

Full Length Research Paper

Comparative analysis of distinct diuretics through urine analysis

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Diuretics are used for different diseases and are taken without knowing their adverse/side effects. To create awareness, four popular diuretics, Lasix, Spiromide, Aldactone and Conium were investigated for their effect on body. These were experimented over four volunteers with single and double doses. The urine of these volunteers was collected for analysis of sodium and potassium. The obtained results showed that the effect of medicine remained up to 6 to 12 h. In this duration, the sodium excreted value went up for a certain period and then became almost normal and same was true for potassium. The increase in dosage increased the rate of excretion of the cations and also prolonged the time period of their effects. It is concluded that although Lasix, a potential diuretic but its effects over body were also severe in terms of excretion of ions etc. Similarly, Spiromide was also noted to be a reasonably effective diuretic and its effects are totally different from Lasix in terms of excretion of ions and body weight loss. The other two medicines (Aldactone and Conium) did not show much effect upon excretion etc.

Key words: Urine, Lasix, Spiromide, Aldactone, Conium.

INTRODUCTION

Any substance that tends to increase the flow of urine, which causes the body to get rid of excess water, is known as diuretic drugs. Substances that augment "diuresis," or the removal of fluids from the body through urination, are considered diuretics. Some people use diuretics as a weight loss aid, usually when a large amount of weight needs to be lost in a short amount of time (Capps et al., 1952). The fact is that diuretics are not proven to promote the loss of fat; they simply remove retained fluid. While the scale may show the loss of a few

pounds, it is a temporary loss. This is not a healthy way to lose weight. Diuretics are widely used and generally safe, but like any therapeutic agents, they may cause side effects. They enjoy a very high clinical reputation for safety and efficacy. However, more than 3 decades of clinical investigation have disclosed a number of abnormalities in fluid electrolyte handling, metabolism and other adverse effects that can complicate therapy with diuretic drugs. These include extracellular fluid volume depletion, associated orthostatic hypotension, and prerenal azotemia (Brown et al., 2003). Others are not a direct action of the diuretic, but can be explained as intranephronal compensation to the diuretic action. Diuretics are used for many reasons. They may be indicated for people who suffer from edema, high blood

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pressure and heart related diseases (Staessen and Wang, 2001). Over-diuretics can lead to dehydration and sometimes severe potassium deficiencies, which can be dangerous (Briggs et al., 1998).

There are four major classes of diuretics and all of them inhibit sodium (and water) re-absorption in different segments of the nephron, therefore, increasing urinary excretion of sodium and urine volume:

- 1) Carbonic anhydrase inhibitors
- 2) Loop diuretics
- 3) Thiazides
- 4) Potassium-sparing diuretics

The first one is a mild alkaline diuresis in the proximal tubule. Acetazolamide are used to reduce the intraocular pressure in glaucoma or to alkalinize urine. The second one is the most potent diuretics and can induce significant volume depletion. These diuretics are organic anions that are secreted in the lumen of the proximal tubule. They bind to the chloride site of the Na-K-2Cl co-transporter in the luminal membrane located in the thick ascending limb of Henle. The Lasix used here is furosemide and is loop diuretic. Loop diuretics may cause a change in the levels of potassium and other electrolytes in the blood. In some cases, loop diuretics may cause a decrease in the amount of magnesium in the blood. The third one is the organic anions secreted by the proximal tubule that bind to the chloride site of the Na-Cl co-transporter in the luminal membrane of the distal convoluted tubule. Thiazides can induce hyponatremia because they inhibit urine dilution and the fourth one is weak because not much sodium is reabsorbed in their site of action. Spironolactone is an aldosterone antagonist useful in the treatment of congestive heart failure and hepatic cirrhosis (Pickkers et al., 1998).

Diuretics side effects are a result of the change in the amount of levels of minerals due to the action of these water pills. Although the side effects of diuretics may be mild and they may be felt during the initial days of treatment, a physician should be consulted in case the side effects persist for a long period of time (Buchet and Lauwerys, 1973).

