COMPLICATIONS OF LONG-TERM STEROID USE

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How the Experts Treat Hematologic Malignancies
Las Vegas, NV
March 18, 2017
DISCLOSURE

No disclosures
Objectives

- Discuss the indications for long-term steroid therapy
- Review physiological and psychological effects of steroids
- Discuss impacts on patients and caregivers
- Outline principles for nursing considerations
Indication for long-term steroid use: Graft vs. Host Disease (GVHD)

- Major complication of allogeneic hematopoietic stem cell transplant (allo-HSCT), affecting overall survival
- Immunologic response following allo-HSCT
- GVHD occurs when immunologically competent donor T lymphocytes (in the transplanted graft) recognize antigens on cells in the recipient’s organs as foreign and mount an immunologic response
- The cells attack or injure the host tissues either directly or through the secretion of inflammatory cytokines

(Faiman, 2016)
Graft vs. Host Disease

- Can be acute, chronic, or an overlap of both
- Chronic GVHD can affect the gastrointestinal tract, skin, mouth, eyes, lungs, and liver among other sites
- Chronic GVHD occurs in 30%-70% of allo-HSCT, and is dependent on patient’s risk factors and cell source

(Faiman, 2016)
Graft vs. Host Disease

• Most cases are diagnosed within the first year (Median is 4-6 months post HSCT) but with 5%-10% diagnosed after the first year
• Patient’s will receive GVHD prophylaxis in the form of systemic immunosuppression starting just before transplant (i.e. tacrolimus, sirolimus, cyclosporin, methotrexate)
• Poorer prognosis than with acute GVHD, being the main cause of late, non-relapse mortality and morbidity, primarily due to infections secondary to the disease itself or its treatments

(Faiman, 2016)
Treating Chronic GVDH – Steroid therapy

- Standard first-line treatment for chronic GVHD is systemic corticosteroid therapy (Methylprednisolone)
- Utilized concomitantly with systemic immune suppression (tacrolimus, sirolimus, cyclosporin)
- Standard dosing is 1mg/kg/per day
- Primary treatment goal is to use the least immunosuppressive dose possible while achieving clinical improvement
- Steroids should be tapered to lowest dose possible, or removed completely as appropriate to diminish the risk and/or severity of long-term steroid associated toxicities

(Faiman, 2016)
Treating Chronic GVDH – Steroid therapy

- Prolonged steroids render the patient at risk for relapse caused by suppression of immunologic graft-vs-disease effect
General effects of long term steroid use

- Metabolic
- Neurologic
- Cardiovascular
- Gastrointestinal
- Dermatologic
- Ophthalmic
- Psychiatric
- Other
Specific effects of long term steroid use

- Hyperglycemia
- Avascular necrosis
- Infection
- Psychosis
How do steroids work?

- Rapid depletion of most circulating T cells due to a combination of effects including:
  - Enhanced circulatory emigration
  - Inhibition of Interleukin-2 (IL-2), a principal T cell growth factor, and IL-2 signaling
  - Impaired release of cells from lymphoid tissues
  - Induction of T cell apoptosis

(Chantham, 2016)
HYPERGLYCEMIA
Hyperglycemia

- In the hospital setting, there is evidence that more than half of the patients receiving high-dose steroids develop hyperglycemia.
- Criteria for the diagnosis of hyperglycemia per the American Association of Diabetes:
  - Blood glucose of $\geq 126$ mg/dL
  - Blood glucose at any time of $\geq 200$ mg/dL
  - HbA1c $> 6.5\%$ or blood glucose $> 200$ mg/dL 2h after an oral glucose load

(Tamez-Perez, 2015)
Hyperglycemia

- Complications of hyperglycemia:
  - Increased cardiovascular mortality associated with increased LDL cholesterol
  - Activation of the coagulation cascade
  - Increased pro-inflammatory cytokine production
  - Increased length of hospital stay
  - Risk of admission to ICU
  - Higher risk of infection
  - Poor wound healing

(Chantham, 2016)
Hyperglycemia management

• Managing steroid induced hyperglycemia:
  - Insulin is the treatment of choice in patients with persistent steroid induced hyperglycemia
  - Typical regimen starts with pre-prandial sliding scale with short acting insulin such as Lispro (Humalog)
  - Initial dosing usually calculated at 0.1 U/kg per meal, and is then modified depending on the glycemic response and the amount of supplementary insulin required to correct the pre-prandial hyperglycemia
  - 0.4 U/mg per meal with a glucose level between 200-300 mg/dL
  - 0.8 U/mg per meal with a glucose level above 300mg/dL

(Tamez-Perez, 2015)
Hyperglycemia management (continued)

- Patients with poor oral intake may be on total parenteral nutrition (TPN), which can exacerbate hyperglycemia due to the dextrose base
- Insulin may be added to the TPN to obtain stable glucose levels
- Educate patients regarding self glucose monitoring as some patients may be discharged home on anti-hyperglycemic medications in the presence of continued hyperglycemia
Hyperglycemia – Nursing Considerations

