

## A Retrospective and Explorative Study of Hypokalemia in Psychiatric Disorders: a Beta<sub>2</sub>-Receptor Related Phenomenon\*

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**Summary.** Since the serum potassium level is under beta<sub>2</sub>-adrenergic influence, we studied serum potassium values on admission in psychiatric patients. Data are reported on 683 patients from nine major diagnostic groups. Among these nine groups significant differences were found concerning the mean serum potassium level and incidence of hypokalemia. Significant differences existed between the alcohol withdrawal and attempted suicide groups compared to the dysthymic, bipolar manic, schizophrenic and nonschizophrenic psychosis groups. Like alcohol withdrawal, attempted suicide is assumed to be a hyper-adrenergic state. Although the relative contribution of factors like nutritional state, aldosterone, insulin, and beta<sub>2</sub>-receptor density or sensitivity is unclear, the catecholamine-potassium relationship deserves further study.

**Key words:** Potassium – Stress – Psychiatric disorders – Hypokalemia

### Introduction

There exists little doubt that one of the mechanisms of hypokalemia in man is a beta<sub>2</sub>-receptor-mediated influx of potassium into skeletal muscle, induced by circulating epinephrine [2, 3, 7, 8]. This epinephrine-induced hypokalemia has been thought to play an important role in a variety of serious medical illnesses, such as myocardial infarction, pneumonia, stroke,

and cerebral trauma [4, 16] in which a 15- to 30-fold rise in levels of epinephrine may occur [3, 4, 13]. This is associated, in experiments with epinephrine infusions, with a 0.8–1.0 mmol/l reduction in serum potassium values [3]. Though in daily life such an increase in levels of epinephrine may not be expected, an increase by a factor of 2 to 10 seems possible, e.g., in healthy frightened subjects [6, 7]. Although interesting, these observations aroused little interest in the field of psychiatry. Yet it might be possible that the serum potassium level can teach us something about activation of the adrenergic system.

It was hypothesized first that known hyperadrenergic states, like alcohol withdrawal [10], would yield a low mean serum potassium level and that in anxiety disorder this might also be expected. Second, anorexia nervosa patients would yield low values (on account of food restriction and vomiting). Thirdly it was interesting whether differences would exist between patients with a major depression and a bipolar manic disorder and, fourthly whether disease duration might lead to a kind of adaptation as reflected in the serum potassium level. Therefore, a retrospective and explorative study of serum potassium values in psychiatric patients on admission was undertaken.

### Method

Retrospectively the serum potassium values on admission were sampled from psychiatric patients admitted to our hospital.

Data are reported on 683 patients, who had their serum potassium values determined, usually within 2 days after admission. These patients were from nine major diagnostic groups, according to DSM-III, (Table 1), except the attempted suicide group, which is not a DSM-III concept.

