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"Treat The Patient With The Disease, Not The Disease Alone"

4-1 PATIENT-CENTERED DECISION MAKING AND HEALTH CARE OUTCOMES: Observational Study

Evidence-based medicine (**EBM**) has been described as the "conscious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients". The process of adapting "best evidence" to the care of the individual patient has been characterized as "contextualizing care" or "patient-centered decision making" (**PCDM**). Inattention to relevant patient context that results in an inappropriate care plan is a type of medical error termed ""contextual error".

Patient's context comprises all that is expressed outside the boundaries of their skin that may be relevant to their care, including their life circumstances, and behaviors. For example, failure to recognize when a worsening chronic condition (eg, diabetes) is due to progressive cognitive disability and deteriorating medical adherence rather than the need for intensified medical therapy is a contextual error. Although dementia is a disease process, it also changes behavior and hence is part of the context of diabetes self-care.

"Contextual red flags" are factors in a patient's life that may adversely affect their care. They should trigger the clinician to explore these factors.

Clinicians may consider 10 domains of a patient's context: Access to care, social support, competing responsibilities, relationship with health care providers, emotional state, financial situation, cultural beliefs, skills and abilities, spiritual beliefs, and attitude toward illness.

Contextualizing care involves identifying the relevance of these domains and adopting the care plan accordingly. For example, if a patient is unable to adhere to a 3-time a day medication because of work responsibilities, modification of the plan to accommodate these circumstances is appropriate.

Physicians are prone to miss contextual errors. One study of primary care physicians reported that appropriate care, based on guidelines and best practice recommendations, was provided 73% of the time. When patients' contextual factors were introduced, appropriate care was provided in just 22%. The cost of contextual errors is high.

This study explored whether PCDM—defined as adapting care to the patient's context—positively affected outcomes. And assessed whether patients' presenting problems were more likely to be solved when contextual issues were addressed.

This study used a structured approach to review medical records (written and recorded) to answer:

1) Are there contextual red flags?
2) If so, did the physician explore them for underlying contextual factors that could be addressed in a care plan, or did the patient volunteer such information?
3) If so, did the physician address the contextual factors in the recommended care plan? The study monitored patients' record for 9 months to determine whether the original contextual red flag was partially or fully resolved.

A "Chart Coder" received the medical record for contextual red flags that should alert the physician to screen for contextual factors. Red flags include: Missed appointments, non-adherence with medication, poor control of a chronic condition, or lack of follow-through with laboratory tests or referrals.

After a coder identified a red flag, a structured process followed:

1) Did the attending physician ask the patient what he or she believed might be causing the red flag problem? (Eg, "Your diabetes has been well controlled until recently. Now your sugar is high, what do you think is going on in your life that might cause this change"?)
2) The Coder determines whether the health care provider noted and pursued (probed) the red flag.
3) If the health-care provider did note the red flag did the patient reveal a contextual factor (Eg. "I've been moved to the night shift, and it is more difficult to take my medicines when I'm supposed to.")
4) If the patient revealed a contextual factor in response to the probe did the attending physician respond to the information? (Eg, "Let's talk about how you could adapt to your medication schedule to fit your new work schedule.")
5) The Coder determined whether the provider recommended a care plan that

substantially approached the model response.

6) If the patient reveals contextual factors without probing, the Coder follows steps 4) and 5).

7. Example:

Red Flag	Criterion	Good outcome	Poor outcome
Non-adherence To agreed plan	Did not follow self care plan (eg, exercise; diet)	Patient adhered to plan next visit	Still not adhering to agreed plan

RESULTS

1. 139 resident physicians in the VA consented to participate.
2. A total of 774 patients participated in the study. Average age = 62; 98% male. Patients wee receiving an average of 10 medicines. 548 red flags were identified.
   - Contextual factors were determined in 208 (38% of 548))
   - Physicians made contextualized plans in 123 (59% of 208)
     - Good outcomes in 71%
     - Bad outcomes in 29%
   - Physicians did not make a contextualized plan in 85 (41%).
     - Good outcome 46%
     - Bad outcome 54%
3. Patients who received a contextualized care plan were more likely to have a positive outcome.
4. When patients saw the same physician at their most recent visit, they were more likely to have a positive outcome than when they saw a different physician.

DISCUSSION

1. Contextualizing care is, in essence, Patient Centered Decision Making.
2. When physicians take into account the needs and circumstances (the context) of their

individual patients when planning their care, health care outcomes can improve.

3. For different categories of contextual red flags there was considerable variability in the degree to which clinicians probed and planned care in response to revealed contextual factors.
4. In addition to, and independently of, whether the plan was conceptualized at a given visit, having the same physician at the most recent clinic visit improved patient outcomes.
5. This study measured individualization of care in unselected patients whose clinical problems and context varied considerably.
6. The findings of this study suggest that when clinicians successfully answer the question "What is the best next thing for this patient at this time?", there is an associated benefit to the patient that is measurable and substantial.
7. This study may be the first to document an association between contextualizing patient care and patient outcomes.

