Who Needs a Therapeutic Phlebotomy?

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Many oncology practices treat patients with benign and malignant hematologic diagnoses. As a result, oncology nurses often are required to care for these patients. One common procedure nurses perform is therapeutic phlebotomy, where about 500 ml of blood is removed through a large-bore needle over 15–30 minutes. The procedure is ordered as a treatment for hereditary hemochromatosis, polycythemia vera, and secondary polycythemia. Before initiating the procedure, nurses must be aware of a patient’s diagnosis, baseline hemoglobin, hematocrit, ferritin, and therapeutic end points. Reviewing these diagnoses will help nurses understand why phlebotomy is an important part of treatment.

Hereditary hemochromatosis is characterized by the abnormal progressive absorption of dietary iron in the intestines, which is then stored in the liver, heart, and other organs. Inherited as an autosomal recessive disorder, the most common genotype that causes hereditary hemochromatosis is HFE C282Y/C282Y (Adams & Barton, 2010). Signs and symptoms often appear in adults aged 50–69. Complications in the liver include fibrosis, cirrhosis, complete liver failure, or hepatocellular cancer. Damage to other organs from iron overload may result in diabetes mellitus, cardiomyopathy, gonadal dysfunction, arthritis, and dementia. Excess iron storage is thought to be toxic to cells. Increased amounts of free radicals are generated that can damage cellular and subcellular membranes. In this disease, the goal of treatment with phlebotomy is to deplete enough iron to normalize the body’s iron stores and prevent or minimize organ dysfunction (McLaren, 2002).

Diagnosis of hereditary hemochromatosis is based on symptoms and laboratory studies. If the patient is asymptomatic, suspicion of iron overload may first be raised when laboratory tests reveal elevated hemoglobin, hematocrit, and ferritin. Normal ferritin in men is about 18–464 mg/dl; for women it ranges from 12–262 mg/dl. Patients with this disorder may present with readings as elevated as 1,000–5,000 mg/dl. Iron saturation also is typically elevated (normal is 15%–50%). A definitive diagnosis can be made on the basis of genotyping for the HFE mutation. A positive result suggests testing of first-degree relatives (particularly siblings and children) (Schriër & Bacon, 2009). A patient suspected of having iron overload but who is negative for the common genetic variants associated with the disease may undergo a specialized liver magnetic resonance imaging scan to visualize liver iron stores. If this imaging procedure is not available, a liver biopsy may be performed.

Treatment of iron overload is based on phenotype (high ferritin and evidence of elevated iron stores), not genotype (Adams & Barton, 2010). Genotype is a pair of genes for a particular characteristic or protein, whereas phenotype is the observable expression of a trait or characteristic that is visible or biochemically detectable (Lashley, 1998). Phlebotomy is the most effective method to deplete iron stores in a patient that is not anemic. Each phlebotomy removes about 500 ml of blood, which contains 200–250 mg of iron. This process then depletes the body’s iron stores by mobilizing approximately the same amount of iron out of the liver. The goal of treatment is to remove the circulating iron as quickly and safely as possible. Depending on the size and overall condition of the patient, phlebotomy can be performed once or twice weekly. The end-point goal of treatment is a serum ferritin in the range of 50–100 mg/dl. Therefore, the length of treatment depends on the baseline level. To prevent anemia, a hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy. Parameters ordered by the provider to hold the treatment will be compared with the most recent hemoglobin and hematocrit usually is drawn before each phlebotomy.
and uncooked seafood. Chelation therapy with deferoxamine is rarely used in hereditary hemochromatosis (only if the patient cannot tolerate phlebotomy) (Schrier & Bacon, 2009).

Polycythemia Vera

Polycythemia vera is defined as a myeloproliferative disorder with clonal proliferation of myeloid cells with varying degrees of maturity and efficiency (Tefferi, 2010). The principal finding is an increase in the number of red blood cells (erythrocytosis), hemoglobin, and hematocrit. An increase in white blood cells and platelets with splenomegaly also may be seen. The peak age range is 50–70 years.

Blood becomes viscous if a patient has too many circulating red blood cells. This creates diminished oxygenation to the tissues. Patients may then present with headaches, dizziness, tinnitus, visual changes, and weakness or, even more seriously, with an arterial or venous thrombus or embolus. Other symptoms may include bleeding, pruritus, peptic ulcer disease, hypertension, gout, and erythromelalgia (a unique syndrome seen in patients with polycythemia vera and essential thrombocythemia char-

acterized by red, painful, burning toes, feet, or fingers). Mortality in patients with polycythemia vera results from thrombosis or embolus, transformation to myelofibrosis or myeloid metaplasia, transformation or acute myeloid leukemia or myelodysplastic syndrome, non-hematologic malignancy, or hemorrhage (Tefferi, 2010).