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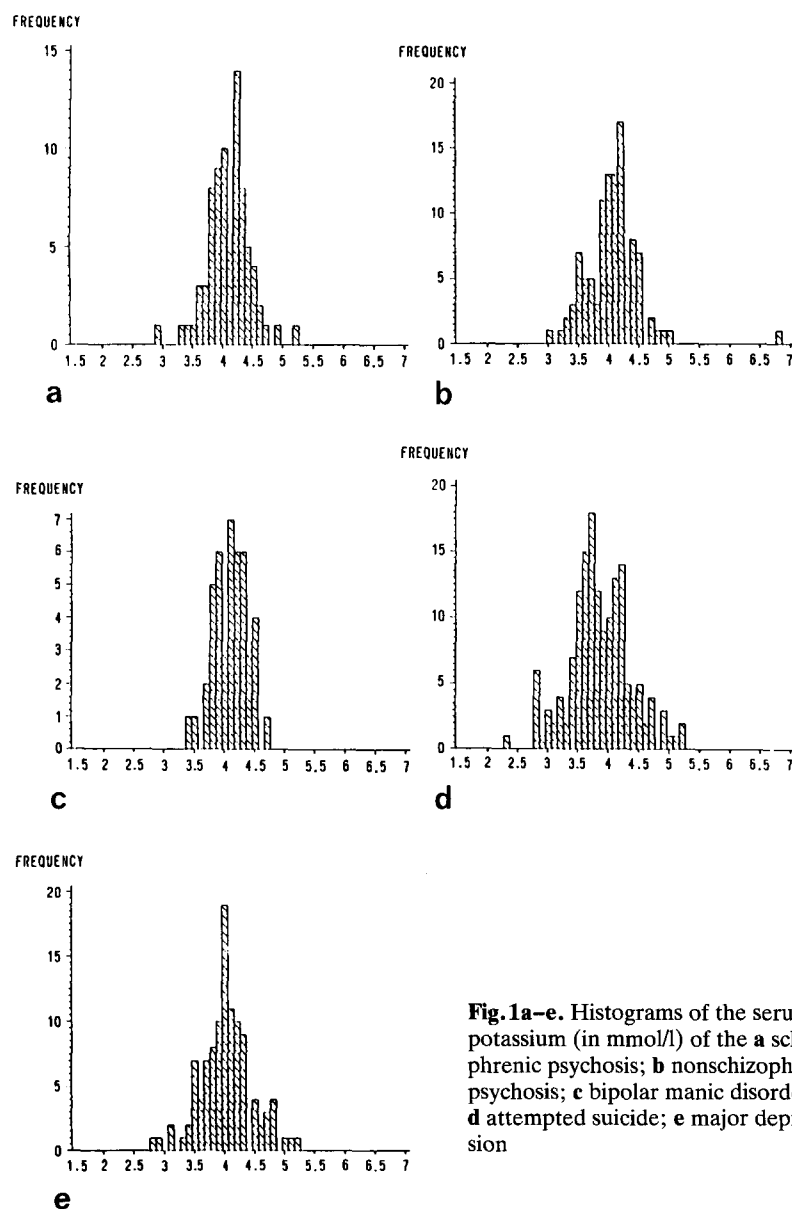
**Table 1.** The mean serum potassium value, SD, percentage of patients with hypokalemia on admission and the number of patients in the nine diagnostic groups

Diagnostic group	Mean serum K <sup>+</sup> value	SD	% HypoK <sup>+</sup>	n
Schizophrenic psychosis	4.08	0.35	12.8	78
Nonschizophrenic psychosis	4.06	0.46	22.2	108
Bipolar manic disorder	4.10	0.28	8.9	45
Attempted suicide	3.85	0.51	45.5	156
Major depression	4.02	0.43	23.1	108
Dysthymic disorder	4.11	0.42	18.5	81
Anorexia nervosa	3.87	0.65	26.9	26
Alcohol withdrawal	3.80	0.61	43.5	46
Anxiety disorder	4.05	0.26	11.4	35

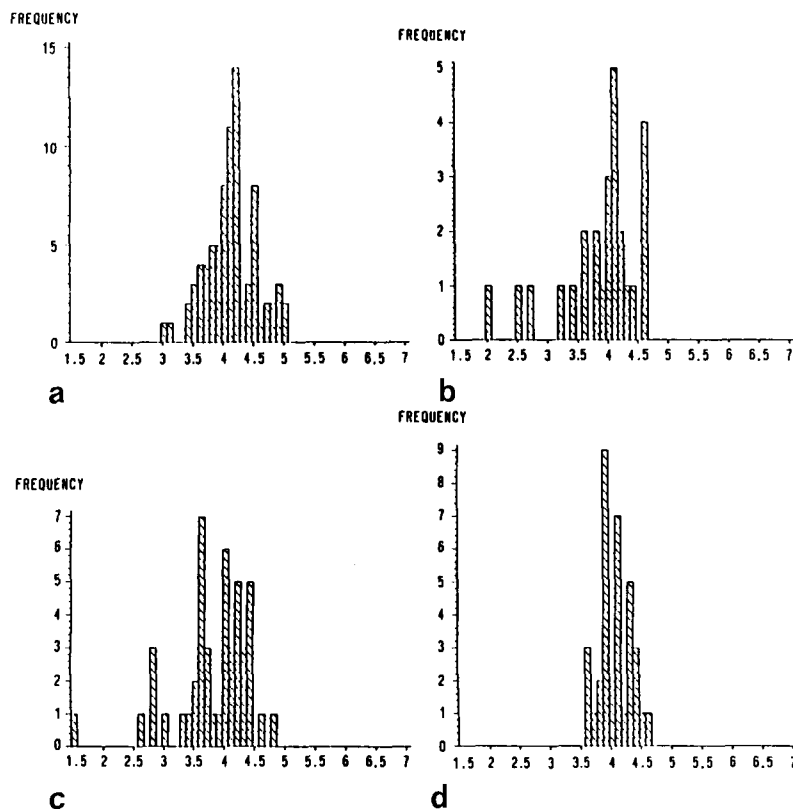
Excluded were patients using medication or suffering from diseases that might influence potassium homeostasis, such as gastrointestinal disorders, use of diuretics, insulin, or beta-blockers etc. Reference values for serum potassium were 3.8 to 5.0 mmol/l, and hypokalemia, therefore, was defined as 3.7 mmol/l or below.