Annals Internal Medicine April 16, 2013;158:573-79 Original investigation, first author Saul J Weiner, University of Illinois at Chicago

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This is an important aspect of primary care medicine. It is rarely considered in the current literature. It is the first article I have read that addresses the subject of circumstances of individual patients which may have an important effect on their care.

However, generalization of the results may be limited because the study was limited to older male veterans.

Contextual factors which limit effective treatment are frequent. The older small town family doctor had a great advantage over the large city specialist in recognizing contextual factors. He knew the living circumstances of the town population without having to probe deeply. He had grown up with them. As the article points out—continuity of care is especially important in deterring contextual factors.

"Non-compliance" with prescribed treatments is common. Some physicians may believe that it is due to carelessness, irresponsibility, self-treatment, and neglect. I believe these are less common reasons for 'contextual errors".

I suggest this article as a featured reading for primary care physicians. It is an update on the old advice to "Treat the patient with the disease, not just the disease."

Physicians must take care not to place blame or criticize a non-compliant patient. There may be a good reason. Explore the reasons with patience, compassion and understanding. Patient my be very reluctant to explore the true reasons for non-compliance with a treatment plan. Consider a young woman who is being subject to violent spousal abuse. She may be reluctant to admit this real reason for her complaints.

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Current Public Health Recommendations Are To Reduce NaCl Intake From About 9-12 Grams Per Day To 5-6 Grams

4-2 EFFECT OF LONGER TERM MODEST SALT REDUCTION ON BLOOD PRESSURE: ***Cochrane Systematic Review and meta-analysis (M-A) of randomized trials. (RCTs)***

The object of this study was to determine the effects of longer term modest salt (NaCl) reduction on BP, hormones, and lipids. It included RCTs with a modest reduction in NaCl intake and duration of at least 4 weeks.

To be included in this study, there could be no concomitant interventions (no non-pharmacological interventions, antihypertension drugs, or other drugs). No children were included.

The mean reduction in NaCl intake was 4.4 grams per day. With this salt reduction the mean BP reduction was 4.18/2.96.

When NaCl intake was reduced by 6 grams per day, systolic BP was reduced by 5.8 mm Hg.

The current public health recommendations are to reduce NaCl intake from about 9-12 grams per day to 5-6 grams. Epidemiological, population based interventions, genetic and animal studies, as well as treatment studies show that such a reduction lowers BP:

A reduction in NaCl , if it lowers BP, would reduce CVD risk. Indeed, prospective cohort studies and outcome trials have shown that a low salt diet is related to a reduced risk of CVD.

A total of 34 trials (n = 3230, age range 22 to 73) met inclusion criteria and were included in this M-A: 22 were in patients withy hypertension, and 12 in normotensive patients. Study duration ranged from 4 weeks to 3 years (median = 5 weeks). Participants were randomized to: 1) Usual diet (controls) vs 2) NaCl restricted diets. Daily NaCl intake was determined by24-hour sodium urinary excretion.

Mean NaCl intake at baseline was 9.4 grams per day. Mean BP was 141/86.

In the intervention group, NaCl intake was reduced by a mean of 4.4 grams per day—similar to current public health recommendations.

The pooled estimate of reduction in BP (intervention vs control) was 3.18/2.06. An estimated reduction of 6 grams NaCl was associated with a decrease in systolic BP of 5.8.

Effect on lipids and hormones:

There was no significant change in any serum lipid when NaCl was restricted.

With NaCl restriction, however, there was a fall in extracellular volume and a compensatory physiological stimulation of the rennin-angiotensin-aldosterone system (r-a-a), greater with larger decreases in NaCl intake and smaller with long-term modest reductions. With modest NaCl reductions there were only small physiological increases in plasma renin activity, aldosterone, and noradrenalin. However, studies were of only 4 to 6 weeks.

Trials in hypertensive patients. (990 patients in 22 trials; median age 50; trial duration a mean of 5 weeks):

With usual NaCl intake, the median intake was 9.5 grams per day. And the median BP was 148/93.

In the salt restriction group, NaCl intake was reduced by 4.4 grams per day. And the mean BP was reduced by 5.39/2.82.

A 6 gram per day reduction in NaCl intake was associated with a fall in in systolic BP of 10.8

Being hypertensive was associated with a greater fall in systolic compared with normotensive participants.

Trials in normotensive patients (2241 individuals with normal BP in 12 trials for a median of 4 weeks).

With the usual salt diet, NaCl intake was a median of 8.9 grams daily. The median BP was 127/77.

