# A Review on Edema

## Aslesha E\*

Department of Pharmaceutics, Mallareddy College of Pharmacy, Hyderabad, Telangana, India

## **Research Article**

## ABSTRACT

Received: 25/08/2016 Accepted: 09/09/2016 Published: 18/09/2016

#### \*For Correspondence

Aslesha E, Department of Pharmaceutics, Mallareddy College of Pharmacy, Hyderabad, Telangana, India

E-mail: aslesha5@ymail.com

**Keywords:** Edema, Oncotic Pressure, Macular edema, Magnetic Resonance Imaging, Diuretics Edema is a swelling which is caused due to accumulation of fluid due to release of fluid from small blood vessels (capillaries) or interstitial spaces to nearby tissues. It may affect a small area or even entire body. The affected body part is considered to be edematous. Edema is most commonly seen in the legs, feet, ankles and it can even affect other body parts. Edema is a side effect in many medications. The article presents information on the types, symptoms, causes, diagnosis and treatment of edema.

# INTRODUCTION

Edema is a swelling which is caused due to accumulation of fluid due to release of fluid from small blood vessels (capillaries) or interstitial spaces to nearby tissues. Swelling may be caused due to the reasons such as pressure within the blood vessels, build-up of fluid following removal of the lymph nodes, inflammation, water retention, hydrostatic Pressure, tissue (interstitial) oncotic pressure. The capillary damage or increased pressure either by injury or inflammation leads to the swelling of the body parts. It may affect a small area or even entire body. The affected body part is considered to be edematous. Edema is most commonly seen in the legs, feet, ankles and it can even affect other body parts. Edema is a side effect in many medications <sup>[1-6]</sup>.

## Types of Edema

#### Peripheral edema

Edema of peripheral vascular system parts like lower limbs (legs, feet and ankles).

#### Pedal edema

Edema of foot is known as Pedal edema.

#### Pulmonary edema

Pulmonary edema is characterized by accumulation of fluids in air spaces and parenchyma lungs. It may lead to respiratory failure.

## Cerebral edema

The accumulation of increased water content in the brain is known as cerebral edema. It may be caused due to ischemic stroke, cancer, or brain inflammation due to meningitis or encephalitis.

#### Angioedema

It is different from hives where swelling is caused underneath the skin rather than surface of the skin. It occurs on the face.

#### Hereditary angioedema

It is a rare genetic condition that affects immune system. Release of fluids from capillaries to the surrounding tissues result in edema. Swelling affects face, genitals and abdomen.

#### Papilledema

Swelling of the optic nerve of the eye which is a result of increased intracranial pressure inside the skull and around the brain (intracranial pressure). It is diagnosed by ophthalmoscopy.

#### Macular edema

Blood retinal barrier is responsible in maintaining homeostasis (restricting movement of plasma constituents into the retina). The disruption caused in the homeostasis leads to macular edema.

#### Dependent edema

Dependent edema is the swelling that occur in the legs and lower body which is affected by gravity and which is position dependent.

#### Scrotal lymphedema

It is caused due to enlargement of the scrotum due to fluid accumulation around the testes.

#### Lipedema

Lipedema is a disorder of the fatty (adipose) tissue that causes swelling of the legs and hips.

#### Idiopathic edema

Accumulation of fluid in tissues no particular cause.

#### Pitting edema

When pressure is applied on the skin and removed, a depression is seen.

#### Non-pitting edema

Edema in which there is no presence of depression when pressure is applied <sup>[7-19]</sup>.

## Symptoms of Edema

- Skin that retains a dimple when pressure is applied for few seconds
- Stretched and shiny skin
- Increased abdominal size
- Swelling or puffiness in the affected area
- Aching body parts
- Weight gain or weight loss
- Raised pulse rate
- Ascites
- Stretched or shiny skin
- Chest pain
- Difficulty in breathing or cough [20-32]

#### **Common Causes**

#### Medications that cause edema

Vasodilators (drugs that open blood vessels), calcium channel blockers (CCBs), NSAIDs (non-steroidal antiinflammatory drugs), estrogens, corticosteroids (like prednisone and methylprednisolone), cytokines, several chemotherapy drugs, and some diabetes drugs (thiazolidinediones).

