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Chapter 11:
Hypertonic Saline

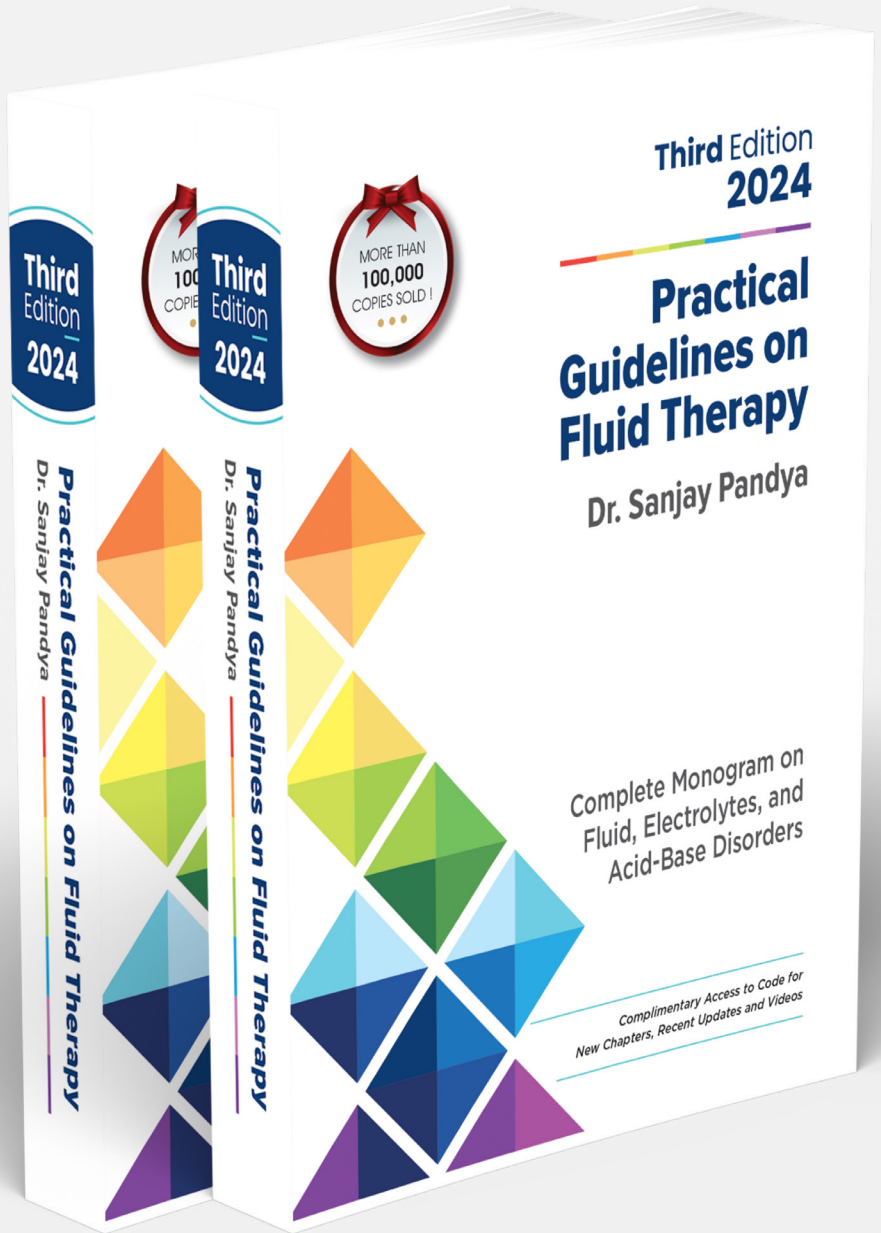

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Table of Contents

11 Hypertonic Saline

Hypertonic saline (HS) is a concentrated form of sodium chloride dissolved in water, and 3% and 5% hypertonic saline are commonly used solutions in clinical practice.

COMPOSITION

Inj. 3% Hypertonic Saline

Each 100 ml of contains:

Sodium	51.3 mEq
Chloride	51.3 mEq
Osmolality	1026.0 mOsm/L

100 ml of 3% NaCl contains: 3 gm of Sodium Chloride

Inj. 5% Hypertonic Saline

Each 100 ml of contains:

Sodium	85.5 mEq
Chloride	85.5 mEq
Osmolality	1710.0 mOsm/L

100 ml of 5% NaCl contains: 5 gm of Sodium Chloride

PHARMACOLOGICAL BASIS

Hypertonic saline solutions have higher sodium chloride concentration and serum osmolality as compared to normal serum values.