The low NaCl diet reduced intake by a mean of 4.4 grams daily. (range 2.3 to 6.9 g/d). The pooled estimate of reduction in BP was 2.42/1.86.

A reduction of NaCl of 6 grams per day was associated with a fall in systolic of 4.3 mm Hg.

DISCUSSION

"Our analysis shows that a longer term modest reduction in salt (NaCl) intake of 4.4 grams per day on average caused significant, and from a population view, important falls in blood pressure in people with both raised and normal blood pressure,"

BP fell, on average, by 5/3 mm Hg in hypertensive people and by 2/1 in normotensive people.

The benefit was present in both white and black persons and in men and women.

"These results provide further support for a reduction in population salt intake, which will result in lower population blood pressure and thereby a reduction in strokes, heart attacks, and heart failure."

The effect of chronic high NaCl intake is a gradual increase in BP throughout life. The International Study of Salt and Blood Pressure (INTERSALT) suggested a strong relation between salt intake and progressive increase in BP with age

The greater the baseline NaCl intake, the greater the fall in BP with NaCl restriction.

The DASH-sodium study (Dietary Approach to Stop Hypertension) randomized over 400 individuals with normal or raised BP were randomized to the normal American diet (control group) or the DASH diet, rich in fruits, vegetables, and low fat dairy. Participants were given 3 levels of NaCl intake (8, 6, and 4 grams daily) in a randomized cross-over manner, each for 4 weeks. The fall in BP was greater in the lower level of NaCl intake (4 grams) compared with 6 to 8 grams.

"It is clear that recommendations to reduce salt from the current levels of about 9 to 12 grams daily to 5-6 grams/d will have a significant effect on BP. A further reduction to 3 grams per day will have a much greater effect on BP. We consider that this should become the long term target for population salt intake". The UK recommendations are to reduce population NaCl intake to 3 grams per day by 2025.

It will be difficult, however, to keep individuals on a low salt diet for a long time because of the widespread presence of salt in nearly all processed, restaurant, and fast foods.

NaCl reduction lowers BP by a similar mechanism to that of thiazide diuretics. Both stimulate the r-a-a system and the sympathetic nervous system.

Patients receiving aggressive diuretic treatment may be severely salt and water depleted. Salt restriction without a reduction in dose of diuretics is known to be dangerous.

CONCLUSION

A modest reduction in salt intake for 4 or more weeks caused significant, and from a population viewpoint, important falls in BP in both hypertensive and non-hypertensive individuals independent of sex and ethnic group.

NaCl restriction was associated with a small physiological increase in plasma renin activity, aldosterone, and noradrenalin. There was no significant change in lipids.

These results support a reduction in population salt intake, which will lower population BP and reduce CVD.

Larger reductions in salt intake will lead to larger falls in systolic BP.

The current recommendations to reduce NaCl intake from 9-12 grams per day to 5-6 will have a major effect on BP. A further reduction to 3 grams will have a greater effect on BP and should become the long-term target for population salt intake.

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First author Feng J He, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry

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Avoidance of a diet heavy with salt should be a universal health intervention. The DASH diet helps.

I doubt, however, if most primary care clinicians stress this point, perhaps because they think it is futile and that most patients cannot comply. However, any reduction in NaCl intake will help.

It is easier to take a pill. Many other interventions will reduce BP.

BP is a substitute endpoint.

The authors did mention a possible adverse effect from too stringent NaCl restriction. A combination of diuretic + very low NaCl intake may lead to hyponatremia and dehydration. The combination should be used with caution.

The main clinical point is that a modest reduction in daily NaCl intakes (eg, by 4 to 5 grams) will significantly reduce BP.

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4-3 EFFECT OF LOWER SODIUM INTAKES ON HEALTH:

Systematic Review and Meat-analysis

(Note: This article persists in quoting results in terms of sodium (Na). Since the greatest Na content of the diet is in the form of salt (NaCl), I have converted most amounts of Na to equivalent amounts of NaCl by multiplying Na by 2.5. (Eg, 2 grams Na = 5 grams of NaCl; 4 grams = 10 grams NaCl.) I believe this will clarify the presentation. Ed.)

Raised BP and hypertension are major risk factors for cardiovascular disease (CVD), and are estimated to contribute to 49% of all coronary heart disease (CHD) and 62% of all stroke events. Hypertension currently affects nearly half of adults globally with an even greater number experiencing raised BP. Raised BP, hypertension, and related non-communicable diseases are among the most important public health problems. Renewed efforts (including non-drug approaches) to reduce them are urgently required.

Sodium is an essential nutrient necessary for maintenance of plasma volume, acid-base balance, transmission of nerve impulses, and normal cell function.

Increased NaCl consumption is associated with increased BP. Reduced NaCl consumption decreases BP.

