

# TREATMENT OF HYPERKALEMIA WITH SALBUTAMOL AND INSULIN

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## ABSTRACT

**Objective:** To see the potassium lowering effect of salbutamol and insulin in hyperkalemia, and to compare this hypokalemic effect when these drugs are administered alone or in combination.

**Place of Study:** This interventional study was conducted in Services Hospital Lahore, for a period of one year.

**Patients and Methods:** Fifteen patients with hyperkalemia were divided into three groups. Group A, B and C received 0.5 mg salbutamol diluted in 100 ml 5% water, glucose 25 gm diluted in 100 ml of water plus 10 units of regular insulin and both salbutamol 0.5 mg diluted in 100 ml of water with 25 grams of glucose plus 10 units of regular insulin respectively. Dextrose was given as infusion over 30 minutes and insulin as iv bolus. Blood samples were drawn at 0, 30, 60, 180 and 360 minutes. Blood pressure, pulse, temperature, respiratory rate and ECG were also recorded.

**Results:** Base line serum potassium levels fell from  $6.4 \pm 0.3$  mmol/L,  $6.5 \pm 0.3$  mmol/L and  $6.5 \pm 0.2$  mmol/L, to  $5.5 \pm 0.2$  mmol/L,  $5.7 \pm 0.2$  mmol/L and  $5.4 \pm 0.3$  mmol/L for groups A, B, and C respectively at 60 minutes. These levels started to creep up again at 180 minutes to  $5.7 \pm 0.1$  mmol/L,  $5.9 \pm 0.2$  mmol/L and  $5.5 \pm 0.4$  mmol/L for groups A, B and C respectively.

**Conclusion:** According to the preliminary report Salbutamol is slightly more effective than insulin in the treatment of hyperkalemia. When administered simultaneously their effect is additive and prolong then administered alone. The number of patients in each group was too small, hence it needs to be studied further.

**KEY WORDS:** Hyperkalemia, Insulin, Salbutamol.

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## INTRODUCTION

Renal failure is associated with predictable abnormalities in composition of body fluids.<sup>1</sup> Three quarters of cases of hyperkalemia are due

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to renal failure, and this hyperkalemia deserves respect as genuine electrolyte emergency.<sup>2</sup> Renal potassium excretion is an effective but time consuming process of potassium homeostasis requiring several hours<sup>3</sup> During this period of several hours extrarenal mechanisms which are in action within minutes help to lower acute potassium load. Insulin and epinephrine are two major physiologic factors which promote this extrarenal potassium disposal<sup>4</sup> Definitive treatment of hyperkalemia is hemodialysis and there is always inevitable delay in starting hemodialysis. In Pakistan hemodialysis is available only in established renal units so it is more important in our clinical practice to lower serum potassium levels immediately.<sup>5</sup> Intracellular shift of potassium is major defense against acute rise in serum potassium levels in patients with renal failure.<sup>6</sup>

Rapid decrease in serum potassium is produced by administration of salbutamol and insulin.<sup>7</sup> Hyperkalemia with electrocardiographic changes is medical emergency and after stabilizing the myocardium with intravenous calcium, intracellular shift of the potassium can be achieved by administration of insulin<sup>8,9</sup> and by administration of salbutamol.<sup>7,10</sup>

Present study was conducted to observe and compare the hypokalemic effects of salbutamol and insulin as observed by other workers and to compare this hypokalemic effect when these drugs are administered alone or in combination.

### PATIENTS AND METHODS

This study was conducted in Services Hospital Lahore for a period of one year. A total of 15 patients with acute or chronic renal failure having serum potassium levels more than 6 mmol/L were included in the study.

*Exclusion criteria:* serum potassium less than 6 mmol/L, Ischemic heart disease, patients already receiving one or more of the following drugs: beta agonist, beta blocker, digoxin and diuretic therapy.

Complete history and physical examination was carried out at admission. Patients were asked about any chronic ailment especially ischemic heart disease. Previous medicines used were asked with a special enquiry regarding those in exclusion criteria. Patients were divided into three groups of 5 patients each.