## Excessive salt intake

Increased sodium content in body results in the swelling of body parts.

#### Menopause and pregnancy

Hormone fluctuations in menopause and pressure by uterus on blood vessels and more water retain in pregnant woman may cause fluid retention.

### Malnutrition

Insufficient vitamins B6 and B5 may cause fluid retention.

#### Burns

Burns causes local swelling.

#### Heat

On high temperatures body doesn't work efficient in removing the fluid from the tissues [33-46].

## Edema Caused by Different Diseases

#### Kidney disease

Kidney function failure in eliminating fluid and sodium from blood causes increased pressure on blood vessels which leads to leaking of liquid. Swelling is caused in legs and eyes.

#### Heart failure

Inability to pump blood effectively (congestive heart failure) leads to the accumulation of the blood in limbs causing edema in limbs.

#### Venous insufficiency

Inefficient blood circulation from peripheral body parts results edema in ankles, legs, feet and hands.

### Chronic lung disease

Accumulation of fluids in lungs leads to pulmonary edema.

## Liver

Liver cirrhosis affects liver function which leads to the fluid retention in legs and abdomen; reduced protein synthesis results decreased plasma oncotic pressure.

#### Diabetes

Swelling in the retina in diabetes is called Diabetic macular edema.

#### Allergies

Some foods and insect bites causes swelling.

#### Brain

Accumulation of water in a brain tumor.

## Obstructive sleep apnea

Increased capillary hydrostatic pressure results in obstructive sleep apnea.

#### Renal disease

Protein loss results in decreased plasma oncotic pressure [47-58].

## Diagnosis

#### Chest X-rays

RRJPA | Volume 5 | Issue 2 | August - September, 2016

## Blood tests

Blood tests are done to check the amount of oxygen and carbon dioxide content (arterial blood gas concentrations) and blood count.

## Urine tests

Urine tests are done to identify if there is any loss of protein from the kidneys.

## Liver function tests:

- The decreased albumin levels in chronic liver diseases lead to blood clotting. Therefore the albumin levels are to be determined to identify the presence of edema.
- Liver biopsy is done to collect a tissue sample by small needle inserted into the liver which is to be analyzed to diagnose liver diseases.

## Heart function tests

- Electrocardiogram (ECG or EKG): It is done determine how long the electrical wave takes to pass through the heart by which we can evaluate pulmonary arterial pressures.
- **Pulse oximetry**: It is used to determine the oxygen in the blood by a sensor which is attached to ear or finger which uses light.
- Echocardiogram: Transducer is the device which generates high frequency sound waves that reflect from the heart tissues, and the image is composed on a monitor which shows the blood flow and also pressure in the heart.
- Cardiac Catheterization and Angiogram: If the specific cause of your pulmonary edema is not determined in Electrocardiogram or Echocardiogram, then cardiac catheterization and coronary angiogram is done. In this method a catheter is sent into the heart chambers to measure the pressure in your heart.
- Magnetic Resonance Imaging (MRI): When confirmation of thrombosis is not obtained by duplex ultrasonography this additional imaging is needed to diagnose the cause of edema. Magnetic resonance aids in the diagnosis of musculoskeletal etiologies and also directly visualizes the lymphatic channels.
- Computerized Tomography of the Heart (CT): It creates detailed pictures of the heart and its arteries which evaluates if there is narrowing or a blockage in arteries. It helps to detect various heart diseases.
- **Transesophageal Echocardiogram (TEE):** Transducer is attached with then catheter and passed through esophagus to have a closer view of heart <sup>[59-73]</sup>.

## Ultrasonography

Venous ultrasonography is the choice of imaging to determine the venous insufficiency. Compression ultrasonography is done for imaging thrombosis. To confirm the chronic venous insufficiency, the duplex ultrasonography is needed <sup>[74]</sup>.

## Lymphoscintigraphy

It is done to determine the lymph flow. In this method indirect radionuclide lymphoscintigraphy shows absent or delayed filling of lymphatic channels.

## Treatment

## Diuretics (water pill)

These drugs increase the production of urine which facilitates the increased water and sodium excretion from the body.