A. High sodium concentration promptly corrects hyponatremia

Sodium concentration of 3% and 5% hypertonic saline is 513 mEq/L and 855 mEq/L respectively compared to normal plasma concentration of 140 mEq/L. As a high sodium concentration of hypertonic saline can rapidly raise sodium and reduce cerebral edema, it is recommended in the treatment of life-threatening hyponatremia. Because of substantially higher concentrations of salt, this solution is selected to provide a large amount of sodium in a small amount of fluid (i.e., in a patient with

euvolemic or hypervolemic hyponatremia who needs salt supplementation, but fluid restriction).

REFERENCES

1. Hinson HE, Stein D, Sheth KN. Hypertonic saline and mannitol therapy in critical care neurology. J Intensive Care Med 2013;28(1):3–11.
2. Busey K, Samai K. Hypertonic Saline for ICP Reduction in Traumatic Brain Injury Patients: An Evolving Practice. J Trauma Nurs. 2017;24(4):222–223.
3. Bunn F, Roberts I, Tasker R, et al. Hypertonic versus near isotonic crystalloid for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev. 2004;2004(3):CD002045.
4. Pfortmueller CA, Schefold JC. Hypertonic saline in critical illness - A systematic review. J Crit Care. 2017;42:168–177.
5. Orbegozo D, Vincent JL, Creteur J, et al. Hypertonic Saline in Human Sepsis: A Systematic Review of Randomized Controlled Trials. Anesth Analg. 2019;128(6):1175–1184.
6. Hashimoto K, Suemaru S, Hirasawa R, et al. Effect of hypertonic saline on the corticotropin-releasing hormone and arginine vasopressin content of the rat pituitary neurointermediate lobe. Endocrinol Jpn. 1990;37(5):599–606.
7. Mazzoni MC, Borgstrom P, Arfors KE, et al. Dynamic fluid redistribution in hyperosmotic resuscitation of hypovolemic hemorrhage. Am J Physiol. 1988;255(3 Pt 2):H629–37.
8. Strandvik GF. Hypertonic saline in critical care: a review of the literature and guidelines for use in hypotensive states and raised intracranial pressure. Anaesthesia. 2009;64(9):990–1003.
9. Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. Semin Nephrol 2009;29(3):282–299.
10. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med 2013;126(10 Suppl 1):S1–42.
11. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur J Endocrinol 2014;170(3):G1–47.
12. Ayus JC, Caputo D, Bazerque F, et al. Treatment of hyponatremic encephalopathy with a 3% sodium chloride protocol: a case series. Am J Kidney Dis 2015;65(3):435–42.
13. Weismann D, Schneider A, Höybye C. Clinical aspects of symptomatic hyponatremia. Endocr Connect. 2016;5(5):R35–R43.
14. Seay NW, Lehrich RW, Greenberg A. Diagnosis and Management of Disorders of Body Tonicity—Hyponatremia and Hypernatremia: Core Curriculum 2020. Am J Kidney Dis. 2020;75(2):272–286.
15. Sterns RH. Treatment of Severe Hyponatremia. Clin J Am Soc Nephrol 2018;13(4):641–649.
16. Okuhara Y, Hirotani S, Naito Y, et al. Intravenous salt supplementation with low-dose furosemide for treatment of acute decompensated heart failure. J Card Fail. 2014;20(5):295–301.
17. Shah S, Kimberly WT. Today's Approach to Treating Brain Swelling in the Neuro Intensive Care Unit. Semin Neurol. 2016;36(6):502–507.
18. Hays AN, Lazaridis C, Neyens R, et al. Osmotherapy: use among neurointensivists. Neurocritical Care. 2011;14(2):222–228.
19. Marko NF. Hypertonic saline, not mannitol, should be considered gold-standard medical therapy for intracranial hypertension. Crit Care. 2012;16(1):113.
20. Ogden AT, Mayer SA, Connolly ES. Hyperosmolar agents in neurosurgical practice: the evolving role of hypertonic saline. Neurosurgery. 2005;57(2):207–215.
21. Ware ML, Nemani VM, Meeker M, et al. Effects of 23.4% sodium chloride solution in reducing intracranial pressure in patients with traumatic brain injury: a preliminary study. Neurosurgery 2005;57(4):727–36.
22. Kamel H, Navi BB, Nakagawa K, et al. Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: A meta-analysis of randomized

clinical trials. Crit Care Med. 2011;39(3):554–9.