## Results

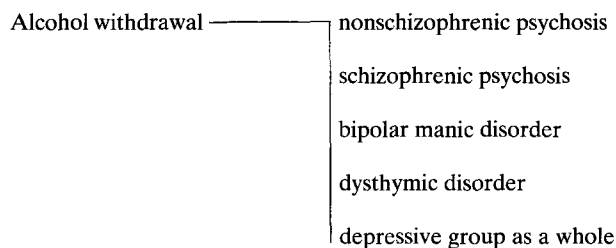
Results are presented in Table 1 and the histograms 1–9 (Figs. 1 and 2). When the dysthymic and major depression groups were combined a mean serum potassium value of 4.06 mmol/l resulted (SD of 0.42) and 21.2% of these patients had hypokalemia, ranking between the anxiety disorder and nonschizophrenic psychotic groups. The mean serum potassium value of the total sample was 3.99 mmol/l (SD



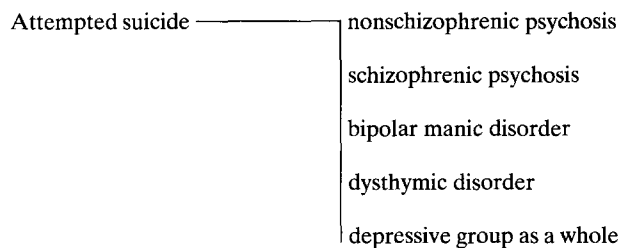
**Fig. 1a–e.** Histograms of the serum potassium (in mmol/l) of the **a** schizophrenic psychosis; **b** nonschizophrenic psychosis; **c** bipolar manic disorder; **d** attempted suicide; **e** major depression



**Fig. 2a-d.** Histograms of the serum potassium (in mmol/l) of the **a** dysthymic disorder; **b** anorexia nervosa; **c** alcohol withdrawal; **d** anxiety disorder



**Fig. 3.** Significant differences between the alcohol withdrawal group and five other groups concerning the mean serum potassium on admission and incidence of hypokalemia



**Fig. 4.** Significant differences between the attempted suicide group and five other groups concerning the mean serum potassium on admission and incidence of hypokalemia

0.46), 26.4% being in the hypokalemic range. The difference between diagnostic groups was highly significant (a one way analysis of variance  $F = 4.94$ ,  $df = 8.675$ ,  $P < 0.001$ ).

Tukey pairwise comparisons showed significant differences at the 0.05 level between on one hand the alcohol withdrawal group and on the other hand the dysthymic disorder, bipolar manic disorder, schizophrenic psychosis, nonschizophrenic psychosis, and the combined depressive group (major depressive and dysthymic disorder) (Fig. 3). Potassium values were significantly lower in the attempted suicide group compared to the dysthymic, bipolar manic, schizophrenic, nonschizophrenic, and depressive group as a whole (Fig. 4). T-tests of the major de-

pressive group against the bipolar manic disorder group yielded  $P = 0.069$ ; combination of the nonschizophrenic psychosis and major depression group tested against the schizophrenic psychosis and dysthymic disorder group yielded  $P = 0.075$  (separate variance estimate, 2-tail probability); the major depression group against the dysthymic disorder  $P = 0.054$  (pooled variance estimate),  $P = 0.046$  (separate variance estimate) ( $F$  value 1.33; 2-tail probability 0.162).

## Discussion

Psychiatric patients may show hypokalemia on admission. The incidence was different between diag-

nostic groups but may be as high as that found in acute serious medical conditions, like acute myocardial infarction, cerebral trauma, or acute surgery [4, 16], especially when a diagnosis of alcohol withdrawal or suicide attempt has been made. The degree of hypokalemia was usually small, although exceptions existed that warranted therapeutic measures.

