribund infants with severe RDS.<sup>17</sup>

In 1996, researchers participated in a pilot study to evaluate the safety and efficacy of partial liquid ventilation in children with ARDS. The research took place in 8 university medical centers across the country. Ten children, ages 1 to 17 years, with a clinical diagnosis of ARDS, were enrolled in the study. During mechanical gas ventilation, the perflubron was instilled down the endotracheal tube at an initial mean dosage of 18.6 mL/kg.<sup>18</sup>

No significant improvement was found in lung mechanics after the partial liquid ventilation therapy, but gas exchange improved in 9 patients. The researchers suggested that partial liquid ventilation could be a safe therapy in treating pediatric patients with ARDS and that a randomized, controlled research study was warranted.<sup>18</sup>

A multicenter phase I-II study was launched in 1994 to ascertain the safety and efficacy of partial liquid ventilation in adult patients with ARDS that were not receiving other treatments, such as extracorporeal life support or surfactant therapy. The clinical trials were performed in 3 surgical and 1 medical intensive care unit by researchers in 4 medical centers across the country.<sup>19</sup>

Nine adult patients ages 37 to 64 years that met the study criteria for clinical diagnosis of ARDS were enrolled. The patients were receiving conventional mechanical ventilation at time of enrollment. Partial liquid ventilation was initiated and continued for up to 96 hours. The dosing of the perflubron was done in 2 phases. The first dose was given in 2.5 to 5 mL/kg increments over a 15- to 30-minute period, waiting 30 minutes between doses. Indications for redosing the perflubron included the absence of a meniscus in the endotracheal tube during transient ventilator disconnection, a tidal volume greater than 70% of baseline, and a  $\text{PaO}_2/\text{FiO}_2$  ratio less than 250. The amount for redosing was 2.5 to 5 mL/kg. As seen with previous studies, mucous plug formation was a side effect of partial liquid ventilation, and frequent suctioning was used to keep the airway clear of secretions.<sup>19</sup>

The variable endpoint for this study was the change in  $(A-a)D_{O_2}$ . During the time frame after the first dose of perflubron, a marked decrease in  $(A-a)D_{O_2}$  was noted. Significant decreases in  $\text{FiO}_2$  were observed after 48 hours of partial liquid ventilation. Seven of the 9 patients survived for 28 days after the partial liq-

uid ventilation, and 5 were discharged home. The researchers concluded that partial liquid ventilation may be performed safely with few adverse effects in adult patients with ARDS. Pulmonary gas exchange showed improvement over the 48 hours after the start of partial liquid ventilation. More randomized, controlled studies are currently in progress to continue to evaluate partial liquid ventilation therapy for patients with differing stages of respiratory dysfunction.<sup>19</sup>

The largest human study involving partial liquid ventilation in adult patients with acute lung injury and ARDS was performed at 18 medical centers across the country between July of 1995 and August of 1996. Researchers evaluated partial liquid ventilation in a prospective, controlled, randomized, exploratory clinical trial. Ninety adult patients, aged 15 to 75 years, that met the inclusion criteria based on the Murray lung injury score were enrolled in the study. These patients had  $\text{PaO}_2/\text{FiO}_2$  ratios greater than 60 and less than 300 with ARDS for less than 24 hours. Randomization was achieved based on a 3 or 6 block design within each facility and had a 2:1 ratio of partial liquid-ventilated to control gas-ventilated patients.<sup>20</sup>

The perflubron was initially given via endotracheal tube based on ideal body weight in 5 mL/kg doses over 5 to 15 minutes, waiting 5 minutes between the first and second, third and fourth, and fifth and sixth doses. The patients were evaluated every 4 hours to ensure a meniscus in the endotracheal tube during periodical disconnection from the ventilator. If no meniscus was visible, 1 to 5 mL/kg of perflubron was administered. The patients' airways were suctioned every 1 to 2 hours to remove debris. The partial liquid ventilation was performed for a maximum of 5 days.<sup>20</sup>

The primary variable evaluated at the conclusion of the study was the mean number of ventilator-free days in each partial liquid ventilation treatment group through day 28 following the first dose of perflubron. The study found a significant reduction in progression from acute lung injury to ARDS; however, no difference in gas exchange, ventilator-free days, pulmonary function, or outcome was observed when comparing the control group to the partial liquid ventilation group. A significant finding was noted in the patients aged 55 years or less. These patients experienced a more rapid weaning from the mechanical ventilator and a trend toward an increase in the 28 ventilator-free days in the partial liquid ventilation group when compared to the gas ventilation group. The researchers identified many variables that still need to be addressed with partial liquid ventilation, including optimal dosing, positioning, and ventilator management.<sup>20</sup>

## Summary

RDS is a potential complication for any patient that has suffered damage to the lungs. It continues to carry a significantly high mortality rate, in spite of multiple conventional treatments currently in use. Liquid ventilation therapy has evolved from an inconceivable notion to a potentially successful rescue treatment for critically ill patients with severe pulmonary dysfunction. The literature has shown that liquid ventilation therapy can improve lung function in certain patients and that ongoing research is needed to improve existing techniques to maximize patient outcomes.<sup>3</sup> As the research continues, more critically ill patients with severe RDS will have the opportunity to participate in this therapy in hopes of improving their chances of survival. It is through literature publications and research documentation that clinical findings with liquid ventilation therapy can be disseminated to the nursing population to increase awareness and provide education on this potentially life-saving treatment.

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