23. Mortazavi MM, Romeo AK, Deep A, et al. Hypertonic saline for treating raised intracranial pressure: literature review with meta-analysis. J Neurosurg. 2012;116(1):210–221.
24. Rickard AC, Smith JE, Newell P, et al. Salt or sugar for your injured brain? A meta-analysis of randomised controlled trials of mannitol versus hypertonic sodium solutions to manage raised intracranial pressure in traumatic brain injury. Emerg Med J. 2014;31(8):679–683.
25. Cook AM, Morgan JG, Hawryluk GWJ, et al. Guidelines for the Acute Treatment of Cerebral Edema in Neurocritical Care Patients. Neurocrit Care. 2020;32(3):647–666.
26. Riou B, Carli P. Hypertonic sodium chloride and hemorrhagic shock. Ann Fr Anesth Reanim. 1990;9:536–46.
27. Vialet R, Albanèse J, Thomachot L, et al. Isovolume hypertonic solutes (sodium chloride or mannitol) in the treatment of refractory posttraumatic intracranial hypertension: 2 mL/kg 7.5% saline is more effective than 2 mL/kg 20% mannitol. Crit Care Med 2003;31(6):1683–7.
28. Battison C, Andrews PJ, Graham C, et al. Randomized, controlled trial on the effect of a 20% mannitol solution and a 7.5% saline/6% dextran solution on increased intracranial pressure after brain injury. Crit Care Med 2005;33(1):196–202.
29. Mangat HS, Chiu Y-L, Gerber LM, et al. Hypertonic saline reduces cumulative and daily intracranial pressure burdens after severe traumatic brain injury. J Neurosurg. 2015;122(1):202–10.
30. Li M, Chen T, Chen SD, et al. Comparison of equimolar doses of mannitol and hypertonic saline for the treatment of elevated intracranial pressure after traumatic brain injury: a systematic review and meta-analysis. Medicine (Baltimore) 2015;94(17):e668.
31. Burgess S, Abu-Laban RB, Slavik RS, et al. A systematic review of randomized controlled trials comparing hypertonic sodium solutions and mannitol for traumatic brain injury: implications for emergency department management. Ann Pharmacother. 2016;50(4):291–300.
32. Alnemari AM, Krafcik BM, Mansour TR, et al. A comparison of pharmacologic therapeutic agents used for the reduction of intracranial pressure after traumatic brain injury. World Neurosurg 2017;106:509–528.
33. Mangat HS, Wu X, Gerber LM, et al. Hypertonic saline is superior to mannitol for the combined effect on intracranial pressure and cerebral perfusion pressure burdens in patients with severe traumatic brain injury. Neurosurgery. 2020;86(2):221–230.
34. Horn P, Munch E, Vajkoczy P, et al. Hypertonic saline solution for control of elevated intracranial pressure in patients with exhausted response to mannitol and barbiturates. Neurol Res. 1999;21:758–764.
35. Schwarz S, Georgiadis D, Aschoff A, et al. Effects of hypertonic (10%) saline in patients with raised intracranial pressure after stroke. Stroke. 2002;33(1):136–40.
36. Harutjunyan L, Holz C, Rieger A, et al. Efficiency of 7.2% hypertonic saline hydroxyethyl starch 200/0.5 versus mannitol 15% in the treatment of increased intracranial pressure in neurosurgical patients—a randomized clinical trial. Crit Care. 2005;9(5):R530–40.
37. Sakellaridis N, Pavlou E, Karatzas S, et al. Comparison of mannitol and hypertonic saline in the treatment of severe brain injuries. J Neurosurg. 2011;114(2):545–548.
38. Lewandowski-Belfer JJ, Patel AV, Darracott RM, et al. Safety and efficacy of repeated doses of 14.6 or 23.4% hypertonic saline for refractory intracranial hypertension. Neurocrit Care 2014;20(3):436–42.
39. Gu J, Huang H, Huang Y, et al. Hypertonic saline or mannitol for treating elevated intracranial pressure in traumatic brain injury: a meta-analysis of randomized controlled trials. Neurosurg Rev 2019;42(2):499–509.
40. Francony G, Fauvage B, Falcon D, et al. Equimolar doses of mannitol and hypertonic saline in the treatment of increased intracranial pressure. Crit Care Med. 2008;36(3):795–800.
41. Cottenceau V, Masson F, Mahamid E, et al. Comparison of effects of equiosmolar doses of mannitol and hypertonic saline on cerebral blood flow and metabolism in traumatic brain injury. J Neurotrauma 2011;28(10):2003–12.
42. Oddo M, Levine JM, Frangos S, et al. Effect of mannitol and hypertonic saline on cerebral oxygenation in patients with severe traumatic brain injury and refractory intracranial hypertension. J Neurol Neurosurg Psychiatry 2009;80(8):916–20.
43. Rozet I, Tontisirin N, Muangman S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. Anesthesiology 2007;107(5):697–704.
44. Boone MD, Oren-Grinberg A, Robinson TM, et al. Mannitol or hypertonic saline in the setting of traumatic brain injury: What have we learned? Surg Neurol Int 2015;6:177.
45. Singla A, Mathew PJ, Jangra K, et al. A comparison of hypertonic saline and mannitol on intraoperative brain relaxation in patients with raised intracranial pressure during supratentorial tumors resection: A randomized control trial. Neurol India 2020;68(1):141–5.
46. Chen H, Song Z, Dennis JA. Hypertonic saline versus other intracranial pressure-lowering agents for people with acute traumatic brain injury. Cochrane Database Syst Rev. 2019;12(12):CD010904.
47. Roquilly A, Moyer JD, Huet O, et al. Effect of Continuous Infusion of Hypertonic Saline vs Standard Care on 6-Month Neurological Outcomes in Patients With Traumatic Brain Injury: The COBI Randomized Clinical Trial. JAMA. 2021;325(20):2056–2066.
48. Han C, Yang F, Guo S, et al. Hypertonic Saline Compared to Mannitol for the Management of Elevated Intracranial Pressure in Traumatic Brain Injury: A Meta-Analysis. Front Surg. 2022;8:765784.
49. Bernhardt K, McClune W, Rowland MJ, et al.