There were remarkable differences between diagnostic groups and it seemed important to investigate these differences against the background of recent findings that indicate an important influence of the adrenergic system on serum potassium.

Concerning our hypotheses, first, alcohol withdrawal patients, who are known to be in a hyperadrenergic state [8], showed the lowest mean serum potassium value and a high percentage of patients with hypokalemia. The alcohol withdrawal group differed significantly from the dysthymic, combined depressive bipolar manic, schizophrenic and nonschizophrenic psychotic groups. This trend toward hypokalemia is in line with recent findings of Manhem et al. [15] who studied the epinephrine-potassium relationship in alcohol withdrawal patients and reported a correlation between plasma epinephrine and potassium levels of  $-0.56$ . It should be noted that other factors, like food intake, may contribute to the hypokalemic trend in this group, while for example alkalosis has been proven unjust [19].

Second, patients with gastrointestinal disturbances were excluded, except anorexia nervosa patients. This group showed – as expected – a low mean serum potassium value with a high incidence of hypokalemia, probably as a result of food restrictive measures.

Unexpected findings in our study were the low mean potassium and high incidence of hypokalemia in the attempted suicide group. This group differed significantly from the dysthymic, combined depressive, bipolar manic, schizophrenic and nonschizophrenic psychotic groups. One is tempted to postulate a hyperadrenergic drive for this group also with the resultant  $\beta_2$ -receptor stimulation and hypokalemic trend. Such a postulate is supported by dexamethasone suppression Test (DST) results, since high DST nonsuppressor values have been reported for both attempted suicide and alcohol withdrawal patients [1] and since DST nonsuppression is supposed to be associated with strain or stress [17].

Alcohol consumption or withdrawal as a possible underlying cause for the noted low serum potassium in the attempted suicide group is unlikely for two reasons. Alcohol consumption was recorded in only a minority of patients ( $n = 26$ ), whereas in 106 patients there had been no use of alcohol, and secondly, there was no significant difference between the serum

potassium of these two groups ( $n = 26$ , mean value  $3.8 \text{ mmol/l}$ , SD  $0.47$ ;  $n = 106$ , mean value  $3.9 \text{ mmol/l}$ , SD  $0.52$ ; T-test  $t = -0.56$ ,  $P = 0.579$ ).

Third, there was a trend ( $P < 0.08$ ) that the bipolar manic differed from the major depression patients and, fourth, that disorders of a relatively short disease duration, viz. major depression and nonschizophrenic psychosis, have lower mean serum potassium values and a higher incidence of hypokalemia than disorders of longer duration such as dysthymic disorder and schizophrenic psychosis. The differences between these groups need further analyses. If the duration of illness plays a role, this may be due to changes in adrenergic drive or in sensitivity or density of the  $\beta_2$ -receptor. Such a kind of adaptation might explain the relative lack of potassium level decrease in anxiety disorder.

Although there are reports on bipolar manic patients being badly nourished [12], it is remarkable that we found a relatively high mean serum potassium value with a very low incidence of hypokalemia. Only a few patients with a bipolar manic disorder used lithium on admission and lithium may induce a mild potassium diuresis [12], so that other factors seem of more importance. Perhaps in this subgroup more weight has to be attributed to  $\text{Na}^+ - \text{K}^+$  pump abnormalities that have been noted [11] or to a lithium-induced change in the epinephrine responsiveness [9].

A hypoadrenergic drive concomitant with euphoric mood in the manic state may also be hypothesized. This is supported by findings of normal cortisol levels in (mild) mania [5]. The increase in potassium level following bodily activity is so short-lasting [4] that this could not play a role [8].

In conclusion, some psychiatric disorder groups showed hypokalemia on admission, in particular the alcohol withdrawal and attempted suicide patients.

It is not known whether these differences were due to level of adrenergic activation, to  $\beta_2$ -receptor density, or to receptor sensitivity changes. Further studies should take other variables into account like nutritional state and influence of insulin and aldosterone.

Theoretically, 31% of variance of the serum potassium level may be due to the level of epinephrine ( $r^2$  in the Manhem et al. experiment [5]), so that serum potassium may serve as a rough indicator of adrenergic activation. We have planned further research on this epinephrine-potassium relation in psychiatric disorders.

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