

# Burden of Extra Sodium Administered Through Intravenous Antibiotic Therapy in Hospitalized Patients: A Neglected Harm in Salt Restricted Cardiac Patients

Arash Eatemadi <sup>1</sup>, Kianoosh homayoon <sup>2</sup>, Mohammed Al Bolushi <sup>3</sup>, Reza Shahrami <sup>4</sup>, Fatemeh Mir Nezhad <sup>5</sup>, Iman Mohammadi <sup>6</sup>

<sup>1</sup> Specialist Infectious Disease, Suhar hospital, Suhar, Sultanate of Oman,

<sup>2</sup> Senior specialist cardiologist, Nizwa hospital, Nizwa, Sultanate of Oman

<sup>3</sup> Clinical Pharmacist, Department of Pharmacy, Suhar hospital, Suhar, Sultanate of Oman

<sup>4</sup> Specialist Infectious Disease, Department of Internal Medicine, Imam Hossein hospital, Neka, Iran

<sup>5</sup> Senior medical officer, Seeb polyclinic, Seeb, Muscat, Ministry of Health, Sultanate of Oman

<sup>6</sup> Senior medical officer, Center for emergency management, Ministry of Health, Sultanate of Oman

**Abstract:- Cardiac patients due to suffering from uncontrolled hypertension or especially advanced heart failure, are sometime advised to salt restriction during hospitalization and even after discharge. A considerable portion of this fragile patients concurrently underwent intravenous antibiotic therapy on or during admission for infectious syndromes such as urinary tract infection or pneumonia. Both antibiotic vials and dissolvent solution contain various amounts of sodium which is harmful for this subset of cardiac patients, especially for long term course. This brief review highlighted the importance of considering sodium content of various antibiotics vials and dissolvent fluids.**

**Keywords:** *Cardiac Patient, Uncontrolled Hypertension, Advanced Heart Failure, Salt Restriction.*

High sodium (Na) consumption (>2 grams/day, equivalent to 5 g salt/day) contributes to high blood pressure and increase the risk of heart disease and stroke. The main source of sodium in our diet is salt. Most people consume too much salt (on average 9-12 grams per day), or around twice the recommended maximum level of intake. WHO Member States have agreed to reduce the global population's intake of salt by a relative 30% by 2025. (1). In addition, Dietary guidelines recommend reducing daily intake of sodium to 500 mg for persons with hypertension or chronic renal disease. (2) Salt intake of less than 5 grams per day, lowers blood pressure, and lowering blood pressure reduces the risk of myocardial infarction, stroke and death. (3,4)

A significant portion of hospitalized cardiac patients receive intravenous antibiotic therapy for several reasons during admission. (5) Although this is common phenomenon, however subset of these patients with advanced heart failure who were put on salt and fluid restrictions, is a matter of concern. (6-8)

A neglected issue in this field, is sodium content of antibiotic vials used for treatment of infectious complications among patients with advanced heart failure who should kept under fluid and salt restriction. The

majority of antibiotics are in form of lyophilized powder for injection which needs to reconstitution and then dissolve in normal saline or dextrose normal saline which are containing sodium. Therefore, cardiac patients already under salt restriction, are vulnerable to receive extra but neglected amount of sodium content through intravenous antibiotic therapy. (9) This practice sometimes could be life threatening, especially when a given patient with advance heart failure is planned to receive a long course of intravenous antibiotic therapy for infectious complications such as infective endocarditis. (10)

We collected antibiotic leaflets of all common injectable antibiotics available in Suhar hospital medical store to check the sodium content of each of them. Moreover, we calculated the amount of sodium per 100 ml of different solutions which are used commonly for dissolving and administration of intravenous antibiotics in the form of lyophilized powder and finally the total daily accumulative amount of Na content delivered to the patient. (Table 1)

Regarding necessity of lowering daily receiving sodium in the patients need to follow salt restriction, it is wise to choose solution with less content of sodium such as 5% Dextrose and 0.45% Sodium Chloride Injection (dextrose half- saline) which its sodium content is half amount of 0.9% Sodium Chloride Injection (sodium content of each 100 ml: 177 & 354 mg, respectively).

Among commonly used antibiotics in our hospital for cardiac patients, intravenous quinolones (levofloxacin and ciprofloxacin) had highest content of sodium and vancomycin was the least. Another important consideration is frequency of administration which determines the accumulative amount of total daily receiving sodium. The clear example is true about Penicillin G Sodium. Although each vial of Penicillin G Sodium has little amount of sodium, however due to high routine dose and its usual frequency, the accumulative sodium burden will be considerably harmful. We mentioned the choice of antibiotic therapy in some of common infectious diseases or complications (Table 2)

Generally, dextrose half- saline solution (especially in non-diabetic patients) in little volume (50 ml per each administration) should be the choice solution for most of routine antibiotic administration in this category of patients.

In conclusion, raising awareness among cardiologists and internal medicine physicians about potential harm of prolonged high dose, high sodium content intravenous antibiotic therapy is an important issue and could be placed in antimicrobial stewardship program (ASP) of the hospital.