The minimum daily requirement of sodium is estimated at 200 – 500 mg (equivalent to 500-1250 mg NaCl). The average daily intake around the world is well above that needed for physiological function, and in many countries is greater than the 2 grams per day, (5 grams of NaCl) the value recommended in 2007 by the WHO.

Cultural context and dietary habits determine the population's intake.

In addition to being the content of table salt, NaCl is added to many foods in their preparation. Many condiments such as soy, fish sauces, and snack foods often contain high amounts. Thus, a diet high in processed foods and low in fruits and vegetables is high in NaCl.

Several recent systematic reviews of randomized controlled trials (RCTs) concluded that reducing NaCl intake decreases BP in adults with and without hypertension.

This review systematically compiled results from RCTs and cohort studies and conducted a meta-analysis (M-A) to quantify the effect of lower compared with higher NaCl intake on

BP, all-cause mortality, CVD, stroke, and CHD. And assessed whether the absolute amount of NaCl consumed, or a relative reduction in NaCl intake, would affect these outcomes.

STUDY

1. Used the methods recommended by the Cochrane Collaboration to search for RCTs and cohort studies on the effect of a lower NaCl intake relative to higher NaCl intake. Included RCTs that allocated one group of participants to decreased NaCl intake (interventions group) and one group to higher Na intake (control group). All studies lasted 4 or more weeks. All achieved an intake difference of at least 2.5 grams of NaCl per day between intervention and control. Determined daily intake of NaCl by 24-hour urinary secretion of Na.
2. Cohort studies had a prospective design that measured NaCl intake in any way, had a duration of one or more years, and reported any outcome of interest. Excluded studies targeting people with acute illness (including type 1 diabetes, acute heart failure, and patients admitted to hospital).
3. Assessed the relation between high and low NaCl intake and BP, renal function, blood lipids and catecholamine levels, and all-cause mortality, cardiovascular disease (CVD), stroke, and coronary heart disease (CHD).

RESULTS

1. Identified 9862 publications reporting on NaCl and at least one outcome of interest; 64 studies from 11 countries contributed to the systematic review and 54 contributed to the M-A.
2. Length of intervention varied from 4 weeks to 36 months. (Most were less than 3 months.) Included 478 with hypertension; 3263 without hypertension.
3. The intervention was dietary advice or education in 12 RCTs.
   One trial supplied prepared food with a known NaCl level; 24 trials had a run-in period where all participants achieved a reduced NaCl intake, and participants received either NaCl or placebo tablets.

4. All studies divided the sample populating according to Na intake at baseline and calculated risk of outcome by NaCl intake group.

5. Effects on BP:

The M-A of 36 studies found that a reduction in NaCl intake significantly reduced BP by 3.3/1.5 mm Hg.

The M-A of 3 comparisons showed a significant decrease of 3.47/1.81 when NaCl intake was less than 5 grams/day.

The M-A of 2 comparisons detected a significant decrease of 3.14/1.70 when the relative reduction in NaCl intake was one third or more of control.

The reduction in systolic pressure was greater in studies of participants with hypertension than in studies without hypertension. (4.06 vs 2.96)

The subgroup in which the relative reduction in NaCl was one third or more of control had significantly greater decrease in BP compared with those consuming more.

Reduced NaCl intake decreased systolic BP in studies of duration of less than 3 months, and in those 3 to 6 months.

Reduced NaCl intake lowered BP regardless of sex, measurement device of method, status of anti-hypertension drugs, of study design.

6 Adverse effects:

Reduced NaCl intake had no significant adverse effect on total cholesterol, LDL-cholesterol, HDL-cholesterol, or triglycerides.

Several studies determined renal function and reported a non- significant reduction in protein excreting.

7. Clinical outcomes:

A. There were insufficient RCTs to assess the effect of reduced NaCl on morbidity and mortality.

B. Cohort studies:

Outcome or subgroup	Effect estimate: Risk ratio high NaCl vs low NaCl	
All cause morality	1.06	NS

All CVD events	1.12	NS
Fatal CVD events	1.08	NS
Stroke overall	1.24	S
Fatal stroke	1.53	S
CHD	1.04	NS
Fatal CHD	1.32	S

(NS = not significant; S = significant

8. All-cause mortality , CVD, and CHD in adults

The M-A of 10 cohort studies reported an increase in stroke with higher NaCl intake (RR = 1.24). and fatal strokes (RR - 1.63) The M-A of 3 comparisons of NaCl intake and CHD mortality detected an increased risk of fatal CHD in those with higher Na intake.

9. This review considered that changes in BP are indirect evidence for the effect of NaCl on risk of CVD, stroke, and CHD. BP is recognized as a reliable biomarker for estimating risk of CVD.