Hypertonic Saline Versus Other Intracranial-Pressure-Lowering Agents for Patients with Acute Traumatic Brain Injury: A Systematic Review and Meta-analysis. Neurocrit Care. 2023.

50. Iqbal U, Kumar A, Arsal SA, et al. Efficacy of hypertonic saline and mannitol in patients with traumatic brain injury and cerebral edema: a systematic review and meta-analysis. Egypt J Neurosurg. 2023;38:54.
51. Hauer EM, Stark D, Staykov D, et al. Early continuous hypertonic saline infusion in patients with severe cerebrovascular disease. Crit Care Med. 2011;39(7):1766–1772.
52. Koenig MA, Bryan M, Lewin IJL, et al. Reversal of transtentorial herniation with hypertonic saline. Neurology. 2008;70(13):1023–1029.
53. Cooper DJ. Hypertonic saline resuscitation for head injured patients. Critical Care and Resusctiation 1999;1(2):161.
54. Joseph B, Aziz H, Snell M, et al. The physiological effects of hyperosmolar resuscitation: 5% vs 3% hypertonic saline. Am. J. Surg. 2014;208(5):697–702.
55. Shrum B, Church B, McArthur E, et al. Hypertonic salt solution for peri-operative fluid management. Cochrane Database Syst Rev. 2016;(6):CD005576.
56. Jarvela K, Rantanen M, Koobi T, et al. Hypertonic saline-hydroxyethyl starch solution attenuates fluid accumulation in cardiac surgery patients: a randomized controlled double-blind trial. Anaesthesiol Intensive Ther 2018;50(2):122–127.
57. Loftus TJ, Efron PA, Bala TM, et al. Hypertonic saline resuscitation following emergent laparotomy and temporary abdominal closure. J Trauma Acute Care Surg. 2018;84(2):350–357.
58. Bulger EM, May S, Kerby JD, et al. Out-of-hospital hypertonic resuscitation after traumatic hypovolemic shock. Ann Surg. 2011;253(3):431–441.
59. Vahidi E, Naderpour Z, Saeedi M. Hypertonic Saline in the Treatment of Hemorrhagic Shock. Adv J Emerg Med. 2017;1(1):e8.
60. Wu MC, Liao TY, Lee EM, et al. Administration of Hypertonic Solutions for Hemorrhagic Shock: A Systematic Review and Meta-analysis of Clinical Trials. Anesth Analg. 2017;125(5):1549–1557.
61. Blanchard IE, Ahmad A, Tang KL, et al. The effectiveness of prehospital hypertonic saline for hypotensive trauma patients: a systematic review and meta-analysis. BMC Emerg Med. 2017;17(1):35.
62. Paterna S, Parrinello G, Amato P, et al. Tolerability and efficacy of high-dose furosemide and small-volume hypertonic saline solution in refractory congestive heart failure. Adv Ther. 1999;16(5):219–228.
63. Paterna S, Di Pasquale P, Parrinello G, et al. Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as a bolus, in refractory congestive heart failure. Eur J Heart Fail. 2000;2(3):305–313.
64. Licata G, Di Pasquale P, Parrinello G, et al. Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as bolus in refractory congestive heart failure: long-term effects. Am Heart J 2003;145(3):459–66.
65. Paterna S, Fasullo S, Parrinello G, et al. Short-term effects of hypertonic saline solution in acute heart failure and long-term effects of a moderate sodium restriction in patients with compensated heart failure with New York Heart Association class III (Class C) (SMAC-HF Study). Am J Med Sci. 2011;342(1):27–37.
66. Engelmeier RS, Le TT, Kamalay SE, et al. Randomized trial of high dose furosemide-hypertonic saline in acute decompensated heart failure with advanced renal disease. Journal of the American College of Cardiology. 2012;59:e958.
67. Gandhi S, Mosleh W, Myers RB. Hypertonic saline with furosemide for the treatment of acute congestive heart failure: a systematic review and meta-analysis. Int J Cardiol 2014;173(2):139–145.
68. Yayla Ç, Akyel A, Canpolat U, et al. Comparison of three diuretic treatment strategies for patients with acute decompensated heart failure. Herz. 2015;40(8):1115–1120.
69. De Vecchis R, Esposito C, Ariano C, et al. Hypertonic saline plus i.v. furosemide improve renal safety profile and clinical outcomes in acute decompensated heart failure: A meta-analysis of the literature. Herz 2015;40(3):423–35.
70. Lafrenière G, Béliveau P, Bégin J, et al. Effects of hypertonic saline solution on body weight and serum creatinine in patients with acute decompensated heart failure. World J Cardiol. 2017;9(8):685–692.
71. Wan Y, Li L, Niu H, et al. Impact of Compound Hypertonic Saline Solution on Decompensated Heart Failure. Int Heart J. 2017;58(4):601–607.
72. Crane A, Hertel C, Hobza, et al. Does hypertonic saline infusion with furosemide improve outcomes for patients with acute CHF exacerbation? Evidence-Based Practice 2018;21(2):5–6.
73. Griffin M, Soufer A, Goljo E, et al. Real world use of hypertonic saline in refractory acute decompensated heart failure: a U.S. center's experience. JACC: Heart Failure 2020;8(3):199–208.
74. Farkas J. Hyperdiuresis: Using hypertonic saline to facilitate diuresis. PulmCrit December 9, 2019. https://emcrit.org/pulmcrit/pulmcrit-hyperdiuresis-using-hypertonic-saline-to-facilitate-diuresis/.
75. Hanberg J, Rao V, Ter M, et al. Hypochloremia and diuretic resistance in heart failure: mechanistic insights. Circ Heart Fail. 2016;9(8):10.
76. Masella C, Viggiano D, Molfino I, et al. Diuretic resistance in cardio-nephrology: role of pharmacokinetics, hypochloremia, and kidney remodeling. Kidney Blood Press Res 2019;44(5):915–927.
77. Regolisti G, Antoniotti R, Pastorini G, et al. Management of congestion and diuretic resistance in heart failure. Nephrology @ Point of Care. 2016;2(1):73–87.
78. Elkins MR, Robinson M, Rose BR, et al. A controlled trial of long-term inhaled hypertonic saline in patients with cystic fibrosis. N Engl J Med