- Loop diuretics: furosemide (Lasix) and butethamine (Bumex),
- Thiazide diuretics: metolazone (Zaroxolyn) and chlorthalidone (Thalitone),

- Potassium-sparing diuretic: spironolactone (Aldactone) and amiloride (Midamor).
- Other Medications:
- ACE inhibitors: enalapril (Vasotec), captopril (Capoten), ramipril (Altace),
- Angiotensin receptor blockers include: losartan (Cozaar),
- Low-dose amphetamines,
- Ephedrine,
- Bromocriptine (Parlodel).

## Anticoagulation therapy

Postthrombotic syndrome is a chronic venous insufficiency occurred following telangiectasias (small, widened blood vessels associated with several diseases). Anticoagulants are used to prevent clot or the development of postthrombotic syndrome.

Eg: Heparin or warfarin.

#### Oxygen therapy

Some diseases like cystic fibrosis, sleep apnea prevent you getting enough oxygen. In this condition oxygen therapy is a medical intervention that provides extra oxygen.

Eg: Nasal Cannula and oxygen regulator.

#### Lucentis (Ranibizumab)

It is a human antibody fragment designed for intraocular use which keeps new blood vessels from forming under the retina.

#### Reduce sodium in diet

The sodium content in the diet may increase edema. Therefore, reducing salt intake helps to control edema.

#### Compression stockings

These stockings compress the skin underneath them which prevents swelling at that part. Stockings are available in different sizes like ankle high, knee high and thigh high. These are preferred on the basis of the swelling area and volume. Mild leg edema due to varicose veins can be treated.

## Body positioning

Elevation of legs in inclined angle may help reducing swelling for people with mild edema. Swollen ankles and feet in a pregnant woman can be treated by body positioning <sup>[75-94]</sup>.

# CONCLUSION

Edema is a swelling which is caused due to accumulation of fluid due to release of fluid from small blood vessels (capillaries) or interstitial spaces to nearby tissues. Edema caused by different diseases, kidney diseases, heart failure, venous insufficiency, chronic lung disease, liver cirrhosis, diabetes, renal diseases etc. It is also caused due to some medications like vasodilators, estrogens, corticosteroids, cytokines, chemotherapy drugs etc. Diagnosis of edema is done by various methods like chest X-rays, heart function and liver function tests, blood tests and urine tests. Ultrasonography and Lymphoscintigraphy are the choice of imaging techniques which are done to confirm the cause if not known from the above methods. Low salt intake and body positioning are the natural ways to treat edema. Body positioning and compression stockings are the natural treatment for foot and ankle edema. Diuretics, anticoagulation therapy and oxygen therapy are the better treatment methods for edema.

## REFERENCES

- 1. Rockson SG. Lymphedema. Am J Med. 2001;110:288-295.
- 2. Kesieme E, et al. Deep vein thrombosis: a clinical review. J Blood Med. 2011;2:59-69.