DISCUSSION

1. Reduction in NaCl intake reduces BP. The quality of evidence was high.
2. These results are consistent with 5 previous systematic reviews in adults with and without hypertension. There was no indication of bias, inconsistency, or imprecision across all studies.
3. RCTs of 4 or more weeks showed no indication that reducing NaCl intake had any adverse effects on blood lipids, catecholamine levels, or renal function.
4. Reduction in NaCl intake decreases BP in people with hypertensions and in those without hypertension. The reduction was greater in those with hypertension.
5. A modest decrease in BP can have important public health benefits. A decrease of 2 mm Hg in the US population could result in an estimated 17% decrease in the prevalence of hypertension, 6% decrease in CHD, and a 15% decrease in risk of stroke. And prevent an estimated 67 000 CVD events and 34 000 strokes every year.

6. The relation between BP and vascular mortality is positive, strong, and linear down to a systolic of 115.
7. Most reductions in vascular events owing to small reductions in BP across the entire distribution will occur among people with moderately raised BP levels, including those within normal range. Thus, almost all reductions in BP are beneficial for health, and modest population-wide reductions in BP can result in important reductions in mortality, substantial health benefits, and meaningful savings in health care costs.
8. The BP reductions in children related to NaCl restriction were small. However, such an effect sustained during childhood and adolescence could result in an appreciable reduction in risk of hypertension in adults. Non-communicable diseases are chronic and take years or decades to manifest. Delaying onset of elevated BP could improve quality of lives and provide substantial cost savings.
9. Reducing NaCl intake reduces blood volume and thus activates the renin-angiotensin-aldosterone and sympathetic nervous systems.
10. The M-A detected a significant association between higher NaCl intake and increased risk of fatal stroke and fatal CHD.
11. The objective of this review was to inform the WHO guideline development process for advising NaCl intake for most people globally.

CONCLUSION

There was a clear benefit of low NaCl intake in persons without acute illnesses. A decrease in Na intake reduced BP.

The effect was detectable in those with and without hypertension.

Results from observational cohort studies also showed a significant association between lower intake of NaCl intake and stroke and fatal CHD.

Lower NaCl intake had no adverse effect on blood lipids, catecholamine levels, or renal function.

BMJ 2013;346:f1326 BMJ April 4 , 2013
http://dx.doi.org/10.1136/bmj.f1326
First author Nancy J Aburto, World Health Organization, Geneva, Switzerland

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This study strongly supports the inverse relationship between NaCl intake and BP.

It does not strongly support the effect of NaCl reduction on clinical endpoints (CHD, CVD). RCTs of only 3 to 4 months duration could hardly be expected to reveal decreases in clinical endpoints, which take years to develop.

I believe any persons with sufficient interest could reduce NaCl intake by half with little effort. Remove the salt shaker. Cook at home with no added salt. Avoid prepared foods with obviously added salt (salted chips and crackers; salted nuts)

Don't forget the influence of potassium on BP. *See the following.*

==========.

Increased K Intake Reduces Bp In People With Hypertension And Is Associated With A Reduction In Stroke

4-4 EFFECT OF INCREASED POTASSIUM INTAKE ON CARDIOVASCULAR RISK FACTORS AND DISEASE: ***Systematic Review and Meta-analysis (M-A)***

Potassium (K) is an essential nutrient that is needed for maintenance of total body fluid volume, acid and electrolyte balance, and normal cell function. In our human ancestors, K intake was very high, often exceeding 200 mmol/d (7.8 grams/d)[a]. Now, K levels have been markedly reduced by food processing . A diet high in processed foods and low in fresh fruits and vegetables is often lacking in K.

(a Note: The article continues to quote K levels in mmol. Most of us in the U.S. consider levels in terms of grams per day. The atomic weight of K is 39. One mole of K weighs 39 grams; one mmol weighs 39 mg; 39 X 200 = 7.8 grams. I will change mmol to grams from here on. Ed.)

Data from around the world suggest that the average K intake in many countries is below 2.7 to 3.3 grams/d. Few countries report an average consumption of 3.5 grams/d. No country reported an average consumption of 4.6 grams/d as recommended in the U.S.

Low K consumption has been associated with elevated BP, hypertension, and stroke. Higher consumption could protect against these conditions. A public health intervention aimed at increasing K intake from food is a potentially cost effective measure to reduce the burden of morbidity and mortality from non-communicable disease.

Previous systematic reviews and M-A have reported conflicting effects of increased K intake on BP.

The WHO initiated this review to inform guidelines on K intake by apparently healthy adults and children without acute illnesses or renal impairment. The M-A asked the following:

1) What is the effect of increased K intake compared with a low intake on BP, all-cause mortality, CVD, stroke, and CHD in apparently healthy adults?
2) What is the effect of increased K intake on BP in apparently healthy children?
3) What is the effect of increased K intake on lipids, catecholamine concentrations, and renal function in apparently healthy adults and children?
4) What is the level of K intake that results in the maximum bereft on BP and risk of CVD?
5) Is the effect of increased K differentially affected by the hypertension status of the population, average sodium or K intake at baseline, type of intervention, method used to determine BP, study design, or duration of interventions?

