

Serum potassium concentrations after suxamethonium in patients with familial amyloid polyneuropathy type I

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Background: Suxamethonium produces an abnormal increase in serum potassium in some neurological diseases and some authors have suggested that it is safer not to use this drug in patients with familial amyloid polyneuropathy (FAP). However, there are no data previously reported to support this hypothesis. The aim of this study was to evaluate the magnitude of the potassium increase produced by suxamethonium in FAP type I. **Method:** Twenty-one FAP Met 30 patients anaesthetised for liver transplantation were studied. Age was 34.9 ± 6.9 years (mean \pm SD), time elapsed from first symptom 5.5 ± 3.2 years and weight was $14 \pm 9\%$ below ideal body weight. Anaesthesia was induced with thiopentone and low-dose fentanyl. Samples for blood gas and electrolytes analyses were drawn before induction and 1 and 5 min after 1 mg/kg of suxamethonium was given for tracheal intubation.

Results: Before induction serum potassium levels were 3.8 ± 0.4 mmol/L. One minute after suxamethonium, values were 3.8 ± 0.4 mmol/L and 5 min after 4.3 ± 0.5 mmol/L. The maximal

increase observed was 1.6 mmol/L (from 3.4 mmol/L to 5.0 mmol/L).

Conclusion: The average increase in plasma potassium concentrations observed in FAP patients after suxamethonium was similar to the increase observed in a normal population by others. Our study can exclude the hypothesis that an anomalous increase in potassium would be a typical and frequent response to suxamethonium in FAP Met 30 patients. However, we cannot exclude that a dangerous rise in serum potassium may exist in a certain percentage of FAP patients.

Received 1 July, accepted for publication 3 December 1996

Key words: Amyloid; anaesthesia; familial amyloidosis; potassium; succinylcholine.

© Acta Anaesthesiologica Scandinavica 41 (1997)

FAMILIAL amyloid polyneuropathy (FAP) or Andrade disease is a hereditary amyloidosis with inherent dominant transmission (1). Type I is the most frequent type (2, 3), with some hundred patients living in Portugal, Sweden and Japan, and some cases noticed in USA, Brazil, England, Spain and other countries. This type of FAP, first reported in 1952 (1), is characterised by sensorial, motor and neuro-vegetative involvement with onset in the lower extremities and later spread to the upper extremities. Cachexy, as a consequence of digestive autonomic dysregulation, or cardiac arrhythmias are the usual causes of death with a very poor quality of life during the last years (2, 3).

As a result of motor involvement, a variable degree of muscle atrophy is observed during the course of the disease (3). Suxamethonium produces an abnormal increase in serum potassium in several neurological diseases (4). Knowing that FAP patients are predisposed to cardiac arrhythmias, and not knowing the effects of suxamethonium on their serum potassium concentrations, it could be argued that it is not safe to

use this drug in patients with this pathology (5, 6). However, in several reports of liver transplantation in FAP patients (7-9), no complications were reported in association with its administration. The aim of this study was to evaluate the magnitude of the increase in serum potassium produced by suxamethonium in patients with FAP.

Patients and methods

The study was approved by the Ethics Committee of the University Hospitals of Coimbra and informed consent was obtained from all patients.

Patients

Twenty-one patients with clinical symptoms, familial history and positive Transthyretin Met 30, anaesthetised for liver transplantation during a 30-month period were included. No FAP patient transplanted in our institution during the same period was excluded due to medical reasons but 4 cases were not included in this study exclusively due to technical reasons.

Nine patients were female and 12 were male and age varied between 25 and 52 years (34.9 ± 6.9 years). The neurological involvement, evaluated with the scale of Maccdo et al. (10), was from 20 to 65 in 100 (36.5 ± 11.5 in 100), time elapsed from first symptom was from 2 to 12 years (5.5 ± 3.2 years). Weight was 52.6 ± 7.7 kg and height 166.6 ± 7.5 cm, indicating that our patients weighed $14 \pm 9\%$ less than their ideal weight, as calculated by the Lorenz formula. Body Mass Index (BMI) was 18.9 ± 2.3 kg/m².