- 3. Villeco JP. Edema: a silent but important factor. J Hand Ther. 2012;25:153-162.
- 4. Studdiford J, et al. Evaluating edema of the hands. J Musculoskel Med. 2009;26:30-36.
- 5. Blankfield RP and Zyzanski SJ. Bilateral leg edema, pulmonary hypertension, and obstructive sleep apnea: a cross-sectional study. J Fam Pract. 2002;51:561-564.
- 6. Ely JW, et al. Approach to Leg Edema of Unclear Etiology. J Am Board Fam Med. 2006;19:148-160.
- 7. Holmes G. The Prognosis in Papilloedema. Br J Ophthalmol. 1937;21:337-342.
- 8. Cho S, et al. Peripheral edema. Am J Med. 2002;113:580-586.
- 9. Veena N, et al. Pedal edema with olanzapine. Indian J Pharmacol. 2009;41:49-50.
- 10. Zhurda T, et al. Acute Postoperative Negative Pressure Pulmonary Edema as Complication of Acute Airway Obstruction: Case Report. J Anesth Clin Res. 2016;7:603.
- 11. Srivastava S. Genetic Variations in Renin-Angiotensin-Aldosterone System (RAAS) Genes Could Contribute to High Altitude Pulmonary Edema: Review. J Pulm Respir Med. 2015;5:296.
- 12. Tandale SR, et al. Acute Pulmonary Edema Following Caesarean Delivery. J Clin Case Rep. 2015;5:481.
- 13. Tilman V. Pulmonary Edema: A Unifying Pathophysiological Formula. J Cardiovasc Dis Diagn. 2015;3:194.
- 14. Pirasath S, et al. Homicidal Strangulation: Uncommon Cause of Noncardiogenic Pulmonary Oedema. J Pulm Respir Med. 2016;6:332.
- 15. Darabont RO, et al. Renal Artery Stenosis and Acute Pulmonary Edema-A Possible Correlation beyond Pickering Syndrome. J Clin Exp Cardiolog. 2015;6:377.
- 16. Paul S, et al. High Altitude Pulmonary Edema: An Update on Omics Data and Redefining Susceptibility. J Proteomics Bioinform. 2015;8:116-125.
- 17. Magon P. Drug-Induced Pulmonary Edema and Acute Respiratory Distress Syndrome in Children. Adv Pharmacoepidemiol Drug Saf. 2015;4:178.
- Al Ghofaily L, et al. Negative Pressure Pulmonary Edema after Laryngospasm: A Revisit with a Case Report. J Anesth Clin Res. 2012;3:252.
- 19. Vaudrey C. Brain Scan-Bone Lysis, Compression and Cerebral Edema. Endocrinol Metab Syndr. 2015;4:i009.
- 20. Mehtap O, et al. A Rare but Fatal Complication Probably due to Imatinib: Cerebral Edema. J Clin Case Rep. 2012;2:176.
- 21. Adukauskiene D, et al. Cerebral edema and its treatment. Medicina. 2007;43:170-6.
- 22. Muir AB, et al. Cerebral Edema in Childhood Diabetic Ketoacidosis. Diabetes Care. 2004;27:1541-1546.
- 23. Mai-Lan Ho, et al. Cerebral Edema. Am J Roentgenol. 2012;199:W258-W273.
- 24. Mahajan S, et al. Cerebral oedema: Pathophysiological mechanisms and experimental therapies. J Neuroanaesthesiol Crit Care. 2016;3:22-28.
- 25. Jha LCSK. Cerebral Edema and its Management. MJAFI. 2003;59:326-331.
- 26. Stern WE, et al. Cerebral Edema. JAMA. 1966;195:8.
- 27. Shiber J. Lingual Angioedema due to ACE-Inhibitor. Trop Med Surg. 2014;2:161.
- 28. Genel S, et al. Therapeutic Perspectives on the Treatment of Urticaria Associated with Angioedema. Pharmaceut Anal Acta. 2012;3:187.
- 29. Kaplan AP. Angioedema. World Allergy Organization Journal. 2008;1:103.
- 30. Rasmussen EHR, et al. Angioedema assessment and treatment. Tidsskr Nor Legeforen. 2012;132:2391-5.
- 31. Ishaque S, et al. Kaala Pathar (Paraphenylene Diamine) Poisoning and Angioedema in a Child: An Unusual Encounter. J Clin Toxicol. 2016;6:294.
- 32. Salemi M, et al. Psychological Correlates in Subjects with Hereditary Angioedema (HAE). J Psychol Psychother. 2014;4:134.
- 33. Csuka D, et al. Hereditary Angioedema Due to C1-Inhibitor Deficiency From a Genetic Point of View. Hereditary Genet. 2015;4:e112.
- 34. Reese AB. Peri-Papillary Detachment of the Retina Accompanying Papilledema. Trans Am Ophthalmol Soc. 1930;28:341-351.
- 35. Dandy WE. Papilledema without intracranial pressure (optic neuritis). Ann Surg. 1939;110:161-168.
- 36. Hejsek L, et al. Navigated Laser Photocoagulation of Chronic Diabetic Macular Edema. J Clin Exp Ophthalmol. 2015;6:414.
- 37. Pitcher JD and Hubschman JP. Management of Diabetic Macular Edema. J Diabetes Metab. 2011;S3:002.
- 38. Qiu TG. Revisit Rescula and Cystoid Macular Edema and Refractory Glaucoma. J Clin Exp Ophthalmol. 2015;6:473.

