

Effect of Laxatives as regulators of colonic potassium secretion in Hemodialysis Patients

Thesis

*Submitted for Partial Fulfillment of
Master Degree in Nephrology*

By

Mustafa Abo Al Khair Mohamed

M.B.B.Ch., Diploma in internal medicine

Under Supervision of

Prof. Magdy Mohamed said El Sharkawy

*Professor of Internal Medicine and Nephrology
Faculty of Medicine –Ain Shams University*

Prof. Hesham Atef Abu Al Lail

*Assistant Professor of Internal Medicine and Nephrology
Faculty of Medicine –Ain Shams University*

Dr. Khaled mohamed Rezk

*Lecturer of Internal Medicine and Nephrology
Faculty of Medicine – Ain Shams University*

**Faculty of Medicine
Ain Shams University
2017**

List of contents

Content	Page
• List of tables	i
• List of figures.....	ii
• List of abbreviations	iv
• Introduction	1
• Aim of the work	5
• Review of literature:	
➤ Potassium Chapter.....	6
➤ Hyperkalemia.....	28
➤ Constipation and laxative therapy.....	63
• Patients& methods	88
• Results	92
• Discussion	106
• Summary	116
• Conclusion	119
• Recommendations	120
• References	121
• Arabic summary	

• List of Tables

Number	Name	page
Table 1	Comparative Amounts of Approximate Potassium Content in Various Food Groups	27
Table 2	Laboratory investigations in hyperkalemia	48
Table 3	Laxatives can be used safely in ESRD	86
Table 4	Laxatives to be used with caution in ESRD	86
Table 5	Laxatives never to be used in ESRD	87
Table 6	Demographic data of included ESRD patients	93
Table 7	Hematological data of included ESRD patients	94
Table 8	Clinical and biochemical parameters of included ESRD patients	95
Table 9	Effect of laxatives on serum potassium level	96

Number	Name	Page
Figure 1	Apparent K ⁺ -H ⁺ exchange (or K ⁺ -HCO ₃ ⁻ cotransport) in skeletal muscle cells	15
Figure 2	lactose and lactulose molecules	69
Figure 3	Bisacodyl molecule	76
Figure 4	Etiology of chronic kidney diseases in the study patients	92
Figure 5	Serum K ⁺ concentrations in the studied groups at the beginning of the study and after medication intake	97
Figure 6	Effect of bisacodyl on inter-dialytic hyperkalemia among group1	98
Figure 7	Effect of osmotic laxative on inter-dialytic hyperkalemia in group2	99
Figure 8	Serum K ⁺ in ESRD patients who did not receive any type of laxatives (group3)	100
Figure 9	Constipation percent among selected ESRD patents.	101
Figure 10	The baseline K ⁺ level in the total constipated patients compared to total non-constipated patients	102
Figure 11	Distribution of K ⁺ level in constipated patients in comparison with non-constipated patients in group 1; pre-and post bisacodyl intake	103

Figure 12	Distribution of K^+ level in constipated patients in comparison with non-constipated patients in group 2; pre-and post-osmotic laxative intake	104
Figure 13	Comparison between both laxatives influence on inter-dialytic hyperkalemia in constipated ESRD patients	105

Abbreviations

5-HT ₄	Serotonin type 4
ACEI	Angiotensin converting enzyme inhibitor
ALT	Alanine transaminase
ARBs	Angiotensin receptor blockers
BK	Big Potassium
BMD	Bone mineral disease
CIC-2	Type 2 chloride channels
CO ₂	Carbone dioxide
CRRT	Continuous renal replacement therapy
D5W	Dextrose 5%
DCT	Distal convoluted tubule
ECF	Extracellular fluid
ECG	Electrocardiogram
ENaC	Epithelial sodium channel
ESRD	End stage renal disease
FDA	Food and Drug Administration
GFR	Glomerular filtration rate
GIT	Gastrointestinal Tract
HD	Hemodialysis