Lasix, Spiromide, Aldactone and Conium are used as diuretics for many reasons. They may be indicated for people who suffer from edema, an intense accumulation of fluids in the body's tissues, and those who suffer from high blood pressure or other heart related diseases. Increasing the production of urine not only releases fluid, but also helps rid the body of excess salts and may reduce blood volume (Birtwhistle et al., 2004). Although it can be administered as single dosage but as there are four volunteers to be chosen, therefore double dosage is much more valuable and productive (Pickkers et al., 1998). We have tried to use and follow all the drugs according to ABCD rules of British Hypertension Society's (BHS) July 29, 2005 (Williams et al., 2004; Birtwhistle et al., 2004). The present work is unique and

novel type because the literature survey reveals that no symmetric study has been carried out about the efficiency of the diuretics and the adverse effects of them (Martinez-Maldonado et al., 1990). The objective of the work is to take different diuretics and investigate them with reference to their action and side effects

MATERIALS AND METHODS

Selection of drugs and subjects

For comparison, the drugs are selected in such a way that the origin, mechanism of action be different from each other and these must be available in the market harmful for the person to take. Keeping in view, these facts the drug selected for this purpose were purely diuretic including, Lasix, Spiromide, Aldactone and Conium (Staessen et al., 2003). Further, the following considerations were kept in mind:

- 1) These drugs are easily available for laboratory study.
- 2) The action be rapid and quick and be at least in 24 h.
- 3) These should increase the volume of urine excreted.
- 4) The medicine must not have dangerous adverse effects so that the model is ready to take these and their lives might not be in danger (Braunwald et al., 2004).

To conduct experiments, four volunteers were chosen as models in hostel dispensary. The four volunteers were divided into two groups. The volunteers were having the same characteristics. Further, the following considerations were made during the selection:

- 1) Physically and mentally normal up to the possible extent.
- 2) Provided with the same dietary intake up to large extent.
- 3) Same age within permissible range and is young.
- 4) Not taking any medicine in those days except the ones provided by us.
- 5) Available throughout the study period that is, the whole year.

Dosing and sample collection

The four volunteers selected were divided into two groups as stated earlier. One group was given a single dosage of the respective diuretic drug and the other provided with a double dosage. In both cases, the sample of urine were taken regularly and analyzed for sodium and potassium (Buchet and Lauwerys, 1973). Before giving the medicine, the urine was collected in early morning on same day and considered to be at zero time. The medicine was given at an appropriate time (normally 8:00 am) on Sunday and the urine samples were collected after each hour at regular intervals of time. These samples were collected in washed, cleaned and tight fattened containers (Carlberg et al., 2004). The samples were collected up to twelve hours (8:00 pm) after giving the medicine. The blank sample was used as a reference for the variation in concentration of various ions after the administration of drugs (Psaty et al., 2004). Quantitative analysis was carried out to determine the variations in concentration in different ions excreted through urine by the intake of the drugs.

Determination of sodium and potassium electrolytes

0.2543 g of NaCl provided by EMerck Germany and analytical grade was taken after drying at 11°C in oven. This amount of

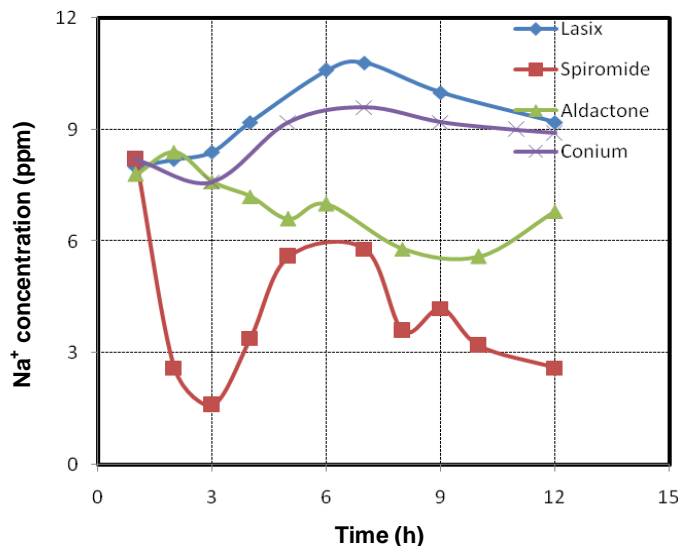


Figure 1. Effect on sodium excretion in urine by single dose of different diuretics.