- 39. Pareja-Ríos A, et al. Management of Diabetic Macular Edema in Current Clinical Practice: A Review. J Diabetes Metab. 2012;S3:004.
- 40. Maalej A, et al. Optical Coherence Tomography for Diabetic Macular Edema: Early Diagnosis, Classification and Quantitative Assessment. J Clinic Experiment Ophthalmol. 2012;S2:004.
- 41. Noma H. Treatment Strategy for Macular Edema with Ischemic Retinal Vein Occlusion. J Vasc Med Surg. 2013;1:e103.
- 42. Silva RA, et al. Intravitreal Ranibizumab for Macular Edema Secondary to Juxtafoveal Retinal Telangiectasia Type 1A. J Clinic Experiment Ophthalmol. 2011;2:195.
- 43. Xie J, et al. Relative Importance and Contribiton of Risk Factors for Diabetic Retinopathy and Macular Edema. J Diabetes Metab. 2014;5:337.
- 44. Nourollahi S, et al. Bucher's Broom and Selenium Improve Lipedema: A Retrospective Case Study. Altern Integr Med. 2013;2:119.
- 45. Qanneta R. Urinary Bladder Distension Presenting with Leg Edema Duo to Venous Obstruction. J Gerontol Geriat Res. 2015;4:217.
- 46. Soussi Tanani D, et al. Signal Management of Disproportionate Reporting in Moroccan Pharmacovigilance: The Lower Limb Edema Induced by Anti-Tuberculosis Drugs. J Pharmacovigilance. 2015;3:161.
- 47. Okuyama E, et al. Clinical Experience of Noninvasive Positive Pressure Ventilation in Patients with Acute Cardiogenic Pulmonary Oedema Treated in a Community Hospital in Japan. 2014;4:196.
- 48. Gordon SK, et al. Continuous 24-Hour Intraocular Pressure Pattern Monitoring in Medically Treated Normal Tension Glaucoma. Surgery Curr Res. 2014;4:193.
- 49. Kodakkattil S. Management of Pregnancy in Woman with Heriditary Angioedema. Gynecol Obstet. 2014;4:194.
- 50. González L, et al. Swelling of Extremities: Primary Lymphedema? Pediat Therapeut. 2012;2:135.
- 51. Colson F, et al. Paclitaxel-Related Lymphedema and Scleroderma-Like Skin Changes. J Clin Case Rep. 2013;3:317.
- 52. Gorman WP, et al. Swollen lower limb. West J Med. 2001;174:132-136.
- 53. Glaser N. Cerebral edema in children with diabetic ketoacidosis. Curr Diab Rep. 2001;1:41-46.
- 54. Luisada AA, et al. Acute Pulmonary Edema. Circulation. 1956;13:113-135.
- 55. Cavanaugh RM. Orthostatic Edema in Adolescents. Pediatrics in Review. 2005;26.
- 56. Murray JF. Pulmonary edema: pathophysiology and diagnosis. Int J Tuberc Lung Dis. 2011;15:155-160.
- 57. Ware LB, et al. Acute Pulmonary Edema. N Engl J Med. 2005;353:2788-2796.
- 58. Tranos PG, et al. Macular edema. Surv Ophthalmol. 2004;49:470-490.
- 59. Vives F, et al. Giant lymphedema of the penis and scrotum: a case report. Autops Case Rep. 2016;6:57-61.
- 60. Yale SH and Mazza JJ. Approach to diagnosing lower extremity edema. Compr Ther. 2001;27(3):242-252.
- 61. Pastor C, et al. Scrotal Lymphedema. Eplasty. 2011;11:ic15.
- 62. Rockson SG. Diagnosis and management of lymphatic vascular disease. J Am Coll Cardiol. 2008;52:799-806.
- 63. Bamigboye AA and Smyth R. Interventions for varicose veins and leg oedema in pregnancy. Cochrane Database Syst Rev. 2007;1:CD001066.
- 64. Rosenfeld PJ, et al. Ranibizumab for Neovascular Age-Related Macular Degeneration. N Engl J Med. 2006;355:1419-1431.
- 65. Singh Y and Everden S. Pulse Oximetry Screening for Detection of Critical Congenital Heart Defects: Why to Bother? J Neonatal Biol. 2016;5:e114.
- 66. Stancanello J. Magnetic Resonance Imaging will Replace Computer Tomography. J Biotechnol Biomater. 2012;2:e113.
- 67. Kotecha M, et al. Monitoring Tissue Engineering and Regeneration by Magnetic Resonance Imaging and Spectroscopy. J Tissue Sci Eng. 2012;S11:007.
- 68. Bernelli C. Pharmacotherapy in the Cardiac Catheterization Laboratory. Cardiol Pharmacol. 2015;4:146.
- 69. Azmanis PN, et al. The Additional Diagnostic Value of Optical Coherence Tomography (OCT) and Its Application Procedure in A Wide Variety of Avian Species. J Clin Exp Ophthalmol. 2015;6:431.
- 70. Omar HR. Acute cardiogenic pulmonary edema with normal BNP: the value of repeat BNP testing. Am J Emer Med. 2015;33:605.e5-605.e6.
- 71. Lee JS. Albumin for End-Stage Liver Disease. Korean J Intern Med. 2012;27:13-19.
- 72. Arthur JB. Papilledema Without Increased Intracranial Pressure. Trans Am Ophthalmol Soc. 1941;39:242-261.