HIV	Human immunodeficiency virus
HUS	Hemolytic Uremic Syndrome
IBS	Irritable bowel syndrome
ICF	Intracellular fluid
ICU	Intensive Care Unit
KCl	Potassium chloride
Mg ²⁺	Magnesium
Na ⁺	Sodium
Na-K-ATPase	Sodium Potassium adenosine triphosphate
NH ₄	Ammonium
NS	Normal Saline
NSAIDs	Non -steroidal anti-inflammatory drugs
PEG	Polyethylene glycol
PGE ₂	prostaglandin E ₂
PO	Per Oral
PR	Per Rectal
RAAS	Renin-angiotensin aldosterone system
RCTs	Randomized controlled Trials
RMP	Resting membrane potential
ROMK	Renal outer medullary potassium channel
RRT	renal replacement therapy

RTA	Renal tubular acidosis
SPS	Sodium polystyrene sulfonate
TP	Threshold Potential
ZS-9	Sodium zirconium cyclosilicate

Effect of Laxatives as regulators of colonic potassium secretion in Hemodialysis Patients

Magdy Mohamed said El Sharkawy, Hesham Atef Abu Al Lail, Khaled Mohamed Rezk, Mustafa Abo Al Khair Mohamed
Faculty of Medicine, Ain Shams University, Cairo, Egypt

Abstract

Background: Hyperkalemia is a potentially life-threatening metabolic problem that is relatively common among CKD patients. The kidneys play a predominant role in the maintenance of long term K balance, while extrarenal tissues, mainly skeletal muscle and liver, provide K buffering by shifting K between ICF and ECF, which is very important in the acute short term regulation of extracellular K. In patients with ESRD, The capacity of the colon for potassium secretion increases to the extent that it makes a substantial contribution to K⁺ homeostasis. This colonic K⁺ adaptive response may represent a major route for active K⁺ secretion in HD patients.

Aim of the study: To study the effect of laxatives (namely osmotic laxatives and colonic stimulant laxatives) on inter-dialytic hyperkalemia in patients maintained on hemodialysis.

Patients and Methods: This prospective study was conducted on 60 patients with ESRD on regular hemodialysis as follows divided into three groups as follow: Group I: This group included 20 ESRD patients who received bisacodyl 5-15 mg /day as a colonic stimulant laxative for two weeks. Group II: This group included 20 ESRD patients who received osmotic laxative 3-9 gm/day for two weeks. Group III: This group included 20 ESRD patients who didn't receive any type of laxatives.

Results: We found that there is significant difference in both study groups between baseline serum potassium and serum potassium after 2 weeks of laxative intake especially in constipated patients. In the first group, after bisacodyl intake, the mean K⁺ level significantly decreased (from 5.61 to 4.90 mmol/L, P=0.01) In the second group, after lactulose intake, the mean K⁺ level significantly decreased (from 5.71 to 4.80 mmol/L, P<0.001) with no significant difference between both bisacodyl group and lactulose group in their K lowering affect (P= 0.676).

Conclusion: Our study suggests that there is significant decrease in serum potassium in ESRD patients after administration of laxative therapy for 2 weeks. This potassium lowering effect is related mainly to treatment and prevention of constipation rather than the drug effect per se.

Keywords: potassium , hyperkalemia, end stage renal disease , constipation , laxative.

Introduction

Potassium is a mineral that is found in many foods. It keeps the heart beating regularly, helps to maintain fluid balance, and allows the nerves and muscles to work properly.(**Bakris and olendzki,2016**).

Potassium is the major intracellular cation, with 98% of the total pool being located in the cells at a concentration of 140-150 mmol/l, and only 2% in the extracellular fluid, where it ranges between 3.5 and 5 mmol/l. A fine regulation of the intracellular-extracellular gradient is crucial for life. (**Zacchia et al., 2016**).