Group A received salbutamol 0.5mg diluted in 100 ml of water administered over a period of 15 minutes. Group B received 25grams glucose in 100ml of water over 15 minutes, plus 10 units of regular insulin as intravenous bolus. Group C received salbutamol 0.5mg and 25grams of glucose diluted in 100 ml of water over 15 minutes, plus 10units of regular insulin as intravenous bolus.

Blood samples were taken immediately before starting the treatment and 30, 60, 180 and 360 minutes after the end of the treatment. Potassium and glucose levels were measured in these samples. Pseudohyperkalemia was

avoided by taking blood samples without application of tourniquet or without doing any exercise like fist clenching for sample collection. Blood pressure, pulse, temperature, respiratory rate were monitored during the study period. Electrocardiography was recorded for each patient at specified interval. During the study period patients were given treatment according the protocol of the group and patients received no other medication effecting serum potassium levels like frusemide, bicarbonate, beta blockers. Any unwanted effects observed or complained by the patient were recorded.

### RESULTS

Results are expressed as mean±standard error of mean (SEM). The level of significance established at a P value of less than 0.05. Not much difference was noted in the mean age of the patients being 52.6±9.2, 51.8±9.3 and 51 ±6.5 years respectively for groups A, B and C respectively. Two out of fifteen patients were females. Serum potassium levels started to fall after initiation of therapy. Change in serum potassium levels induced by each treatment modality are mentioned in Table-I. At 30 minutes serum potassium level decreased from 6.4 ±0.3 mmol/L to 5.7±0.3 mmol/L in group A, from 6.5±0.3 mmol/L to 5.9±0.2 mmol/L in group B and from 6.5±0.2 mmol/L to 5.5 ±0.3 mmol/L in group C. In all three groups maximum fall was noted at 60 minutes. Serum potassium levels recorded at 60 minutes being 5.5±0.2 mmol/L, 5.7 ±0.2 mmol/L and 5.4 ±0.3 mmol/L in groups A, B and C respectively.

Table-I: Changes in absolute values of serum potassium induced by three treatment modalities.

	Group A mmol/L	Group B mmol/L	Group C mmol/L
0 min	6.4 ± 0.3	6.5 ± 0.3	6.5 ± 0.2
30 min	5.7 ± 0.3	5.9 ± 0.2	5.5 ± 0.3
60 min	5.5 ± 0.2	5.7 ± 0.2	5.4 ± 0.3
180 min	5.7 ± 0.1	5.9 ± 0.2	5.5 ± 0.4
360 min	5.9 ± 0.1	6.0 ± 0.2	5.8 ± 0.3

Results are mentioned as Mean ± SEM.

Table-II: Decrement in mean serum potassium in each treatment group.

	Group A mmol/L	Group B mmol/L	Group C mmol/L
30 min	-0.7 ± 0.1	-0.6 ± 0.1	-1.0 ± 0.1
60 min	-0.9 ± 0.3	-0.8 ± 0.2	-1.1 ± 0.1
180 min	-0.7 ± 0.3	-0.6 ± 0.1	-1.1 ± 0.2
360 min	-0.5 ± 0.3	-0.5 ± 0.2	-0.7 ± 0.2
Max	0.9 ± 0.3	-0.8 ± 0.2	-1.1 ± 0.1

Results are mentioned as Mean ± SEM.

After 180 minutes of termination of therapy serum potassium levels started to rise again in all the groups. Serum potassium levels noted at this time being  $5.7 \pm 0.1$  mmol/L,  $5.9 \pm 0.2$  mmol/L and  $5.5 \pm 0.4$  mmol/L in groups A, B and C respectively. These levels being nearly the same to that noted at 30 minutes after the termination of therapy. Although at 360 minutes potassium levels rose further but they remained below to the levels at the start of therapy. Levels being  $5.9 \pm 0.1$  mmol/L,  $6 \pm 0.2$  mmol/L and  $5.8 \pm 0.2$  mmol/L for groups A, B and C respectively.

In Table-II mean decrements in serum potassium induced by each treatment modality is mentioned. Maximum decrement was noted in group C through out the study period. Blood sugar levels were found to rise in all three groups treated. This rise was found to be significantly higher in group A. Changes noted in three groups are mentioned in Table-III. No significant change was noted in heart rate, blood pressure, temperature, respiratory rate and electrocardiogram. All the treatment modalities were well tolerated. No side effect in any patient was noted.

