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ESTIMATED SODIUM CONTENT IN PRESCRIPTION MEDICATION: GIVING HEALTHCARE PROVIDERS INFORMATION ON THE ESTIMATED SODIUM CONTENT IN PRESCRIPTION MEDICATIONS IN AN EASY-TO-USE FORMAT

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Abstract. Reducing the sodium intake in an individual's daily diet is a priority for many healthcare providers. Consequently, there is an enormous volume of literature on reducing the sodium content in an individual's food intake; however, there are very few medical journal articles that specifically discuss the sodium content in prescription drugs
Keywords: Sodium, Prescription Medications, Chronic Heart Failure

Background

Since the 1980s, the Food and Drug Administration (FDA) has declared a "war on sodium" but this battle has not yet reached prescription drugs. [1] In 1995, the New England Journal of Medicine (NEJM) published a letter to the editor, "Declaring the Sodium Content of Drug Products." The letter stated, "The FDA recommended that makers of prescription drugs declare the sodium content if it exceeds 5 mg per single recommended dose and issue a warning if the sodium dose content exceeds 140 mg. Until the initiatives have been implemented, this information should be obtained from the manufacturer."[2] Over 15 years have passed since this letter was addressed to the editor and there are still no discussions noted in the FDA Drug Safety Oversight Board Meetings Public Summaries on requiring drug manufacturers to list the sodium content of prescription medications.[3] Phone conversations with the FDA confirm that there are no regulations for drug manufacturers to list the sodium content in prescription drugs.[4] Sodium reduction is still present in the news but there are no strategies discussing the sodium in prescription drugs.[5] The Code of Federal Regulations Title 21 under section 201.64 requires sodium to be labeled in over-the-counter drug products if the single recommended dose of the product contains 5 mg of sodium or more.[6] No discussion can be found to explain the regulatory differences between prescription drugs and non-prescription medication.

Current dietary guidelines recommend that adults should not consume more than 2,300 mg of sodium per day. Seventy percent of the US population (older than 40 years, African American and/or with high blood pressure) is recommended to consume less then 1,500 mg of sodium per day. [7] There are no studies that discuss how much prescription drugs contribute to the sodium intake in a daily diet. It can be speculated that patients with the most health issues are receiving more drug prescriptions. It is also possible that these prescriptions contain sodium and could exacerbate an already chronic condition. Health care providers have been working with their patients to reduce their sodium intake through their diets but may unknowingly be giving sodium to a patient in the form of prescription drugs. Prescribers may, therefore, be harming their most vulnerable patients by not being aware of the sodium content of prescribed medications.

Disclosing sodium content may change or modify the outcomes of research studies. For example, a

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recent study shows that PEG is better than lactulose for chronic constipation.[8] Lactulose does not contain sodium but some PEG laxatives contain high amounts of sodium (2,500 to 10,000 mg), depending on the dosage.[9] Some PEG laxatives contain magnesium citrate and are a low sodium product (35 mg).[10] Sodium content should be discussed and disclosed in a product selection. Due to the nature of PEG laxatives, it is hard to determine the actual amount of sodium absorbed by the bowels and its effect on total bodily sodium levels. We are proposing that sodium content in drugs should be listed in research articles to give medical providers information to make a more informed choice. In addition, more research needs to be done to show the effect of sodium in medication and its effect on the individual. Some medications, like PEG, might not have an effect on total sodium intake due to their laxative nature. It has been proposed that a lone sodium molecule (without a chloride molecule) may not be a significant contributor to changes in blood pressure.[11] More research is required to determine if the sodium content in prescription drugs affects the health of patients.