- Obtain baseline blood glucose level
- Careful monitoring of pre-prandial blood glucose and administration of insulin as directed
- Careful monitoring of the signs and symptoms of hypo and hyperglycemia in patients receiving systemic corticosteroid therapy
- Monitor for skin breakdown and wound healing
- Collaborate with interdisciplinary team, such as endocrinology, regarding blood glucose management
Hyperglycemia – Nursing Considerations (continued)

• Provide patient education regarding diet, exercise as appropriate, and s/s of hypo/hyperglycemia
• For patients with poor oral intake due to mucositis, encourage low glycemic nutritional supplements, such as Glucerna, to be taken around regular meal times and continue pre-prandial glucose monitoring
AVASCULAR NECROSIS
Avascular Necrosis

• What is avascular necrosis?
  – Bone tissue death from ischemia as a result of disrupted blood supply to the affected area, bone and cell tissue death, or disruption of bone repair mechanisms
  – Typically occurs in areas of terminal circulation, commonly the femoral head
  – Multiple studies report an incidence of approximately 5%-20% in long-term allogeneic transplant survivors

(Faiman, 2016)
Avascular Necrosis

- Studies indicate that it appears earlier in transplant recipients than in patients treated with steroids for other chronic illnesses.
- The mean time from transplant to diagnosis is approximately 12-13 months.
- Progressive, resulting in joint destruction in 3-5 years if not treated

(Faiman, 2016)
Avascular Necrosis

• Risk Factors
  – GVHD
  – Older age
  – Primary diagnosis of acute leukemia
  – Total Body Irradiation (TBI)
  – **Steroid therapy**
Avascular Necrosis

- **Diagnosis:**
  - Preferred method of diagnosis is magnetic resonance imaging (MRI), and to a lesser extent, radiographic images

- **Clinical Manifestations:**
  - Groin pain with femoral head disease, as well as thigh and buttock pain
  - Weight bearing or motion induced pain
  - Pain at rest occurs in two-thirds of patients, and night pain occurs in one-third of patients
Avascular Necrosis on Imaging
Avascular Necrosis

• Treatment
  – Reduced or non-weight-bearing ambulation through the use of crutches and/or activity limitation
  – Pain control
  – Physical therapy
  – Core decompression for early stage disease, whereby the medullary space is decompressed by opening the area of dead bone from the outside, thereby restoring blood circulation to the necrotic bone and relieving pain
  – Total joint replacement in late-stage disease

(Faiman, 2016)
Avascular Necrosis – Nursing Considerations

- Baseline assessment of pain, including intensity, frequency, duration, quality, as well as exacerbating and alleviating factors
- Administration of appropriate analgesia, with follow-up assessment of the presence or improvement of pain
- Patient education regarding the treatment plan, including pain control and safety
Avascular Necrosis – Nursing Considerations

- Collaboration with the interdisciplinary team, including orthopedics, pain specialists, and physical/occupational therapy, particularly regarding the safe use of assistive devices as well as transfer techniques
- Assess the need for assistance with or monitoring of ambulation and toileting and ADL’s
- Offer bedside commode
INFECTION
Infection

- Systemic glucocorticoid therapy is associated with an immediate increase in the risk of infection
- This is particularly true with common bacterial, viral, and fungal pathogens

(Chantham, 2016)
Infection – Etiology

- Systemic corticosteroid use creates a dose-dependent inhibitory effect on phagocyte function.
- Phagocytes are a critical component of the innate immune response, and glucocorticoids affect the function of various phagocytes, including neutrophils, monocytes, and macrophages.
- Steroids decrease the immune response by impairing the migration of neutrophils to the sites of inflammation and infection, as well as diminishing production of monocyte/macrophages and inhibiting their function.
Infection – Risk Factors

• Dose
  – Infection risk is directly related to dose and duration of therapy
  – Risks begins to diminish as soon as high-dose therapy is complete
  – With long term, low dose therapy, there may be longer lasting inhibition of immune response due to effects on phagocytic cell function
  – For these reasons, glucocorticoid sparing therapies and alternate day dosing are advisable when possible

(Chantham, 2016)
Infection – Risk Factors

- Patient-specific factors
  - Underlying disease
  - Combination with other immunosuppressive drugs
  - Hospitalization
  - When used in combination with other immunosuppressive drugs, there is a risk of both newly-acquired infections and reactivation of latent viral infections

(Chantham, 2016)
Infectious processes

• Bacterial
  • Pneumocystis jirovecii (formerly Pneumocystis carinii)
  • Staphylococcus aureus