sodium was then dissolved in 1000 ml of de ionized water to form 100 ppm stock solution of NaCl. For this purpose, 1 L volumetric flask was used. This solution was further diluted to give reference solution of 5, 10, 20, 30, 40 and 50 ppm (Brown et al., 2000). These reference solutions were taken into test tubes, the flame photometer was switched on at least half an hour before the measurements were taken. Deionized water was then taken in a test tube and the sucker of flame photometer was inserted into it. The instrument was adjusted to zero and the standard solution was sucked by flame photometer gradually, and the emission for each reference concentrations was determined and noted. The emission was plotted versus concentration to get a standard graph which was then used to determine the Na⁺ concentration in a given urine sample. In the same the cooled urine sample were sucked by photometer and absorption was noted. From these results and using standard graph the concentration of sodium was determined. For potassium detection, 1.9 g of dried KCl was dissolved in 1000 ml of de ionized water in a volumetric flask. This gave 100 ppm stock solutions. From this solution, reference solution of 5, 10, 20, 30, 40, and 50 ppm was prepared. These solutions were used for the determination of K⁺ urine samples. The analysis were carried out by flame photometer and the method used was the same as that for sodium determination.

Statistical analysis

Quantitative analysis was carried out to determine the variations in concentration in different ions excreted through urine by the intake of the drugs

RESULTS AND DISCUSSION

The urine collected from the models after administration of single dosage of Lasix was diluted to several times and was analyzed for sodium and potassium. For sodium, the dilution factor was 200. For potassium, the urine samples were diluted to 50 times. The results obtained for sodium

analysis after the intake of single dosage of Lasix, Spiromide, Aldactone and Conium shows that sodium excretion increases with time and reaches to maximum after 6 hours and then goes down, as shown in Figure 1. When the diuretics were administered in double dose, it can be noted from the results the maximum exertion reaches much earlier than that of single dosage while the maximum excretion value is almost the same as observed for single dosage, as shown in Figure 2. Similarly, the excretion levels go down very fast and come to the normal value within 12 h time (Figure 2). We can see that the maximum effect of the medicine, whether the dosage is single or double. Furthermore, this dosage may affect the amount of the urine excreted by the body but it does not affect the amount of sodium excreted along with the urine.

The urine analyses for potassium were also performed on the same models. The results show that the contents of potassium in urine go down after taking the medicine Lasix and the decrease is very sharp and reaches to minimum value in 4 h. The effect of the medicine dies away and the potassium approaches to a normal value, within 4 h (Figure 3). The results obtained for double dosage intake are shown in Figure 4, showing that potassium decreases and reaches to minimum value and then to the normal as in the case of single dosage. The difference between single and double dosage is that the minimum approaches fast that is, within 3 h for double dosage and the decrease is also a bit higher/greater as compared to single dosage. Though the effect of the medicine remains even up to 12 h but the effect is very short. In this case, we also observed that the potassium excretion decreases with time and approaches to minimum, as observed in case of Lasix (Figure 5). The observations made are very much similar to that of single

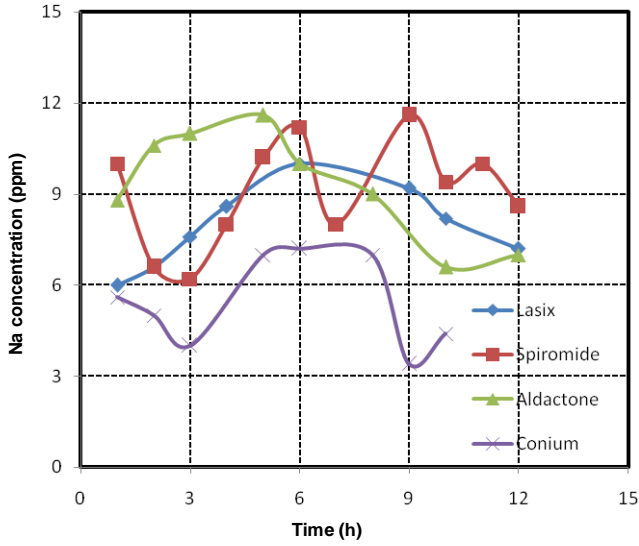


Figure 2. Effect on sodium excretion in urine by double dose of different diuretics.

