Ribavirin: The Need for Exposure Precautions

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Ribavirin is used in the treatment of respiratory syncytial virus (RSV) in high-risk patients, including patients who have undergone hematopoietic stem cell transplantation, to reduce mortality from RSV pneumonia. It is classified as a hazardous drug with potential for carcinogenicity and teratogenicity. Very few recent studies have examined the risk of exposure, and recommendations for exposure precautions are lacking. Administration should include the use of personal protective equipment and terminal cleaning of the patient room after each administration. This article examines ribavirin use among patients who have undergone hematopoietic stem cell transplantation and have RSV-related pneumonia and explores safety considerations for staff. Nursing leaders on a hematopoietic stem cell transplantation unit addressed gaps in knowledge about ribavirin therapy, and completed a review of the hospital’s ribavirin policy, which led to policy revisions, increased knowledge about the safe administration of ribavirin, and improvements in staff and patient education.

Respiratory syncytial virus (RSV) is a common, community-acquired respiratory virus that causes acute respiratory tract infections (Avetisyan, Matsu-son, Sparrelid, & Ljungman, 2009). RSV infections typically occur in the fall, winter, and spring, with the season lasting about four months (Centers for Disease Control and Prevention [CDC], 2013). RSV can affect individuals of all ages, and almost all children by the age of two years have been infected with RSV (CDC, 2013). In the general population, RSV causes mild upper respiratory infections. Typically, only a small percentage of individuals develop severe disease (CDC, 2013). Those at highest risk include premature infants and those with compromised immune systems (CDC, 2013). The virus can cause severe lower respiratory tract infections or pneumonia that is associated with significant morbidity and mortality in those who are immunocompromised (Avetisyan et al., 2009).

In the hematopoietic stem cell transplantation population, RSV can occur in 3.5%-35% of patients during RSV season (Avetisyan et al., 2009). Patients undergoing transplantation have impaired T-cell immunity, which increases their risk of acquiring RSV and also decreases their ability to clear the virus, leading to more severe infections and longer duration of infections (Shah & Chemaly, 2011). Risk factors for RSV in the transplantation population include male gender, allogeneic transplantation, myeloablative conditioning, cyto-megalovirus seropositivity, lymphopenia, and those who have not yet engrafted (Hynicka & Ensor, 2012). RSV-related lower respiratory tract infections are associated with airway inflammation, necrosis, edema, and increased mucus production leading to pulmonary congestion and productive cough (Latchford & Shelton, 2003). RSV infections in this population also can cause delayed engraftment or graft failure (Hynicka & Ensor, 2012). Because of the nonspecific symptoms that occur with RSV, diagnosis can be difficult and often delayed. Diagnosis is established using laboratory testing, with viral culture being the gold standard for detection (Hynicka & Ensor, 2012).

Prevention

RSV is spread through large droplet aerosols (Hynicka & Ensor, 2012), and the virus can shed for up to 22 days, increasing the risk of transmission (Latchford & Shelton, 2003). Prevention includes avoiding exposure, with hand washing being the best way to minimize transmission to others (Hynicka & Ensor, 2012). Other prevention strategies include strict isolation policies and the use of prophylactic medications to prevent infections.
Implications for Practice

- Increase safety related to ribavirin administration through awareness of safe-handling guidelines.
- Incorporate multidisciplinary coordination of ribavirin treatment into workflow.
- Prevent spread of respiratory syncytial virus by becoming familiar with proper isolation techniques in inpatient and outpatient settings.

