



Critical Care Therapy and Respiratory Care Section

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| Category: | Clinical |
| Section: | Aerosol Therapy |
| Title: | Aerosolization of Ribavirin in Mechanically Ventilated Patients |
| Policy #: | 07 |
| Revised: | 09/00 |

1.0. DESCRIPTION

- 1.1 Definition: Ribavirin is an antiviral drug shown to have *in vitro* activity against respiratory syncytial virus, influenza virus, and herpes simplex virus. The drug may be aerosolized via the Small Particle Aerosol Generator (SPAG-2) nebulizer developed specifically for this use. The generator produces aerosolized particles of ribavirin solution appropriate in size (95 percent of nebulized particles are less than five microns in diameter) for delivery to the pulmonary site of infection.
- 1.2 Indications: The efficacy of aerosolized ribavirin therapy for mechanically ventilated patients remains controversial. Current FDA approval indicates its use in ventilated patients with diagnosed respiratory syncytial virus pneumonia only. However, ribavirin aerosolization may be indicated for patients with respiratory failure of another viral origin who are not responding to other therapies. Aerosolization of ribavirin in a mechanically ventilated patient carries with it a number of risks: these must be carefully considered prior to initiation of therapy (see 1.4 Complications and 1.6 Adverse Reactions).
- 1.3 Contraindications:
 - 1.3.1 Ribavirin is contraindicated in female patients who are or may become pregnant, or who are breastfeeding during exposure to the drug. Prior laboratory studies show there may be some potential for teratogenic effects from the drug.
 - 1.3.2 Aerosolization of ribavirin may be contraindicated in patients with chronic cardiopulmonary diseases such as asthma and chronic obstructive pulmonary disease due to the potential for bronchospasm with inhalation of the drug.
- 1.4 Complications:
 - 1.4.1 There exists a potential for clogging of the expiratory limb of the ventilator circuit with precipitated drug. It is essential that the procedure for proper set-up and maintenance of the ventilator circuit during ribavirin therapy be strictly followed, and that the ventilator be monitored appropriately for increases in expiratory resistance.

- 1.4.2 The drug may precipitate in the artificial airway or the patient's airways causing mucus plugging, swelling of secretions, and/or defects of oxygenation and ventilation. Careful attention to secretion characteristics and good bronchopulmonary hygiene is imperative.
- 1.4.3 The aerosolized particles of ribavirin may be irritating to some patients causing bronchospasm.

1.5 Precautions:

- 1.5.1 Health care personnel who are pregnant or breastfeeding or who may become pregnant in the near future should avoid caring for patients who are undergoing ribavirin therapy. Titers of ribavirin in the blood are still measurable even four weeks after administration of the drug.
- 1.5.2 Aerosolization of ribavirin should be performed in a negative flow isolation room to minimize the risk of potential effects to other patients, health care personnel, and others. Additionally, Clinical Center policy recommends that drug therapy should be administered during the hours of 7:00 pm and 7:00 am.
- 1.5.3 Appropriate protective clothing should be worn by all persons entering the patient's room during ribavirin aerosolization (see 2.0 Equipment). When the ventilator circuit is broken to allow for manipulations to the system, or if the patient requires suctioning, the SPAG-2 should be turned off and safety goggles worn to minimize the potential effects ribavirin exposure. It is recommended that an in-line suction catheter be placed into the patient's circuit prior to the initiation of therapy to further reduce exposure.

1.6 Adverse Reactions and Interventions

- 1.6.1 If an increased expiratory resistance is noted during ventilator monitoring, i.e., the expiratory phase of the respiratory cycle shows a noticeable slowing, the end expiratory pressure level shows an increase, audible signs of increased expiratory resistance are heard, or the patient exhibits signs of an increased expiratory work of breathing, discontinue ribavirin therapy and notify the physician. Do not resume ribavirin aerosolization until completely new ventilator circuitry can be installed.
- 1.6.2 If the patient exhibits signs of bronchospasm, a trial of bronchodilator therapy may be appropriate. Persistent wheezing associated with defects in oxygenation and/or ventilation should be assessed relative to the indications for continued ribavirin aerosol therapy.
- 1.6.3 Anemia has been associated with ribavirin therapy. Patients should be monitored for a decrease in the red blood cell count throughout therapy.
- 1.6.4 Health care professionals who are particularly sensitive to the drug's aerosolization, either in exhibiting airway hyperreactivity, eye irritation, or who exhibit signs of rash as a result of handling the

drug, should avoid caring for patients undergoing ribavirin therapy. Proper attire (see 2.0 Equipment) should be worn whenever the drug is handled in any way or when entering a room during aerosol therapy.