Sodium is necessary in the drug manufacturing process as the sodium molecule is used for solubility and the stabilization of drug molecules. Studies have shown that sodium in the blood serum can cause volume expansion and a rise in blood pressure[12], which may harm patients with chronic heart failure and chronic renal failure. It has been suggested that if sodium levels in prescription medications were reduced by 50%, the length of hospital stays could be reduced by one day [13] and the cost of hospitalization from heart failure could be reduced by $ 5.6 billion annually. [14, 15][14] Some research shows that a "9.5% reduction in population sodium intake would result in a 1.25-mm Hg decrease in mean Systolic Blood Pressure (SBP) of persons aged 40 to 85 years. This blood pressure reduction in turn, would avert 513,885 strokes and 480,358 MIs and increase life-years lived by more than 1.3 million over the lifetime of U.S. adults aged 40 to 85 years alive today, saving $ 32.1 billion in direct medical costs."[16] In order for providers to reduce sodium, they need to be informed on the sodium content of prescription drugs and if the FDA will not require drug manufacturers to list this information, it is necessary for third parties to fill this role by creating easy-to-use guides for practitioners and by sharing this information with the medical community.

Methods

From September 13-20, 2010, we searched the two online drug databases [17,18] , for drugs that contain sodium in their name, formula, and/or filler in order to comprise a list of 393 drugs that contain sodium. From this list, we searched for drug packet inserts for the listed drugs. Package inserts were downloaded and saved in .pdf format. If no drug packet insert was found, a general search was conducted to find out if the drug was discontinued and/or no longer prescribed for human consumption. If so, no further action was taken on these drugs. Some drugs did not provide enough information for a correct calculation. In such cases, calls were made to gather information from the drug manufacturer. Some manufacturers would not disclose the proper information for calculations. If the drug packet insert listed the sodium content, this information was placed on the spreadsheet. If no drug sodium content was listed on the packet insert, a calculation of the estimated sodium content was conducted, based on the drug formula and molecular weight from the standardized periodic table. This information was placed on the spreadsheet.

Epocrates© [19] and the drug packet insert dosing information were used to calculate the low and high range of the normal prescribed daily dosage. Max daily dosing was used for the high range of the dosage. Epocrates.com was used as a drug reference because over 1,000,000 healthcare professionals and 45% of US physicians use Epocrates© as a drug reference.[20] If a dose was based on a patient's weight, we used a measure of 70 kg (except for Timentin®, which was 60 kg). If a dose was based on body surface area, we used a measure of 1.7 ms for dosing. If a packet insert did not contain enough information, we attempted to contact the drug manufacturer for more information. Some drugs did not present enough information to make a correct calculation. Some manufacturers would not disclose the proper information for the calculations.

Using the estimated mg/g of Na and daily dose of the medication, we calculated an estimated sodium intake per day. From the estimated sodium dosing range, we selected drugs that contained a daily estimated sodium range of 140 mg or greater per day. The medications were then separated by function (antibiotics, bowel prep etc.) in an easy-to-understand format. All work papers, calculations, and notes are available for review (upon request).

Results

See table I

Discussion

Some prescription drugs contain sodium. More studies are necessary to determine if the sodium in prescription drugs will affect certain patient populations. It is important that the amount of sodium in prescription drugs is disclosed in an easy-

to-understand format and widely disseminated, so that providers can make an informed decision when prescribing drugs. We recommend that the above table be reviewed and changed annually, as new drugs become available, as drug formulas change, and/or more information becomes available.

Limitations

Drug manufacturers are not required to disclose the amount of sodium in the drug's formula and/or filler. This study could have missed drugs that contain high amounts of sodium and more drugs could have been added to the drug databases since we conducted our search (Sept 2010). Furthermore, some patients may not be compliant with their medications or take them as prescribed. Sodium intake without a chloride molecule may not affect blood pressure and/or fluid retention. Moreover, short-term high doses of sodium for acute hospitalization may not change a patient's health. Sodium content may vary between production batches, according to the molecular formula (complex molecules such as heparin) and in the fillers and/or items containing sodium that are used to adjust pH (sodium hydrochloride) and solubility. Furthermore, providers could be prescribing medications outside the ranges listed in the drug packets and/or electronic drug references. This research is based on drugs prescribed in the United States (US) and is, consequently, missing drugs used outside the US. Some medications- even if ingested- may not affect total bodily sodium levels. For example, GoLYTELY® has a laxative effect, which may result in the excretion of sodium without absorption. In addition, many drugs were discontinued during the research period. It is possible that these drugs were temporarily discontinued (Pentothal®, Pantoprazole®) and may return to market at after a specified period. Moreover, some drugs may have restricted distribution in the US, such as Xyrem®. We have only listed drugs that are administered through PO, IM, IV, or rectally. Medications administered through other means (transdermally or optically) may affect the client's sodium intake, but are not discussed in this paper.