2006;354(3):229–40.

79. Flume PA, O'Sullivan BP, Robinson KA, et al. Cystic fibrosis pulmonary guidelines: chronic medications for maintenance of lung health. Am J Respir Crit Care Med 2007;176(10):957–69.
80. Wark P, McDonald VM. Nebulised hypertonic saline for cystic fibrosis. Cochrane Database Syst Rev 2018;9(9):CD001506.
81. Elkins M, Dentice R. Timing of hypertonic saline inhalation for cystic fibrosis. Cochrane Database of Systematic Reviews 2020;2(2):CD008816.
82. Donaldson SH, Bennett WD, Zeman KL, et al. Mucus clearance and lung function in cystic fibrosis with hypertonic saline. N. Engl. J. Med. 2006;354(3):241–250.
83. Elkins MR, Bye PT. Mechanisms and applications of hypertonic saline. R Soc Med 2011;104(Suppl 1):S2–5.
84. Reeves EP, McCarthy C, McElvaney OJ, et al. Inhaled hypertonic saline for cystic fibrosis: reviewing the potential evidence for modulation of neutrophil signalling and function. World J Crit Care Med. 2015;4(3):179–191.
85. Tildy BE, Rogers DF. Therapeutic options for hydrating airway mucus in cystic fibrosis. Pharmacology 2015;95(3–4):117–132.
86. Rubin BK. Aerosol medications for treatment of mucus clearance disorders respiratory care 2015;60(6):825–832.
87. George JC, Zafar W, Bucaloiu ID, et al. Risk Factors and Outcomes of Rapid Correction of Severe Hyponatremia. Clin J Am Soc Nephrol 2018;13(7):984–992.