An integrated system including an 'internal' and 'external' control prevents significant fluctuations of plasma levels in conditions of K(+) loading and depletion. (**Zacchia et al., 2016**).

The kidneys play a predominant role in the maintenance of long term K balance, while extrarenal tissues, mainly skeletal muscle and liver, provide K buffering by shifting K between

ICF and ECF, which is very important in the acute short term regulation of extracellular K.(**McDonough , 2002**).

Normally, the level of potassium in your body is balanced by eating foods that contain potassium and getting rid of excess potassium in the urine. However, some people with chronic kidney disease cannot get rid of enough potassium in their urine because the kidneys do not work well. In these people, the level of potassium in the blood can become higher than normal, causing a condition known as hyperkalemia (hyper = high, kal = potassium, emia = in the blood) (**Bakris and Olendzki, 2016**).

During the development of end-stage renal disease (ESRD), many patients remain normokalemic for long periods, although renal excretory function deteriorates progressively. This can be explained by an increase in the K^+ secretory capacity of remaining functional renal tubules . However, this response cannot entirely explain the maintenance of K^+ homeostasis in such patients, because urinary K^+ excretion is generally substantially lower than in healthy individuals .(**Nina Kononowa et al., 2013**)

As the number of nephrons declines, compensatory hormonal and non-hormonal mechanisms are activated to maintain homeostasis of electrolytes and minerals, and to limit the accumulation of waste products. These mechanisms not only involve the kidneys but also the colon. It is noticed that many patients with progressive CKD remain normokalemic despite a deteriorating excretory renal function (**Mathialahan et al.,2005**).This observation is only partly explained by an adaptive increase in renal tubular potassium excretion. It has long been known that fecal potassium losses in patients with CKD are elevated, suggesting either decreased intestinal absorption or increased secretion (**Ruben Poesen et al.,2013**)

The BK channel plays an important role in potassium homeostasis in later stages of chronic kidney disease and ESRD. Under normal circumstances, the majority of total body potassium excretion occurs via the kidney. However, as renal function declines, the colon plays an increasingly important role in potassium excretion. The distal colon becomes a potassium secretory organ, especially in patients with ESRD (**Sandle and Hunter , 2010**)

Under basal conditions, potassium secretion is about threefold greater in ESRD patients compared to those with normal renal function **(Mathialahan et al.,2005)**.This potassium lowering effect can be impaired by constipation as enteral elimination of potassium can be decreased by constipation and therefore lead to hyperkalemia.**(Pani et al., 2014)**

Interdialytic hyperkalaemia is a serious problem in hemodialysis patients, which might be reduced by enhancement of colonic potassium secretion by laxative therapy.**(lehnhardt Anja and Markus Kemper, 2011)**

AIM oF THE WoRK

To study the effect of laxatives (namely osmotic laxatives and colonic stimulant laxatives) on inter-dialytic hyperkalemia in patients maintained on hemodialysis.

Potassium Chapter

Potassium is the most abundant cation in the intracellular fluid, it is a metallic inorganic ion with atomic weight of 39 . (**Rastegar, 1990**). The total body potassium content is approximately 50 mEq/kg, and is distributed asymmetrically in the body.(**Sejersted et al., 2000**).

Potassium level and distribution

The majority of potassium About 98% is intracellular, and approximately 75% of the intracellular component is in muscle while the minority about 2%, is extracellular and of this extracellular component, about 0.4% of the total body potassium is measurable in the plasma and the intracellular potassium concentration is on average 150 mEq/l. .(**Schaefer et al., 2005**).

Normal serum potassium is 3.5 to 5.5 mEq/l ; however, plasma potassium is 0.5 mEq/l lower. Total body potassium is lower in females and in older patients, while serum potassium concentration is independent of sex and age .(**Rastegar, 1990**).

Measurement of Potassium

Potassium can be measured in serum, plasma (lithium heparin) or heparin-anticoagulated whole blood. Potassium is released from platelets during clotting , therefore, plasma and