2.0 EQUIPMENT

- 2.1 Negative flow isolation room
- 2.2 Siemens 300 ventilator
- 2.3 SPAG-2 nebulizer
- 2.4 Oxygen source gas hose
- 2.5 Disposable ventilator circuit
- 2.6 Disposable corrugated tubing
- 2.7 Three disposable filters
- 2.8 Two T-piece adapters
- 2.9 One one-way valve
- 2.10 Miscellaneous adapters for connections of one-way valve and filters
- 2.11 Water column relief valve
- 2.12 Wright respirometer
- 2.13 Ribavirin solution (as prepared by the pharmacy)
- 2.14 Latex gloves
- 2.15 Particulate respirator or HEPA filter mask
- 2.16 Safety goggles
- 2.17 “Aerosol Therapy in Process” sign

3.0 PROCEDURE (See attached diagram)

- 3.1 Nebulizer assembly:
 - 3.1.1 Pour the ribavirin solution into the nebulizer reservoir.
 - 3.1.2 Insert the nebulizer stem (with three tubings attached) into the swage fitting on the nebulizer cap, and tighten.
 - 3.1.3 Place the nebulizer cap (with gasket in place) onto the nebulizer reservoir, and twist clockwise until sealed. Be certain that the nebulizer cap is tight to avoid leakage of solution during therapy.

Ensure that the nebulizer tubes are not sitting flush against the bottom of the reservoir.

- 3.1.4 Place the assembled nebulizer into the SPAG-2 housing, and snap it into place in the bracket.
 - 3.1.5 Connect the drying air flow (black hose) quick coupling to the larger fitting on the cap. Connect the nebulizer air flow (blue hose) quick coupling to the smaller fitting on the cap. Each of these hoses should be pressed into position while twisting until they “snap” into place.
 - 3.1.6 Insert the drying air chamber into the side port of the SPAG-2 housing, and press it firmly onto the nebulizer cap outflow port. The flow direction arrow must point away from the nebulizer.
- 3.2 Inspiratory limb assembly:
- 3.2.1 Cut the inspiratory side of the patient ventilator circuit an appropriate number of segments from the wye (see the attached Ribavirin Equation Sheet and Appendix 1), and insert the T-piece here.
 - 3.2.2 Attach the one-way valve to the side port of the T-piece using the appropriate adapters.
 - 3.2.3 Connect a length of corrugated tubing from the one-way valve to the side port of the SPAG-2 drying chamber.
 - 3.2.4 Immediately after the outflow of the drying chamber, attach another T-piece and a length of corrugated tubing to accommodate the water column relief valve.
 - 3.2.5 Attach the opposite end of the corrugated tubing to the port on the water column relief valve marked “INLET.”
 - 3.2.6 Attach an additional length of corrugated tubing to the outlet port.
 - 3.2.7 Attach a filter to the end of this.
- 3.3 Expiratory limb assembly:
- 3.3.1 Insert two filters into the circuit just proximal to the heated Star filter. Ensure that a water trap is located proximally to the filters to prevent excess pressure buildup from water in the filters.
- 3.4 Oxygen source gas assembly:
- 3.4.1 Connect an oxygen source gas hose from a flowmeter to the source gas pressure inlet on the front of the SPAG-2.
- 3.5 Operating procedure for non-heated wire circuits for use with volume cycled ventilator modes.

See SPAG-2 Instructions for use for specific instructions for ribavirin aerosolization when using a heated wire circuit and/or a pressure cycled ventilator.