**Table: 1: Na content of various antibiotics, administration solutions and daily accumulative amount**

Antibiotic	antibiotic content per vial (mg)	Routine dose (mg)	Na content per vial (mg)	Total Na amount with 100 ml of N/S <sup>1</sup> or D/S <sup>2</sup> solution (mg) Per injection	Total Na Amount with 100 ml of D/hS solution <sup>3</sup> (mg) Per injection	Total daily receiving Na (mg) with routine doses
<b>Acyclovir</b>	500 mg	500 mg-750 mg/q8h	49 mg	403 - 428	226 – 250.5	678 - 1284
<b>Amikacin</b>	500 mg	1000 - 1500 mg/OD	20	394- 414	187- 237	187- 414
<b>amoxicillin -- clavulanate</b>	1.2 g	1.2 g/q8h	63	417	240	720 - 1251
<b>Ampicillin</b>	1 g	1 – 2 g/q6h	66	420 - 486	243 - 309	972 - 1944
<b>Azithromycin</b>	500 mg	500 mg/OD	114	468	291	291- 468
<b>Cefazolin</b>	1 g	1-2 g/q8h	48	402 - 450	225 - 273	675 - 1350
<b>Cefuroxime</b>	750 mg	0.75-1.5 g/q8h	41	395 - 436	218 - 259	654 - 1308
<b>Ceftriaxone</b>	1 g	1-2 g/q12h	83	437- 520	260 - 343	520- 1040
<b>cefotaxime</b>	1 g	1-2 g/q8-6h	48	402- 450	225 - 273	693 – 1800
<b>Ceftazidime</b>	1 mg	1-2 g/q8h	54	408 - 462	231 - 285	693 - 1386
<b>Ciprofloxacin*</b>	200 mg	400 mg/q12h	354	708	708	1062
<b>Clarithromycin</b>	500 mg	500 mg/q12h	23	377	200	400 - 754
<b>Clindamycin</b>	300 mg	600 – 900 mg/q8h	23	400 - 423	223 - 246	669- 1269
<b>Cotrimoxazole</b>	480 mg TMP	960 mg /q12h	39	432	255	510 - 864
<b>flucloxacillin</b>	500 mg	1-2 g/q6h	26	406 - 458	229 - 281	916 - 1832
<b>Fluconazole*</b>	200 mg	400 mg/OD	354	354	354	708
<b>Gentamicin</b>	80 mg	Up to 400mg/OD	23	Up to 754	Up to 577	Up to 577 - 754
<b>Levofloxacin*</b>	500 mg	500-750 mg/ OD	354	354	354	354 - 531
<b>Linezolid*</b>	600 mg	600 mg/q12h	114	114	114	228
<b>Meropenem</b>	1 g	1-2 g/q8h	90	444	267	801 - 1332
<b>Metronidazole*</b>	500 mg	500 mg/q8-6h	310	310	310	930- 1240
<b>Penicillin G Sodium</b>	1mU	3-4 mU/q4h	46	492 - 618	315 - 441	1890 - 3708
<b>Piperacillin-tazobactam</b>	4.5 gr	4.5 g/q8-6h	217	571	394	1182 - 2284
<b>Vancomycin</b>	500 mg	1 g/q12h	0	354	177	354- 708
<b>Voriconazole</b>	200mg	200 mg/q12h	218	572	395	790 - 1144

\*RTU: ready to use drug

<sup>1</sup> 0.9% Sodium Chloride Injection, USP (Na content of each 100 ml: 354 mg)

<sup>2</sup> 5% Dextrose and 0.9% Sodium Chloride Injection, USP (Na content of each 100 ml: 354 mg)

<sup>3</sup> 5% Dextrose and 0.45% Sodium Chloride Injection, USP (Na content of each 100 ml: 177 mg)

**Table 2: Suggested antibiotic therapy for common infectious syndromes according to sodium content and total daily Na load in salt restricted patients**

<i>Infectious syndrome</i>	<i>Suggested antibiotic regimen</i>	<i>Comment</i>
<b>Community-acquired pneumonia</b>	Ceftriaxone PLUS Azithromycin	ceftriaxone provides the lowest total daily Na compare to other cephalosporines and amoxicillin --clavulanate to the patient. Also, Azithromycin over clarithromycin.
<b>COPD exacerbation</b>	Azithromycin	Azithromycin comparing to clarithromycin, cefuroxime, amoxicillin –clavulanate has the lowest total daily Na load
<b>Nosocomial pneumonia</b>	Ceftazidime or Levofloxacin +/- Vancomycin	They have less Na content compare to Piperacillin-tazobactam
<b>Pyelonephritis</b>	Ceftriaxone +/- Amikacin	Each vial of amikacin has less Na content compare to gentamicin and the amount to daily used vials of amikacin is less than gentamicin
<b>Unknown origin sepsis</b>	Meropenem +/- vancomycin	Total daily Na content provided by meropenem is less than Piperacillin-tazobactam
<b>Meningitis</b>	Ceftriaxone PLUS Vancomycin +/- Ampicillin	Ceftriaxone provides total daily sodium less than cefotaxime.
<b>Cellulitis</b>	Cefazolin or Amoxicillin --clavulanate	They are preferred over flucloxacillin. (if MRSA is suspected, choose Vancomycin)
<b>Intra-abdominal infections (IAIs)</b>	Ceftriaxone PLUS Metronidazole Or Meropenem (severe cases)	Metronidazole is preferable over Clindamycin for IAIs. Meropenem provides less total Na load over Piperacillin-tazobactam

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