Clinical Resource Guide: Edema

INTRODUCTION TO EDEMA & FLUID OVERLOAD

Edema is swelling due to fluid buildup in tissues and is a common symptom in various advanced illnesses. It may be generalized throughout the body or localized to a specific area. While it may have various causes, the result is an imbalance in hydrostatic pressure and vessel wall permeability. Edema can cause significant distress and reduced quality of life, especially when mobility and independence are reduced. Treatment goals include reducing discomfort, improving function and quality of life, and preserving skin integrity.

Pharmacist Corner Objectives

1.) Identify potential causes of edema and fluid overload
2.) Learn how to grade edema
3.) Understand the pharmacologic and non-pharmacologic management of edema

CAUSES OF EDEMA

Source	Examples
Allergic reactions	Angioedema, chemosis, anaphylaxis
Organ failure	Cardiac, renal, hepatic failure
Malignancy	Ovarian, uterine, gastrointestinal cancers
Medications	Acyclovir, amlodipine, carvedilol, celecoxib, clonidine, estrogen, gabapentin, hydralazine, hydrocortisone, ibuprofen, megestrol, metoprolol, naproxen, pioglitazone, prednisone, rosiglitazone, verapamil
Lymphatic impairment	Inefficient lymph transport secondary to infection, inflammation, surgical removal
Pulmonary	Pneumonia, pleural effusion, cardiogenic, chest wall trauma, high altitude-induced, malignancy, immersion/swimming-induced, sepsis
Critical illness	Head trauma, burns, cerebral infarction, tumor, cerebral hemorrhage, deep vein thrombosis, autoimmune
Endocrine	Hypothyroidism, Cushing’s syndrome, Graves’ disease
Dietary	Sodium intake, malnutrition-induced hypoalbuminemia, chronic alcohol abuse, obesity-induced immobility

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EDEMA GRADING

The edema grading (0-4+ pitting) scale measures the extent of edema by gently pressing a finger on the swollen area for 5-15 seconds. After releasing, the depth of the dimple (pit) is measured as follows:

- Grade 1: Immediate rebound with 2mm pit.
- Grade 2: <15-second rebound with 3-4mm pit
- Grade 3: 15-60 second rebound with 5-6mm pit.
- Grade 4: 2 to 3 minutes rebound with 8mm pit.

NON-PHARMACOLOGICAL MANAGEMENT

Non-pharmacological management of edema varies based on the cause.
Interventions may include fluid & salt intake monitoring, reducing alcohol, reducing or discontinuing contributory medications, elevating extremities, or utilizing compression wraps or garments. For symptomatic ascites, or the accumulation of fluid in the peritoneal space, fluid removal via paracentesis may be performed for temporary relief. Specific drainage, massage, and decongestive techniques may be performed by massage or physical therapists specially trained in lymphedema management.

PHARMACOLOGICAL MANAGEMENT

ROUTE	STARTING DOSE	ROUTES	COMMON FORMULATIONS	NOTES
Loop Diuretics				
Bumetanide	0.5mg QD	PO, IV, IM	**Tablets**: 0.5mg, 1mg, 2mg **Injection**: 0.25mg/ml	• PO dose = IV dose • Useful if resistant to furosemide • PO duration of action is typically 4-6hr
Furosemide	20mg QD	PO, SL, PR, SC, IM, IV	**Tablets**: 20mg, 40mg, 80mg **Oral solution**: 10mg/ml, 8mg/ml **Injection**: 10mg/ml	• Often initiated first-line • 40mg PO = 20mg IV • PO duration of action is typically 6-8hr
Torsemide	10mg QD	PO, IV	**Tablets**: 5mg, 10mg, 25mg, 100mg **Injection**: 10mg/ml	• PO dose = IV dose • Useful if resistant to furosemide • PO duration of action is typically 6-8hr

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Thiazide-Type Diuretics				
Metolazone	2.5mg QD	PO	**Tablets**: 2.5mg, 5mg, 10mg	• May be added to a loop diuretic for refractory symptoms • Administer 30-60 minutes before loop diuretic for optimal effect
Hydrochlorothiazide	25mg QD	PO	**Capsules**: 12.5mg **Tablets**: 12.5mg, 25mg, 50mg	• Ineffective if CrCl <30 ml/min unless combined with a loop diuretic • Avoid use in history of gout
Chlorothiazide	250mg QD	PO, IV	**Tablets**: 250mg, 500mg **Oral Suspension**: 250mg/5ml **Injection**: 500mg	• Ineffective if CrCl <30 ml/min unless combined with a loop diuretic • Avoid use in history of gout
Chlorthalidone	50mg QD	PO	**Tablets**: 25mg, 50mg, 100mg	• Ineffective if CrCl <30 ml/min unless combined with a loop diuretic • Avoid use in history of gout
Carbonic Anhydrase Inhibitor				
Acetazolamide	250mg QD	PO	**ER capsules**:500mg **Tabs**: 125mg, 250mg	• Primarily used to reduce intracranial pressure in cerebral edema
Potassium-Sparing Diuretics				
Spironolactone	25mg QD	PO	**Tablets**: 25mg, 50mg, 100mg	• Drug of choice for ascites • Avoid use if CrCl<10 ml/min • Aldosterone antagonist
Eplerenone	25mg QD	PO	**Tablets**: 25mg, 50mg	• Avoid use if CrCl <50 ml/min • Aldosterone antagonist • High potential for hyperkalemia and drug interactions
Triamterene	50mg QD	PO	**Tablets**: 50mg, 100mg	• No aldosterone activity • Avoid use if CrCl <50 ml/min • Avoid use if history of gout
Amiloride	5mg QD	PO	**Tablets**: 5mg	• Primarily combined with thiazides to prevent hypokalemia • Avoid use if CrCl <50 ml/min

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PHARMACOLOGICAL MANAGEMENT: CLINICAL PEARLS

1. Monitor for dehydration, dizziness, orthostatic hypotension.
2. Weight loss should be limited to 0.5kg-1kg per day.
3. Thiazides and loop diuretics contain a sulfa group and carry a slight risk of reaction in patients with a documented sulfa allergy. Although many patients with sulfa antibiotic allergies can tolerate diuretics, avoid if the patient has a history of anaphylaxis or severe reaction.
4. Avoid evening doses of diuretics when possible to reduce sleep disruption.
5. Subcutaneous furosemide may be helpful in situations where absorption and effectiveness of oral diuretics is diminished.
6. Keep skin clean and moisturized to minimize the risk of breakdown and infection risk.
7. Empiric potassium supplementation upon initiating a loop diuretic may be appropriate, especially at higher doses.
8. Prednisone has more mineralocorticoid activity than dexamethasone resulting in increased sodium and water retention. Use dexamethasone in patients with edema.
9. Approximate equivalent oral doses of loop diuretics are furosemide 40mg = bumetanide 1mg = torsemide 20mg.

SUMMARY

Edema is a commonly experienced symptom at end of life with multiple etiologies. Refractory edema, such as that seen in advanced metastatic cancer, is one of the more challenging clinical concerns in hospice. Adequate management of edema is an important principle of hospice and palliative care.

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