Isolation

In healthcare settings, using isolation precautions is important until symptoms have cleared and the virus is no longer detectable (Latchford & Shelton, 2003). Isolation precautions can be difficult to follow in outpatient treatment areas; therefore, having procedures in place is important to minimize transmission in these areas. These should include bypassing waiting rooms, moving patients directly into treatment rooms, and implementing droplet precautions if patients have respiratory symptoms (CDC, 2011). Treatment areas should be cleaned appropriately between each patient. Patients should be given instructions to wear masks when traveling to healthcare settings, as well as to minimize close contact with other patients and visitors (CDC, 2011). This strategy is the current practice in the authors’ clinic. This clinic also follows hospital guidelines during flu season, including the practice of universal masking for all staff and visitors entering the rooms or treatment areas of any adult patient undergoing stem cell transplantation. Visitors also are instructed to avoid the inpatient and outpatient areas if they have any respiratory symptoms to help prevent the spread of infection.

Palivizumab

Palivizumab is a monoclonal antibody used to prevent RSV infections and has been shown to reduce hospitalization rates in infants when used prophylactically (Shah & Chemaly, 2011). This transplantation center does not currently use palivizumab in the adult hematopoietic stem cell transplantation population; however, it has been shown to be well tolerated in this population (Shah & Chemaly, 2011). Further studies need to be done because no randomized trials in this group have evaluated efficacy (Shah & Chemaly, 2011).

Treatment

Treatment strategies for RSV include antiviral therapy, IV immunoglobulin, monoclonal antibodies, and steroids, which often are used in combination with each other (Hynicka & Ensor, 2012). The drug of choice, ribavirin, is a known teratogen and carcinogen. When administered in an aerosolized mode, a number of safety issues need to be considered. Ribavirin is a nucleoside analog that has antiviral activity against RNA viruses and is considered to be the treatment of choice (Hynicka & Ensor, 2012). A recent retrospective analysis of RSV infections in patients undergoing transplantation found that the use of aerosolized ribavirin significantly reduced the risk for progression of upper respiratory tract infections to lower respiratory tract infections and decreased mortality (Shah et al., 2013).

Available in three forms—aerosolized, IV, and oral—the aerosolized form is the preferred treatment route because it decreases the potential systemic toxicities that can occur with other forms (Hynicka & Ensor, 2012). Side effects can include nausea, headache, bronchospasm, rash, conjunctivitis, and anemia (Krilov, 2002). Ribavirin typically is delivered via a small particle aerosol generator for 12-18 hours per day continuously or on an intermittent dosing schedule (Hynicka & Ensor, 2012). If administering the aerosolized form, patients must be placed in a negative pressure room to reduce second-hand exposure.

Ribavirin is teratogenic in animal studies; however, data in humans are limited. Adverse outcomes to animal fetuses were found in hamsters, rats, and rabbits, but not in studies of primates in nonaerosolized settings (Krilov, 2002). To date, no documented adverse pregnancy outcomes in humans have been associated with secondhand exposure. Studies examining healthcare worker exposure risks have found minimal absorption by healthcare workers; however, because ribavirin can be detected in the environment after administration and studies have been unable to show that a 100% safety guarantee exists, concerns related to exposure continue and precautions must be taken (Krilov, 2002). The lack of recent studies examining the risk of healthcare workers exposed to ribavirin is concerning, and a need exists to increase the available data to ensure that healthcare workers are protected.

Recommended Safety Precautions for Nursing Staff

To date, no nationally recognized standards for safety precautions exist for ribavirin use. However, because of the potential for carcinogenicity and teratogenicity when administering ribavirin, healthcare workers must be mindful of reducing the risk of secondhand exposure. During administration of aerosolized ribavirin, healthcare personnel should not enter the patient’s room unless necessary, and the room should be cleaned one hour after each administration to remove any residue from the aerosolized drug (Hynicka & Ensor, 2012). However, if staff must enter the room, they should wear protective personal equipment, including gowns, gloves, shoe covers, and powered air purifying respirator masks (Latchford & Shelton, 2003).