## DISCUSSION

Renal failure is associated with vast range of abnormalities and hyperkalemia is the most dangerous one requiring immediate measures to lower potassium levels.<sup>11</sup> D'Silva (1936) was first one to demonstrate the role of catecholamines in potassium homeostasis. Todd and colleagues, compared epinephrine and norepinephrine and found first one more potent in lowering serum potassium levels. Administration of salbutamol and fenoterol

resulted in immediate and significant hypokalemia.<sup>12</sup> Salbutamol when administered intravenously or through nebulization lowered serum potassium levels and maximal decrease observed at 30 minutes being  $0.92 \pm 0.01$  mmol/L.<sup>7</sup> Potassium lowering effect of nebulized salbutamol and insulin was compared with bicarbonate administration as a pre-requisite in patients on hemodialysis. Both modalities lowered serum potassium levels within 15 minutes and maximum fall noted with insulin was  $0.85 \pm 0.06$  mmol/L.<sup>13</sup>

In yet another study potassium lowering effect of salbutamol and insulin was compared when administered alone and in combination. All the treatment modalities induced fall in serum potassium levels. In this study maximum fall was noted in group treated with salbutamol and insulin at 60 minutes and was  $1.05 \pm 0.2$  mmol/L.<sup>14</sup>

Comparison of our study to that of Lens and colleague showed all treatment modalities decreased serum potassium levels significantly in both studies. Serum potassium levels fell at 30 minutes and maximum fall was noted at 60 minutes in all groups. Decrease in mean potassium levels was slightly more in group treated with salbutamol than insulin. These results were comparable in both studies.

Liou and colleagues<sup>7</sup> demonstrated maximum fall in potassium levels at 30 minutes after salbutamol infusion while in our study maximum fall noted was at 60 minutes, which is identical to that of Lens and coworkers.<sup>14</sup>

Allon and Shanklin<sup>13</sup> in their study demonstrated potassium lowering affect of insulin maximum at 60 minutes as in our study

Table-III: Changes in blood glucose during treatment in three groups.

	Group A mg/ 100ml	Group B mg/ 100ml	Group C mg/ 100ml
0 min	158 ± 35	135 ± 47	151 ± 49
30 min	199 ± 65	177 ± 75	189 ± 78
60 min	217 ± 44	163 ± 58	156 ± 35
180 min	203 ± 52	131 ± 25	157 ± 21
360 min	194 ± 49	113 ± 44	151 ± 22

Results are mentioned as Mean + /- SEM.

and that by Lens and colleagues.<sup>14</sup> Decrease induced by insulin in serum potassium levels almost remain the same in three studies compared. Reduction in potassium levels by insulin was quantitatively lower than produced by salbutamol probably due to the stimulation of beta-2 adrenergic receptors in pancreas resulting in insulin release which causes an additive effect.<sup>15</sup>

Decrease in mean serum potassium levels noted in our study was lower than noted in previous study by Lens and colleagues, which could be explained by the fact that fall in potassium levels depends upon the levels at start of treatment which is most important factor in determining the subsequent magnitude of hypokalemia following beta agonist therapy.<sup>12</sup>

If we closely look at the individual groups it is clear that decrease in mean potassium levels was noted to be more potent and prolonged in group treated with both salbutamol and insulin. Serum potassium levels started to rise progressively after 60 minutes in all the treatment groups and this is similar to previous studies. Comparative analysis of all the above mentioned studies showed that a fall in serum potassium levels was induced by all the modalities used. Decrease induced in serum potassium levels was more in groups treated with salbutamol then insulin. This decrease produced was even more significant when salbutamol and insulin were administered together.

While treating hyperkalemic patients with salbutamol risk of insulin induced hypoglycemia can be prevented. If risk of hypoglycemia is minimal then insulin can also be used for the treatment of hyperkalemia.

It is concluded that salbutamol is slightly more effective than insulin for treating hyperkalemia. When both agents are administered together their effect is additive and persists for a longer period. So both of these agents be used simultaneously in the treatment of hyperkalemia.

*Limitations of the study:* The number of patient in each group was too small. This is a preliminary report and it need to be studies further.

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