STUDY

1. Conducted this review by the methods recommended by the Cochrane Collaboration.
2. Primary outcomes of interest were: BP, all-cause mortality, fatal and non-fatal stroke, and CHD. The primary outcome in children was BP.
3. Also examined potential adverse effects such as changes in lipids, catecholamine, and renal function, and any other reported adverse effect.

4. After elimination of studies that did not meet inclusion criteria, 35 studies were included in the meta-analysis. Fourteen countries were represented.

    Randomized controlled trials (RCT; high K vs low K) in adults (n = 21)

    Cohort studies in adults (n = 11)

    RCTs in children (n = 1)

    Cohort studies in children (n = 1)

5. K supplements (16 trials) were given mainly as K-chloride in varying amounts:

    <3.5 grams

    3.6 to 4.6

    4.6 to 5.8

    Over 5.8

    In 3 trials, participants received dietary advice only.

6. Duration of intervention = 2 to 4 months.

RESULTS

1. 127 038 participants were included in the M-A
2. Cohort studies divided the sample population on the basis of K intake at baseline and measured all-cause mortality
3. Effect estimates of increased K intake in adults:

    Overall:

    In the M-A of 21 RCTs, increased K intake reduced BP 5.9/3.8 mm Hg.

    Heterogeneity was present for both systolic and diastolic.

    Subgroup analysis:

    A. Hypertension: Participants with hypertension (17 trials) supplemental K was associated with a decrease in BP of 5.3/3.1 mm Hg. Intake of supplemental K of 3.5 to 4.6 grams was related to the greatest reduction in BP (-7.1/4.0). Without hypertension (3 trials)—no effect.

    B. Effect on stroke: Relative risk supplements vs no supplements = 0.76

    C. Effect depending on sodium intake: Those with high Na intake (> 4 grams daily)

had the greatest reduction on BP from K supplementation (-6.9/2.8)

D. Effect on CHD and CVD: No benefit from supplemental K.

4. Children (2 studies): No effect on BP
5. The M-A of 9 studies comparing higher dietary K intake with lower intake detected a protective effect on stroke (RR = 0.76).
6. Increased K intake decreased BP regardless of type of BP measurement device, whether or not BP lowering drugs were used, or the study design.
7. Potential adverse effects:

   There was no significant adverse effect of K supplements on lipids, catecholamines, or serum creatinine.

DISCUSSION

1. This M-A of RCTs in adults confirm that increased K intake reduces BP, without any adverse effects on lipids, catecholamines, or renal function.
2. There was a beneficial effect of K on risk of incident stroke.
3. These results are consistent with previous M-A comparing high K with lower K intake, although some studies reported no effect.
4. This review is the first in children. Further high-quality RCTs are required to clarify effects of K in children.
5. K had no detectable effect on BP in RCTs conducted exclusively in people without hypertension. However, these studies were of relatively short duration and did not consider the effect that increased K intake may have over time in preventing hypertension.
6. Given the high prevalence of hypertension in adults, and the relatively low K intake globally, populations around the world would probably benefit from increased K intake.
7. The decrease in BP caused by increased K intake can have important public health

benefits. For example, a decrease of 2 mm Hg in diastolic in the US population could prevent an estimated 67 000 CHD events and 34 000 stroke events every year. A 5 mm decrease in systolic in the UK could reduce prevalence of hypertension by 50%.

8. Both K intake through supplements, and through dietary changes, reduce systolic BP. Increasing K intake by dietary changes can reduce BP.
9. Other researchers have found that, in people without renal dysfunction, increased K consumption from food is safe. People with impaired renal function can be at risk of hypekalemia from increased K intake. In people without renal impairment, the body is able to excrete excess K up to 15 grams/d. No cases of toxicity from food have been reported. In this M-A, no study reported major adverse effects in the increased K groups vs control groups.
10. What is the optimum K intake? In this M-A, intake above 4 grams/d did not seem to have any additional benefit. If a person consumes 3.5 grams/d, or more, and the WHO recommendation of sodium intake is less than 2 grams, then the molar relationship Na/K is approximately one to one, a ratio considered beneficial to health.
11. Supplemental K is more effective in reducing BP at higher levels of Na intake (> 4 g/d; the general intake of most populations), so increased K intake should benefit most people in many countries. However, this study found a significant decrease in BP when Na intake was 2 to 4 grams/d. Increased K intake can be beneficial even in individuals who decrease Na intake. Benefit on BP may be increased when reductions in Na intake is combined with increased intake of K.
12. The results from cohort studies support the claim that dietary sources of K from food can reduce systolic BP. All cohort studies considered groups of varying dietary intake of K and showed a beneficial effect of higher intake of K from food on risk of stroke
13. The WHO guidelines recommend that adults and children who have no renal impairment consume more than 3.5 grams/d for beneficial effects on BP and reduced risk of related CVD diseases.