- Alguire PC and Mathes BM. Chronic venous insufficiency and venous ulceration. J Gen Intern Med. 1997;12:374-383.
- 74. Roever L, et al. A Ultrasonography Image of Abdominal fat. Emerg Med. 2015;5:246.
- 75. Clark AL, et al. Causes and treatment of oedema in patients with heart failure. Nature Reviews Cardiology 2013;10:156-170.
- 76. O'Brien JG, et al. Treatment of edema. Am Fam Physician. 2005;71:2111-2117.
- 77. Warren AG, et al. Lymphedema: a comprehensive review. Ann Plast Surg. 2007;59:464-472.
- 78. Morrison RT. Edema and principles of diuretic use. Med Clin North Am. 1997;81:689-704.
- 79. Aziz F, et al. Non-Cardiogenic Pulmonary Edema in Salicylate Posioning. J Clinic Case Reports. 2012;2:111.
- 80. Blum A. Angioedema-Induced by Angiotensin Converting Enzyme Inhibitors. J Clin Case Rep. 2012;2:153.
- 81. Genel S, et al. Angioedema Associated with Urticaria can be a Silent Killer. 2013;4:128.
- 82. Raiten J. Anticoagulation Therapy Following Embolic or Hemorrhagic Stroke in the Patient with a Mechanical Heart Valve. J Anesthe Clinic Res. 2011;2:160.
- 83. Hirai I, et al. Hyperbaric Oxygen Therapy for Pancreatic and Gastrointestinal Disease. Pancreatic Dis Ther. 2013;S4:006.
- 84. Tezuka D, et al. An Oxygen Therapy Prevents Ventricular Arrhythmia in Patients with Diastolic Heart Failure and Sleep Apnea. J Sleep Disord Ther. 2014;3:162.
- 85. Lim CH, et al. Graduated compression stockings. CMAJ. 2014;186:E391-E398.
- 86. Moffatt C. Variability of pressure provided by sustained compression. Int Wound J. 2008;5:259-65.
- 87. Callam MJ, et al. Hazards of compression treatment of the leg: an estimate from Scottish surgeons. Br Med J. 1987;295:1382.
- 88. Eberhardt RT and Raffetto JD. Chronic venous insufficiency. Circulation. 2005;111:2398-409.
- 89. Carvalho CA, et al. Reduction of Pain and Edema of the Legs by Walking Wearing Elastic Stockings. International Journal of Vascular Medicine. 2015;ID 648074.
- 90. Sachdeva A, et al. Elastic compression stockings for prevention of deep vein thrombosis. Cochrane Database Syst Rev. 2010;7:CD001484.
- 91. Staub NC. Pulmonary edema: physiologic approaches to management. Chest. 1978;74:559-564.
- 92. Dean E. Effect of body position on pulmonary function. Physical Therapy. 1985;65:613-618.
- 93. Narahari SR, et al. How Does Yoga Work in Lymphedema? J Yoga Phys Ther. 2013;3:135.
- 94. Hodge LM. Decongestive Physiotherapy for the Treatment of Lymphedema. J Blood Lymph. 2012;2:e107.