Diagnosis is made on the basis of symptoms and laboratory studies. In some cases, bone marrow biopsy and aspirate may be conducted. Common laboratory results include a hematocrit higher than 55%–60% (normal is 39%–50% for men, 36%–44% for women), leukocytosis, thrombocytosis, and an elevated vitamin B12 level. More than 90% of patients exhibit a mutation in the JAK2 kinase gene. Specifically this point mutation, called JAK2 V617F, permanently turns on pathways implicated in erythropoietin receptor signaling (Finazzi & Barbui, 2007; Vannucchi, Guglielmelli, & Tefferi, 2009). Bone marrow biopsy typically shows hypercellularity and hyperplasia of all cell lines with low or absent iron stores. Bone marrow fibrosis may be seen.

The treatment goal is to minimize the clinical, laboratory, and long-term complications. The mainstay of treatment in low-risk patients with polycythemia vera is phlebotomy: reduction of the hematocrit is thought to reduce the patient’s risk for thrombotic events (Vannucchi et al., 2009). The target usually is a hematocrit of less than 45% in men and less than 42% in women. Other treatments are individualized and may include hydroxyurea or low-dose aspirin. The use of alpha interferon may be needed for patients who have refractory pruritis or are refractory to other medications. Patients with gout will need allopurinol. Less often, radioactive phosphate p32 may be used (Tefferi, 2010).

Secondary Polycythemia

Many entities other than polycythemia vera may cause abnormally high red blood cells, hematocrit, and hemoglobin. Relative polycythemia results in depletion of extracellular fluid volume from vomiting, diarrhea, caffeine, diuretics, or smoking (Tefferi, 2007). However, the major cause of true secondary polycythemia is the stimulation of erythropoiesis, usually from overproduction of erythropoietin, which is not a finding in polycythemia vera. Increases in erythropoietin are driven by erythropoietin-secreting tumors, hypoxia, and miscellaneous causes. Erythropoietin-secreting tumors are renal cell carcinomas, hepatocellular carcinoma, hemangioblastoma, and uterine fibroids. The most common hypoxemic condition is chronic lung disease in addition to right to left cardiac shunt, obstructive sleep apnea, obesity, living at a high altitude, and chronic carbon monoxide exposure. Other practices that increase erythropoietin levels are using androgens such as testosterone, taking anabolic steroids, or doping with erythropoietin injections or packed red blood cells (Hocking, 2002; Tefferi, 2007).

Patients may present with complaints of headaches, visual changes, dizziness, tingling, and confusion. Diagnosis is made on the basis of laboratory studies, a meticulous history, and physical examination. Expected laboratory results include elevated red blood cells, hematocrit, hemoglobin, and erythropoietin levels and a negative JAK2 mutation. Abnormal blood chemistries and renal and liver functions may help determine the cause. Taxi drivers, underground parking attendants, or people exposed to faulty ventilation from fireplaces or furnaces are subject to chronic carbon monoxide inhalation. A blood carboxyhemoglobin value greater that 5% suggests polycythemia related to carbon monoxide poisoning (Tefferi, 2007). Physical examination includes a head-to-toe assessment with attention to vital signs, oxygen saturation, respiratory pattern, neurologic status, and vision. Evaluation for heart murmurs, plethora, cyanosis, hepatosplenomegaly, or Cushçingoid syndrome should be included.

The best treatment for secondary polycythemia is to remove the cause or to change a patient’s behavior toward the cause of secondary polycythemia. For example, erythropoietin-secreting tumors should be excised or otherwise treated, a smoker should stop smoking, an obese patient should try to lose weight, a patient with sleep apnea should use a continuous positive airway pressure machine (usually after evaluation in a sleep study), and anyone taking anabolic steroids or self-injecting erythropoietin is best served by quitting these practices (Hocking, 2002). As for patients with chronic lung disease or other clinical causes of hypoxia, a
limited phlebotomy program may be needed in an effort to reduce symptoms. Most physicians will use a higher hemoglobin or hematocrit threshold to start a program for these patients compared to individuals with polycythemia vera. One recommendation is to conduct a phlebotomy in a man only when the hemoglobin level is higher than 18.5 mg or the hematocrit level is higher than 52%. The respective levels for women are higher than 16.5 mg or higher than 48% (Tefferi, 2007). The number and frequency of phlebotomies is individualized based on improvement in the patient’s symptoms and the hemoglobin and hematocrit levels. Whether phlebotomy reduces the risk of adverse events in patients with secondary polycythemia is unknown.

Figure 1 reviews the nursing responsibilities and points of care when performing a phlebotomy. The major side effect seen with this procedure is hypovolemia accompanied by hypotension, rapid pulse, and light-headedness. Ways to prevent hypovolemia include instructing the patient to maintain ample hydration before and after the procedure, instructing the patient to change position slowly after the procedure, and both careful review by the nurse of pertinent laboratory values and careful monitoring of serial vital signs before, during, and after the phlebotomy.

**Conclusion**

Therapeutic phlebotomy is the first-line treatment for hereditary hemochromatosis and low-risk patients with polycythemia vera. It can be an effective treatment to improve symptoms in some cases of secondary polycythemia as well (see Table 1). Oncology nurses in a variety of settings may be asked to do a phlebotomy in a patient without cancer. An understanding of these diagnoses to include the pathology that warrants a therapeutic phlebotomy and an awareness of what to monitor when the procedure is ordered will enhance patient care.

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**References**