CONCLUSION

High quality evidence shows that increased K intake reduces BP in people with hypertension and is associated with a lower risk of stroke.

Increased K intake is potentially beneficial to most people who have no renal impairment to prevent and control elevated BP and stroke.

BMJ (http://dx.doi.org/10.1136/bmjf1378) Original investigation, first author Nancy J Aburto, Department of Nutrition for Health and Development, WHO Geneva, Switzerland.

The beneficial effect of K on BP and the deleterious effect of Na on BP has been observed for years. This article seems to be the best synthesis of data to date.

I do not know of any articles recommending K supplementation (pills of KCl) to treat hypertensions. We rely on increased dietary intake of K in vegetable, legumes, and fruits, which also offer other health benefits.

Some "Nutrition Facts" on food labels do include K content. We should aim for a ratio of K to Na of about 3 to 2. (The article mentions a ratio based on molarity (39/23).

Small reduction in BP in the population result in large benefits in reduction of CVD.

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Increase Fluid Intake, Cut Down On Soft Drinks, Consider Thiazides, Allopurinol And Citrate

4-5 MEDICAL MANAGEMENT TO PREVENT RECURRENT NEPHROLITHIASIS IN ADULTS: *Systematic Review and Clinical Guidance from the American College of Physicians*

Lifetime incidence of kidney stones (KS) is approximately 13% in men and 7% in women. Although often asymptomatic, incidental stones are identified in approximately 5% of individuals who have abdominal ultrasound or CT scans.

In patients with asymptomatic stones who are followed with serial radiography, 11% to 33% develop symptoms or undergo a procedure within 3 to 4 years. Without specific treatment after a symptomatic stone event, the recurrence rate is 35% to 50%.

About 80% of KS are composed of calcium oxalate, calcium phosphate, or both. Uric acid and struvite (magnesium ammonium phosphate) stones are less common.

Many patients with KS have low urine volume and biochemical abnormalities (hyper-calcemia, hyper-oxaluria, hyper-uricosuria, and hypo-citrateuria.

Low fluid intake or low calcium intake increases stone risk. Evidence for many other dietary factors is mixed.

Risk is increased by medical conditions including primary hyper-parathyroidism, obesity, diabetes, gout, intestinal malabsorption, and anatomical abnormalities.

This review includes more recent randomized controlled trials, comparative treatments, and combination regimens.

STUDY

1. Conducted a widespread review of Randomized Controlled Trials (RCTs) that involved dietary or pharmacological treatment to prevent recurrent KS in adults and reported clinical outcomes including symptomatic an/or radiographic stone recurrence or change in stone size.
2. Treatment efficacy was assessed according to patient characteristics, baseline and follow-up biochemical measures, and study duration.

RESULTS

1. Included a total of 28 RCTs: 8 dietary and 20 pharmacological. 23 included only calcium stones; 3 were limited to struvite stones; 2 included any type of stone.
2. Six trials reported symptomatic stone recurrence; 8 reported radiographic recurrence; 18 reported a composite recurrence outcome.
3. Duration of trials was 1 to 5 years. Most trials were of fair quality.
4. Dietary therapy to prevent stone recurrence:

A. Increased fluid intake:

Two RCTs assigned participants with a history of 1 past calcium stone to: 1) increased fluid intake to maintain urine output greater than 2 to 2.5 liters/day vs no treatment. In one trial, increased fluid intake was associated with reduced risk for composite stone recurrence. (risk ratio [RR] = 0.4) Results of the second trial did not reach statistical significance.

B. Decreased soft drink intake:

One large trial randomized men with more than 1 past KS of any type and soft drink consumption greater than 160 mL/d to
1) reduced intake vs 2) no treatment. The intervention significantly reduced symptomatic recurrent stones. (RR = 0.83). Benefit seemed to be limited to participants who more frequently consumed soft drinks acidified by phosphoric acid. Total fluid intake was similar in both groups.

C. Multicomponent diets:

One RCT considered participants with 1 or more past calcium stones and hypercalcemia who were on increased fluid intake and avoidance of excess oxalate. They were randomized to: 1) diet including 1200 mg calcium, low animal protein, and low sodium vs 2) low calcium diet (400 mg). The higher calcium + low protein diet was associated with lower risk of of stone recurrence. (RR = 0.52)

5. Pharmacological therapy for preventing stone recurrence:

A. Thiazides vs placebo or control:

Six RCTs assigned participants with recurrent calcium stones to 1) thiazides vs 2) placebo or control. Five trials included increased fluid intake and decreased oxalate in both study groups. There was moderate strength evidence that thiazides decreased stone recurrence. (RR = 0.52), although thiazides did not reduce recurrence of symptomatic stones. Those receiving thiazides were more likely to withdraw for any reason or for adverse effects.