Special Mention

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Estimated Daily Sodium Intake from Select Prescription Medication		
Drug Name	**Sodium (Na) mg/g**	**Esitmated daily sodium dose**
Antibiotics		
(Ampicillin Sodium; Sulbactam Sodium) (IV, IM)	115 mg/1.5g [0]	460 mg to 920 mg
Ancef® (Cefazolin Sodium) (IV, IM)	48 mg/g [0]	36 to 576 mg
Bactocill® (Oxacillin Sodium) (IV)	92.4 mg/g [0]	92.4 to 554 mg
(Cefazolin Sodium) (IV, IM)	48 mg/g [0]	36 to 576 mg
Cefizox® in Dextrose 5% in Plastic Container (Ceftizoxime Sodium) (IV)	57 mg/g [1]	57 to 684 mg
Cefobid® (Cefoperazone Sodium) (IV, IM)	34 mg/g [0]	136 to 408 mg
Cefotan® (Cefotetan Disodium) (IV, IM)	80 mg/g [0]	80 to 480 mg
(Cefotaxime Sodium) (IV, IM)	50.5 mg/g [0]	25 to 606 mg
(Cefotetan Disodium) (IV, IM)	80 mg/g [0]	80 to 480mg
(Cefoxitin Sodium) (IV, IM)	53.8 mg/g [0]	108 to 646 mg
(Ceftriaxone Sodium) (IV, IM)	83 mg/g [0]	83 mg to 333 mg
(Cefuroxime Sodium) (IV, IM)	54.2 mg/g [0]	122 to 488 mg
(Chloramphenicol Sodium Succinate) (IV)	52 mg/g [0]	182 mg to 364 mg
Claforan® (Cefotaxime Sodium) (IV, IM)	50.5 mg/g [0]	51 to 606 mg
Fortaz® in Plastic Container (Ceftazidime Sodium) (IV, IM)	54 mg/g [0]	108 to 324 mg
Foscavir® (Foscarnet Sodium) (IV)	230 mg/g [1]	1288 to 2898 mg
Geocillin® (Carbenicillin Indanyl Sodium) (Tablet)	23 mg/tab [0]	184 mg
Mefoxin® (Cefoxitin Sodium) (IV)	53.8 mg/g [0]	161 to 645 mg
(Nafcillin Sodium) (IV)	76.7 mg/g [0]	230 to 460 mg
(Oxacillin Sodium) (IV)	92.4 mg/g [0]	92 to 554 mg
(Penicillin G Sodium) (IV, IM)	38 mg per million units [0]	38 to 912 mg
(Piperacillin Sodium) (IV, IM)	42.5 mg/g [0]	510 mg to 1,020 mg
Rocephin® (Ceftriaxone Sodium) (IV, IM)	83 mg/g [0]	83 mg to 333 mg
Timentin® (Ticarcillin/Clavulanic Acid) (IV)	103.6 mg / gram [0]	1,285 to 2,486 mg
(Tobramycin Sulfate) (IV, IM)	1.6mg/2 mL vial: 23.52 mg/30 mL vial: [0]	210 to 1,050 mg
Unasyn® (Ampicillin Sodium; Sulbactam Sodium) (IV, IM)	115 mg/1.5g [0]	460 mg to 920 mg
Zinacef® (Cefuroxime Sodium) (IV, IM)	52.4 mg/g [0]	79 to 472 mg
Zosyn® (Piperacillin Sodium; Tazobactam Sodium) (IV)	64 mg /g [0]	864 to 1,152 mg
Anti-Inflammatory		
Anaprox® (Naproxen Sodium) (PO)	50mg/550mg [0]	36 to 150 mg
Colazal® (Balsalazide Disodium) (Capsule)	86 mg/750 mg [0]	258 mg to 774 mg
Gastrocrom® (Cromolyn Sodium) (PO)	90 mg/g [1]	72 to 144 mg
Naprelan® (Naproxen Sodium) (PO)	50mg/550mg [0]	36 to 150 mg
Bowel Prep		
Golytely® (PEG-3350) (PO)	Dosing is per one treatment	11,511 mg
Nulytely® (PEG- 3350) (PO)	Dosing is per one treatment	4,406 mg
Osmoprep® (Pravastatin Sodium) (Tablet)	313 mg per Tablet [1]	10,336 Total (6,260 Day 1; 3,756 Day 2)
Visicol ® (Sodium Phosphate Monobasic Monohydrate) (PO)	313 mg/ 1.5g [1]	12,520 mg