• Fungal
  • Mucormycosis
  • Aspergillosis
  • Candida

• Viral
  • Herpes zoster
  • Cytomegalovirus
Infection prophylaxis

- **Anti-PCP**
  - Bactrim, atovaquone, dapsone
- **Bacterial**
  - Amoxicillin, azithromycin, cephalosporins
- **Fungal**
  - Fluconazole, posaconazole, voriconazole
- **Viral**
  - Acyclovir, valacyclovir, ganciclovir, valgancyclovir
Infection – Nursing Implications

- Assess patient for risk factors, including diagnosis, length and dose of steroid therapy, lab values such as WBC/ANC, presence of combined immune suppressive therapies, and co-morbidities such as diabetes or steroid induced hyperglycemia.
- Assess patient for signs of infection such as fever, chills, and alterations in vital signs such as tachycardia, tachypnea and hypotension.
Infection – Nursing Implications (continued)

- Administer prophylactic therapies including antivirals, antifungals, and antibiotics
- Careful monitoring and treatment of hyperglycemia
- Aseptic technique and copious infection prevention modalities
- Patient/family education regarding hand washing and infection prevention
Be aware that patients taking glucocorticoids may not manifest signs and symptoms of infection as clearly due to the inhibition of cytokine release and associated reduction in inflammatory febrile responses, which can impair early recognition of infection.
PSYCHOSIS
Psychosis – Definition

- Definition:
  - A heterogeneous mixture of neuropsychiatric symptoms involving affective, behavioral, and cognitive manifestations (Dubovsky, 2012)
  - Diverse affective, behavioral, and cognitive syndromes have been lumped together under the term *steroid psychosis* whether or not the patient has been psychotic (Dubovsky, 2012)
Psychosis – Risk factors

• Risk Factors:
  • Dose and length of treatment: Long term treatment results in more depressive symptoms whereas pulse-dose or short-term treatments manifest in manic symptoms
  • Gender: Affects more women than men
  • Metabolic: Hepatic and renal dysfunction results in higher free levels of prednisolone

(Sirois, 2003)
Psychosis – Risk factors (continued)

• Risk Factors:
  – Drug-drug interaction: Inhibition of steroid metabolism by drugs such as -azoles or estrogen containing oral contraceptives
  – Chemotherapy: May lead to damage of the blood-brain barrier, predisposing patient to neuropsychiatric effects
  – Psychiatric history: May predict mood responses to corticosteroid treatment

(Sirois, 2003)
Psychosis – Onset and incidence

- Onset and incidence:
  - Onset varies from hours to days to weeks
  - Incidence is 2% to 60%, reflecting the variability in definitions, variability in dose, and the heterogeneous nature of steroid-induced neuropsychiatric reactions
Psychosis – Manifestations

- Manifestations:
  - Depression
  - Mania
  - Agitation
  - Mood lability
  - Anxiety
  - Insomnia
  - Catatonia
  - Depersonalization
  - Delirium
  - Dementia
Psychosis – Treatment Modalities

• Treatment modalities for steroid-induced psychosis:
  – Steroid discontinuation, alternate day dosing, or dose reduction by taper to allow the adrenal glands to resume cortisol production
  – Mood stabilizers/antipsychotics
  – Minimal data supporting the efficacy of anti-depressants
  – Lithium not widely used as steroid therapy can cause changes in sodium levels, increasing risk for lithium toxicity

(Dubovsky, 2012)
Psychosis – Consideration for Withdrawal

• Recurrence of symptoms for which steroids were used
• Acute renal insufficiency
• “Steroid withdrawal syndrome”
  – Sleep and appetite disturbance
  – Poor concentration
  – Agitation/Psychosis
  – Suicide
  – Fatigue
  – Joint pain
  – Weakness

(Dubovsky, 2012)
Psychosis – Nursing Considerations

- Assess for symptoms for which steroids were prescribed to facilitate appropriate steroid taper
- Screen for anxiety, depression, suicidal ideation, and other symptoms of psychosis and report to members of the health care team
- Facilitate psychiatric or psychology consults
- Provide emotional support to patients and their families
- Facilitate a safe, calm, and reassuring environment to hospitalized patients
General considerations

- Steroids can impact quality of life, affecting appearance, mobility, vision, sex life, as well as subjecting patients to chronic pain, joint contractures, and end-stage lung disease, sometimes leading to irreversible organ damage
  
  (Faiman, 2016)

- Presence of Cushing’s Syndrome, another side effect of steroid therapy, can cause considerable body image issues due to the presence of “moon-face”, “buffalo hump”, stretch marks, acne, facial hair growth, hair loss, ruddy skin or skin darkening
  
  (Margulies, 2017)
Steroid Side Effects
Steroid Side Effects
General considerations

• The diagnosis of a hematological malignancy, as well as the effects and implications of the accompanying therapies such as steroids, cause disruptions in multiple domains, including the physiological, psychological, social, and spiritual (Faiman, 2016)

• These effects can impact both the patient, their caregiver, children, and extended family
References


References (continued)