B. Citrate vs placebo or control:

Six trials randomized participants with predominantly calcium stones to 1) citrate vs 2) placebo or control. There was moderate strength evidence that citrate reduced risk of composite stone recurrence. (RR = 0.25) Citrate participants were more likely to withdraw.

C. Allopurinol vs placebo or control:

Four RCTs assigned participants to 1) allopurinol vs 2) placebo or control. Allopurinol reduced risk for composite stone recurrence. (RR = 0.59) Adverse events were infrequently reported.

6. Pretreatment stone composition and biochemistry measures to predict treatment efficacy in preventing stone recurrence:

In 2 RCTs in patients with elevated uric acid in serum or urine, participants randomized to 1) allopurinol vs 2) control had a significantly lower risk of recurrent stones than controls. (RR = 0.59) However, rates of symptomatic recurrence did not seem lower with allopurinol vs control in trials of participants without high uric acid levels.

7. Other baseline biochemical measures did not seem to predict efficacy of dietary or drug treatment compared with control for recurrent stone. Specifically, baseline calcium levels made no statistically significant difference in the efficacy of increased fluid intake, diet, thiazides, citrate, or allopurinol vs control. Similarly, baseline citrate levels made no statistically significant difference in the efficacy of increased fluid intake, diet, thiazides, or citrate compared with control.

8. On-treatment biochemistry measures to predict treatment efficacy in preventing recurrence:

In 4 thiazide trials that reported follow-up urinary calcium levels, 3 reported

statistically significant decrease in calcium among participant assigned to thiazide but not to controls. This suggests that reduction in urinary calcium levels may predict thiazide efficacy in preventing stone recurrence.

DISCUSSION

1. Increased fluid intake more than halved the risk for composite or radiographic stone recurrence and seemed well tolerated, although the strength of evidence for these findings was limited by study quality and size.

2. Reducing intake of soft drinks acidified by phosphoric acid in men with high intake modestly decreased risk of recurrent symptomatic stone.

3. However, these subgroup results were based on post hoc analyses, and generalizability to other populations is uncertain.

4. Results were inconsistent about whether other dietary interventions added benefit to increased fluid intake.

5. Among pharmaceutical treatments, thiazides, citrate, and allopurinol each decreased risk for recurrent calcium stone more than increased fluid intake alone. But, statistical power was low. And it is not known if low doses of thiazides are effective.

6. Data directly comparing pharmaceutical treatments to prevent stone recurrence are extremely limited.

7. No trial examined the effect of any therapy to reduce risk of recurrent uric acid stones.

8. Because most patients had calcium stones, increasing fluid intake in all patients with KS,

with or without adding thiazide or citrate might reduce recurrence risk. However, no trial tested this strategy.

9. No trial compared allopurinol with thiazides and citrate in patients with high uric acid levels. We do not know whether allopurinol should be the preferred therapy in these patients.

10. The available data limit this review in several ways: 1) Few data existed for some treatment comparisons. And trials and small sample sizes were small.. In these cases, determining whether insufficient evidence for treatment benefit reflects inadequacy of the treatment or limitations in the data may be impossible. 2) Most trials reported few data on treatment harms, thus limiting confidence around risk estimates for some outcomes. 3) Nearly all trials enrolled adults with idiopathic calcium stones. Results may not be generalizable to individuals with conditions predisposing to KS, to those with non-calcium stones, or to children. 4) Few trials reported symptomatic stone recurrence. Most trials were driven by radiographic stone recurrence—a surrogate outcome that may be less relevant to treatment decisions. 5) Only 1 trial recruited patients from primary care. 6) This trial was limited by inconsistent reporting and categorization of baseline biochemistry levels.

CONCLUSION

Increased fluid intake substantially reduced risk of recurrent calcium stones.

In men with high soft drink consumption, decreasing intake reduced stone risk. Benefit may be limited solely to drinks fortified by phosphoric acid. Results were mixed for the potential benefit of other dietary interventions.

In individuals with multiple past calcium stones, most of whom increased fluid intake, thiazides, citrate, and allopurinol each further reduced risk of stone recurrence.

Other than uric acid levels, baseline biochemistry measures did not predict efficacy of any treatment.

Withdrawals were low in trials using increased fluid intake; were high in long-term trials evaluating other dietary interventions. And variable in pharmacological trials.

Reports of adverse events were poor.

Existing gaps in RCT evidence may require clinicians to use other sources of evidence to inform their clinical management of patients with KS.

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We have much more to learn. Meanwhile, primary care clinicians will benefit patients plagued by stones by suggesting some of these interventions.

I congratulate the authors on their detailed analysis of the various limitations of trials. Few studies are so forthcoming.