Tabel I. Results: Estimated Daily Sodium Intake from Select Prescription Medication

Diuretics		
Diuril® (Chlorothiazide Sodium) (IV)	72 mg/g [0]	36 to 144 mg
Electrolyte Management		
Kayexalate® (Sodium Polystyrene Sulfonate) (PO)	100 mg/g [0]	1,500 to 6,000 g
Kionex® (Sodium Polystyrene Sulfonate) (PO)	1500 mg/60 ml [0]	1,500 to 6,000 g
Normocarb HF 25® (Magnesium Chloride; Sodium Bicarbonate; Sodium Chloride) (IV)	140 mEq/L [0]	773 mg
Normocarb HF 35® (Magnesium Chloride; Sodium Bicarbonate; Sodium Chloride) (IV)	140 mEq/L [0]	773 mg
(Sodium Bicarbonate) (IV)	11.5 mg/ml to 22.9 mg/ml 0	Dosing depends on pH
GI Drugs		
Zegerid® (Omeprazole; Sodium Bicarbonate) (PO 20 mg, 40 mg Capsule)	304 mg/ for the 40 mg capsule [1]	304 to 608 mg (40 mg Capsule)
Metabolic Disorders		
Ammonul® (Sodium Benzoate; Sodium Phenylacetate) (IV)	30.5 mg/ml [0]	5,337 to 12,810 mg
Neurologics		
Depacon® (Valproate Sodium) (IV)	138 mg/g [1]	97 mg to 580 mg
Depakote® (Divalproex Sodium) (Tablet)	74 mg/g [1]	155 to 311 mg
Xyrem® (Sodium Oxybate) (PO)	182 mg/g [0]	1,092 to 1,638 mg
IV Fluids		
Ringer's Lactate (IV)	130 mEq/L of Na	2,290 mg per Liter
0.45% Sodium Chloride (IV)	77 mEq/L of Na	1,771, mg per Liter
0.9 % Sodium Chloride (IV)	154 mEq/L of Na	3.524 mg per Liter
Amount of sodium 0.45 % sodium chloride (IV, IM)	10 ml	18 mg
Amount of sodium 0.45 % sodium chloride (IV, IM)	20ml	35 mg
Amount of sodium 0.45 % sodium chloride (IV, IM)	100 ml	177 mg
Amount of sodium 0.45 % sodium chloride (IV, IM)	500 ml	886 mg
Amount of sodium 0.9% sodium chloride (IV, IM)	10 ml	35 mg
Amount of sodium 0.9% sodium chloride (IV, IM)	20ml	71 mg
Amount of sodium 0.9% sodium chloride (IV, IM)	100 ml	354 mg
Amount of sodium 0.9% sodium chloride (IV, IM)	500 ml	1771 mg
[0] Sodium Content listed in Packet Insert	[1] Sodium Content Calculated	

Tabel I. *(continued)* Results: Estimated Daily Sodium Intake from Select Prescription Medication