- 3.5.1 Post the “Aerosol Therapy in Process” sign on the patient’s **closed** door with the appropriate hours of ribavirin aerosolization clearly documented. This step must be completed prior to turning on the SPAG-2.
- 3.5.2 Fill the water column relief valve with enough water to exceed the end expiratory pressure level in the patient-ventilator system by 2-5 cm H₂O. This pressure differential must be maintained throughout therapy. When the water pressure level is appropriate, the water will bubble during the inspiratory phase of the ventilator and cease bubbling during the expiratory phase. Consult the SPAG-2 Instructions for Use for specific instructions for troubleshooting the relief valve (pg. 19).
- 3.5.3 Turn on the flowmeter to flush.
- 3.5.4 Adjust the source gas pressure gauge on the front of the SPAG-2 to read 26 PSI on the pressure manometer.
- 3.5.5 Turn the nebulizer flowmeter to 6-10 LPM. The nebulizer output will determine the correct setting. During the course of nebulization the volume of solution should be noted and the flow adjusted accordingly. Optimally, the solution should be nebulized at a rate of 12.5-15.0 ml/hour. Additionally, if it is noted that ribavirin solution is leaking from the nebulizer, stop treatment to ensure that the nebulizer cap is tight.
- 3.5.6 Turn the drying air flowmeter OFF. During nebulization of ribavirin through a mechanical ventilator, no flow is necessary for the drying chamber; if the drying air flowmeter is utilized, the flow characteristics may cause a defect in drug delivery.
- 3.5.7 Confirm that the nebulizer is producing a good aerosol by visualizing the three “spray spots” on the wall of the reservoir. These should be approximately one inch in diameter. Refer to the SPAG-2 Instructions for Use for troubleshooting tips.
- 3.5.8 During aerosolization, the exhaled tidal volume must be measured and recorded every two hours with a Wright respirometer in the expiratory limb of the circuit. The digital display on the 300 for exhaled tidal volume will be falsely high due to the addition of the continuous flow from the SPAG-2 unit.
- 3.5.9 Maintain the humidifier temperature between 33 and 37 degrees C. to minimize precipitation of the ribavirin.
- 3.5.10 The filters must be changed every two hours as follows:
 - 3.5.10.1 Discard the filter closest to the patient.
 - 3.5.10.2 Move the filter occupying the rear position to the front (closest to the patient).

3.5.10.3 Place a new filter in the rear position.

3.5.11 Discard the disposable circuit components for ribavirin nebulization after termination of therapy each day, and replace the ventilator circuit and the Star filter. Wipe down the SPAG-2 unit with alcohol.

4.0 POST PROCEDURE

4.1 Disposal of ribavirin solution:

4.1.1 Any ribavirin solution which has not been completely nebulized at the termination of therapy, or solution recalled due to the discontinuance of therapy should be returned to the pharmacy in its original container inside of a Ziploc bag so that appropriate disposal may occur. Do **not** dispose of the solution on the unit.

4.2 Equipment processing:

4.2.1 Disassemble the nebulizer and drying chamber parts, rinse in water, and pasteurize. It is not necessary to clean the water column relief valve while administering therapy to the same patient. However, the water column must be changed daily. After therapy has been completed in a patient, process the relief valve in the same fashion as the other equipment.

4.2.2 When it has been determined that no further therapy will be delivered, wipe the SPAG-2 housing with Dispatch prior to removing it from the patient's room.

5.0 CHARTING

5.1 Record the initiation and discontinuance of therapy each day on the "Comments" side of the Continuous Ventilation Record. This note should include an evaluation of the patient's tolerance of the therapy, any adverse effects and action taken, and the efficiency of nebulization. The flowrate used for nebulization should also be noted.

6.0 REFERENCES

6.1 SPAG-2 Instructions for Use.

6.2 Virazole (ribavirin) Prescribing Information Sheet.

6.3 Communication with ICN Pharmaceuticals, Inc. pharmacological and technical support [1(800)572-7400].

6.4 Clinical Center Policy: Guidelines for Preparation and Administration of Aerosolized Ribavirin.

SIGNATURE: _____
Assistant Section Chief, CCTRCS, CCMD

DATE: _____

SIGNATURE: _____
Section Chief, CCTRCS CCMD

DATE: _____

SIGNATURE: _____
Medical Director, CCTRCS CCMD

DATE: _____

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