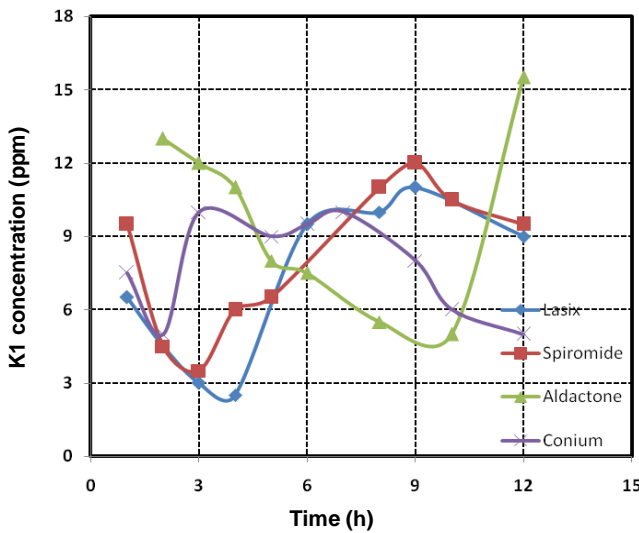


Figure 3. Effect on potassium excretion in urine by single dose of different diuretics.

dose of Spiromide (Figure 6). The third medicine, Aldactone was also given to four persons with two single and two double dosages. It was also observed that the medicines have not sharp diuretics effect (Figure 7), as compared to the medicine discussed earlier. The fourth and last medicine used was Conium which was a homeopathic drug. It was noted the excreted value of sodium firstly decreases as in the case of single dosage but the rate of decrease with bit slower down (Figure 8). However, the extent of decrease remained the same.

From these observations, we can say that this medicine can be composed of two compounds one may be having a short time and other long time effect. This action of medicine may be useful for patient or can be

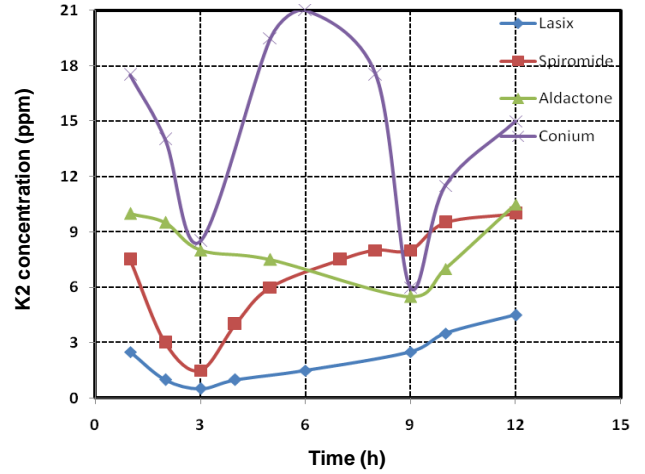


Figure 4. Effect on potassium excretion in urine by double dose of different diuretics.

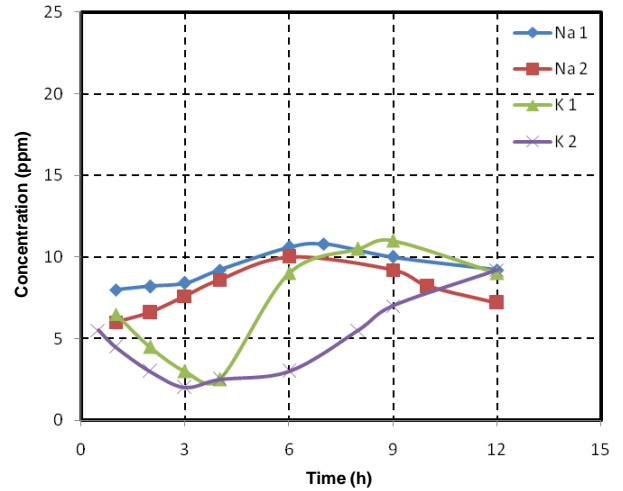


Figure 5. Lasix single and double dose effects on sodium and potassium excretion.