Safety Concerns

Historical practice on the authors’ hematopoietic stem cell transplantation unit mandated that staff members who are pregnant, planning to become pregnant in the next six months, or planning to impregnate a partner in the next six months were not allowed to enter the room during treatment. This caused significant stress because the majority of the staff were women of child-bearing age; therefore, care for patients

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with RSV was limited to older staff members. Although older staff did not have concerns regarding the teratogenicity of the drug, they were concerned with the carcinogenic potential. To address staff concerns related to the safety of ribavirin administration, a work group was formed and diverse stakeholders were consulted. Staff members were interviewed, and their questions and concerns were summarized. A literature review provided data about exposure risks of healthcare workers during ribavirin administration. The hospital's policy was examined for gaps in information or the need for clarification. Hospital safety officers were consulted concerning risk for exposure, testing for possible exposure, and to clarify information in the policy.

Interventions

The findings from the work group were used to revise the hospital policy and online learning modules for staff. Changes in practice were designed to protect healthcare workers, patients, and visitors (see Figure 1). The revised policy described, in detail, drug administration, preparation of the patient for ribavirin treatment, and standards for cleaning the environment after each administration. Clarification for the disposal of residual drug after treatment was obtained from the safety office, which recommended that, despite the lack of U.S. Environmental Protection Agency regulations for ribavirin disposal, the drug should be treated like other hazardous drugs and discarded in hospital-designated waste containers. Dialogue with the safety office also led to the introduction of a new protocol to outline a procedure for analyzing ribavirin exposures. This protocol includes observing the preparation of the solution and evaluating the administration procedure to identify potential exposure. Wipe tests will be instituted to measure the existence of residual drug in a patient’s room after cleaning occurs. The wipe tests will use 25 mm glass fiber filters in a defined area of 100 cm² and will be analyzed by Analytics Corporation. Because no regulatory standards exist for airborne or surface contamination after ribavirin administration, the information will be compared against a recommendation by the California Department of Health Services, which suggested a limit of 2.7 ug/m³ as an eight-hour, time-weighted average (Charney, 1999). Data from these observations will be used to determine the need for changes to current cleaning techniques, as well as to determine risk of secondhand exposure to healthcare workers in this setting. Following the risk assessment, the safety office will communicate its finding related to potential exposure to the staff.

With the help of the work group, a standard is now in place for multidisciplinary coordination for all patients who are starting ribavirin treatment that includes nurses, physicians, respiratory therapists, and support staff to plan the initiation of treatment and identify who is responsible for each aspect of the treatment. This includes the creation of a cleaning schedule during the treatment period to identify who is responsible for the cleaning and to ensure that all shifts are covered. Education for the staff focused on the changes to the protocol that were made and focused on answering the questions that were raised prior to the protocol revision. This education was presented at unit staff meetings, oncology journal club, and oncology grand rounds, and was shared with other units that administer ribavirin in the hospital. The hospital’s online learning module was updated to be more comprehensive and include the updated information from the revised protocol. In addition, the hospital’s patient education handout was updated to reflect current practice. Ribavirin education in the cancer center has become standard during orientation and is given annually to all staff. The nursing staff need to continue taking the initiative to ensure safe practice related to the administration of ribavirin. With each administration, nurses should assess for safety issues and report any issues to the safety office for review. As the use of alternate routes for ribavirin administration becomes more popular, safety related to these practices should be assessed fully prior to the start of therapy.
Conclusion

Safe ribavirin administration is the shared responsibility of a multidisciplinary team, including nurses, physicians, respiratory therapists, and environmental services. Collaboration among all team members ensures coordination of care and can reduce staff-related stress and potential safety risks for all involved. As the National Institute for Occupational Safety and Health’s list of hazardous drugs continues to expand, so must the emphasis on safe-handling practices (Nixon & Schulmeister, 2009). Historical data suggest that ribavirin is a carcinogen and teratogen; however, data are limited and research is needed to determine the nature of exposure risks for diverse hospital staff given contemporary use of aerosolized preparations of this drug. This article reviewed data regarding the safety of ribavirin administration and one institution’s response to the need for standards of patient care, drug administration, and environmental safety.

References


