Antineoplastic Chemotherapy: Infusion Reactions, Cytokine Release Syndrome

Site Applicability

PHC

Practice Level

Basic Skill: Registered Nurses

Need to Know

There are 3 different kinds of reactions that a person may experience as a result of parenteral cancer chemotherapy drug treatment:

1. Allergic Reactions
   - Hypersensitivity
   - Anaphylaxis
2. Cytokine Release Syndrome
3. Tumor Lysis Syndrome

The three kinds of reactions are discussed in separate practice standards – this standard discusses cytokine release syndrome.

Cytokine Release Syndrome

Cytokine Release Syndrome (CRS) is an inflammatory symptom complex that occurs in association with the administration of parenteral T-lymphocyte engaging therapies such as rituximab (or another monoclonal antibody).

When these agents are administered, the body's immune system is activated:

- Lymphocytes begin to proliferate (particularly T-lymphocytes)
- Inflammatory cytokines, small proteins used in cell signaling, are released. Sometimes there is an overproduction of cytokines and the inflammatory response flares out of control.

The incidence and severity of CRS depends on the:

- Inducing agent
- Magnitude of immune cell activation
- Disease burden – presumed to be due to increased lymphocyte activation. Patients with greater than 50×10^9/L circulating lymphocytes have increased rates of CRS symptoms.

Symptoms

The symptoms of CRS include:

Constitutional	▪ Fever ± rigors ▪ Malaise ▪ Fatigue ▪ Myalgias and arthalgias
Skin	▪ Rash
Gastrointestinal	▪ Nausea ▪ Vomiting ▪ Diarrhea
Respiratory	▪ Dyspnea ▪ Tachypnea ▪ Hypoxemia
Cardiovascular	▪ Tachycardia ▪ Hypotension ▪ Widened pulse pressure
Renal	▪ Elevated creatinine
Hepatic	▪ Hyperbilirubinemia
Neurologic	▪ Headache ▪ Confusion; delirium; word finding difficulty ▪ Hallucinations ▪ Tremor

Symptoms indicate that the patient's immune system is responding to the treatment and typically develop within 30 minutes to two hours after the initiation of the infusion, although symptoms may be delayed for up to 24 hours. The majority of reactions occur after the first or second exposure to the agent, but between 10 and 30 percent occur during subsequent treatments. In general, the likelihood of the patient experiencing CRS declines with each subsequent course of therapy.

The majority of symptoms are mild and flu-like, however, some patients may experience potentially life-threatening inflammatory syndrome complications, including hypotension, pulmonary edema, and coagulopathy resulting in multi-organ system failure.

Risk Factors

The risk for CRS increases in the following situations:

- First exposure/infusion to T-lymphocyte activating drugs (up to 77% of patients develop a reaction during initial exposure to riTUXimab)
- Chemotherapy-naïve patients
- Patients with lymphoma or leukemia, especially those with high circulating lymphocyte counts
- Patients more than 60 years old

Guideline

Preparedness

1. Equipment

All care settings where patients receive chemotherapy drugs should ensure that there is easy and ready to use access to:

- Oxygen
- Ambu-bag (resuscitation bag-valve-mask)
- Suction
- IV access, supplies, and fluids

2. Medications

- Sometimes it is difficult to distinguish between a hypersensitivity reaction and CRS – ensure that the preprinted prescribers orders for hypersensitivity reactions have been completed and are in the patient's chart (PH581 Hypersensitivity Reaction Orders for Chemotherapy)
- Ensure emergency medications are available on the unit
- Ensure that antihistamines are available on the unit (diphenhydramine, ranitidine)

3. Patient Health History

Prior to the initiation of treatment with any chemotherapy or biotherapy drug:

- Obtain a detailed history of allergies and reactions to previous drug treatment – *a previous history of reactions, even to structurally unrelated drugs, increases the patient's risk of subsequent reactions*.
- Ensure that the caution sheet is updated, completed and faxed
- Complete a thorough baseline assessment including:
    - Vital signs
    - Oxygen saturation
    - Breath sounds
    - Presence of any rashes

4. **Prophylaxis**

   Pharmacologic prophylaxis with antihistamines and acetaminophen, with or without glucocorticoids, is recommended.

Monitoring

Patients should be monitored with constant visual observation during initiation, at all dose increases and for 30 minutes after infusion is completed.

Treatment and Management

a. Stop infusion and switch to emergency IV tubing
b. Infuse sodium chloride 0.9% IV 100 mL/hour
c. Notify physician
d. Administer anti-histamines as ordered – usually diphenhydrAMINE 25 to 50 mg IV direct or IM if IV access no longer available
e. Monitor vital signs Q5 minutes until stable
f. Observe the patient until symptoms resolve, which usually occurs within 30 minutes
g. Resume infusion (usually at a slower rate) as per physician's orders
h. Administer additional antihistamines as ordered

The symptoms of CRS are an indicator of response in the setting of immune-based therapies. It isn't known to what extent the cytokines mediating the symptomology are required for antitumor effects, so therefore, the goal of management and treatment of CRS is to control the symptoms and prevent life-threatening toxicity, while maximizing the potential for antitumor effects.

Documentation

1. Nursing documentation as per unit procedure: record assessment, nursing interventions, patient's response and vital signs
2. Medication Administration Record—any medications given

Patient and Family Education

Patients and families must be informed of:

- Why the patient is at risk for CRS
- Potential side effects of the drugs, including the risk of a reaction and the associated symptoms
- The rationale for the implemented preventative measures
- The symptoms of CRS. It is essential that patients understand the importance of reporting any of the following symptoms:

▪ Dyspnea; increase in respiratory rate ▪ Heart racing ▪ Confusion; word finding difficulties; hallucinations ▪ Fever ± rigors ▪ Rash ▪ Headache	▪ Tremor ▪ Malaise; fatigue ▪ Myalgias and arthalgias ▪ Nausea, vomiting ▪ Diarrhea

Ensure that patient and family questions have been answered and that their concerns have been addressed. Provide emotional support to the patient and family.

Related Documents

1. B-00-13-10153– Chemotherapy: Hypersensitivity (Allergic) Reaction
2. B-00-13-10202 - Chemotherapy – Infusion Reactions: Tumor Lysis Syndrome
3. B-00-13-10148 – Administration of Parenteral Antineoplastic Drugs (Hematology)
4. BD-00-12-40091 - Anaphylaxis: Initial Emergency Treatment
5. PHC-PH581 –Chemotherapy Hypersensitivity Pre-Printed Orders

References

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3 Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 (2017). Retrieved May 31, 2018 from

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