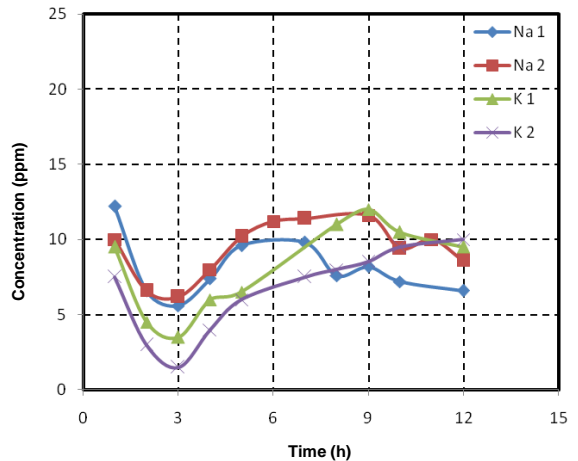


Figure 6. Spiromide single and double dose effects on sodium and potassium excretion.

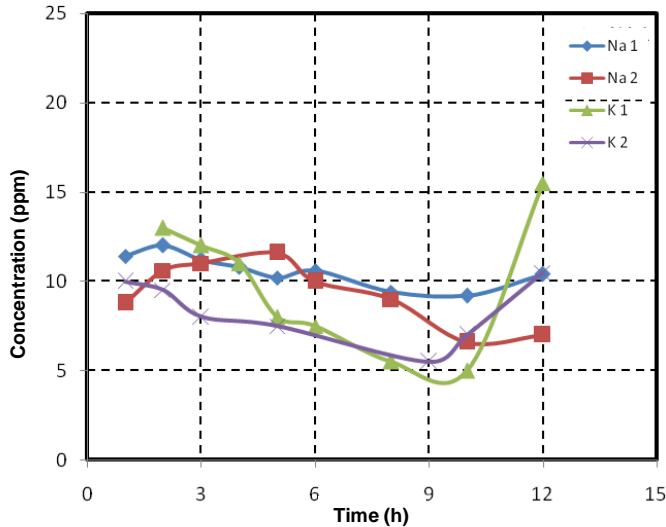


Figure 7. Aldactone single and double dose effects on sodium and potassium excretion.

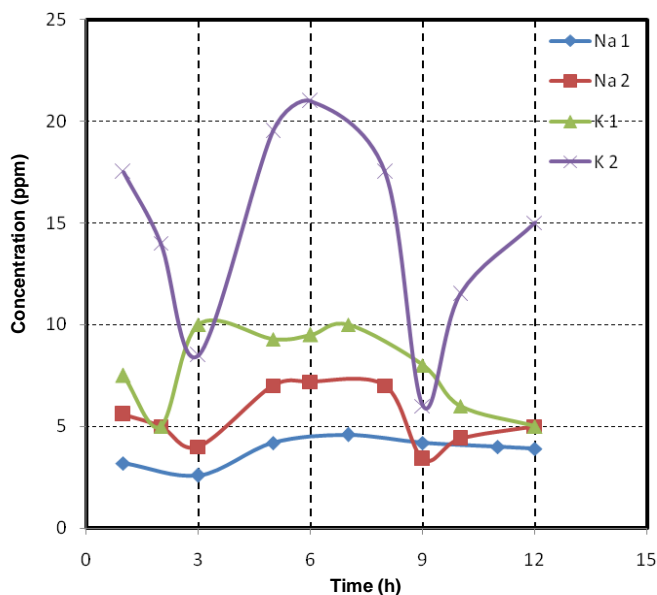


Figure 8. Effect of Conium on sodium and potassium excretion after single and double dose of administration.

dangerous for others depending upon the disease and the requirements of the model patient.

Conclusions

If we compare the observation made as analysis of urine and the report made by the model, the following statement can be made about these drugs:

The first two medicines (Lasix and Spiromide) investigated disturb the body system very much either by increasing or decreasing the excreted amount of sodium

or potassium up to a large extent. However, they were very good as a diuretic that is the amount of water excreted from the body as urine also increases up to a large extent which is considered to be the primary task of such medicine. Aldoctone, used for study purpose showed very little change in sodium or potassium with time from equilibrium value. Therefore, we can say that it can be very safe drugs but on the other hand the urine excretion was not very high after administration of drugs as noted by the models. Therefore, we can say that though this medicine is a good at one hand but does not perform its own primary function for which it is used.

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