To evaluate pre-operative cardiac involvement, conventional EKG, 24-hour electro-cardiography Holter study and cardiac echocardiogram were done in all patients. Four patients had previous pace-makers justified by conduction disturbances. Two of these 4 patients presented EKG and imagiological evidence of left atrium hypertrophy. Two other patients presented first degree AV blockade. Six patients had rare premature ventricular contractions, one of which also presented a single episode of ventricular tachycardia. In the remaining 9 patients, the Holter records were normal.

Methods

Pre-anaesthetic medication was instituted with diazepam. The dose varied from 5 to 10 mg given per os, 1 to 2 h before anaesthesia, or in slow intravenous injection, in the operating room. No other drug was administered before induction. An arm or a forearm vein and a radial artery were catheterised. Values and curve of EKG and systemic arterial pressure were monitored with an AS3 monitor (Datex, Finland).

A rapid sequence induction was done with 1 to 2 µg/kg of fentanyl and 4 to 6 mg/kg of thiopentone, followed by 1 mg/kg of suxamethonium and the insertion of an orotracheal tube. Patients were then ventilated with air/oxygen by a Siemens 900D ventilator.

Samples for analysis of arterial blood gases and plasma concentrations of potassium, sodium and ionised calcium were drawn immediately before induction and 1 and 5 min after the administration of suxamethonium. Analyses were immediately performed in a ABL 505 Analyser (Radiometer, Copenhagen), adjacent to the operating room. For blood sampling heparinized syringes were used (QS 50, Radiometer, Copenhagen).

Statistics

The 3 samples (baseline, 1 min and 5 min) were compared by Analysis of Variance for repeated measurements followed, when appropriate, by Tukey test. Linear regression analysis was performed to determine the correlation of the potassium increase and age,

evolution of the disease, neurological score, body mass index and ratio weight/ideal weight. $P < 0.05$ was considered as statistically significant. All data are expressed as mean \pm standard deviation.

Results

Before induction, plasma potassium concentrations were 3.8 ± 0.4 mmol/L. One minute after suxamethonium its values were 3.8 ± 0.4 mmol/L and 5 min after 4.3 ± 0.5 mmol/L. Values at 5 min were significantly different from baseline values (increase 0.5 ± 0.6 mmol/L, $P < 0.01$) and from values at 1 min ($P < 0.01$). The maximal increase observed in one patient was 1.6 mmol/L and the maximal absolute value was 5.0 mmol/L (Table 1).

With linear regression, no statistically significant association was found between the increase in potassium and age ($r = 0.21$), years elapsed from first symptom ($r = 0.14$), neurological score ($r = 0.17$), BMI ($r = 0.17$), and ratio weight/ideal weight ($r = 0.03$).

No differences were observed among the 3 samples in partial pressure of carbon dioxide (39.6 ± 4.5 mmHg, 40.2 ± 4.5 mmHg and 38.7 ± 4.5 mmHg, respectively, at baseline, 1 min and 5 min). No differences were observed in sodium (139.4 ± 3.1 mmol/L, 137.9 ± 3.6 mmol/L and 138.9 ± 2.8 mmol/L) or ionised calcium (1.20 ± 0.05 mmol/L, 1.18 ± 0.08 mmol/L and 1.20 ± 0.09 mmol/L, respectively).

Table 1
Plasma concentrations of potassium (mmol/L) were measured before anaesthetic induction (baseline) and 1 minute (1 min) and 5 minutes (5 min) after 1 mg/kg of suxamethonium.

	n	Baseline	1 min	5 min
1	1	3.4	3.3	4.5
2	2	4.5	4.3	4.9
3	3	3.9	3.8	4.3
4	4	3.3	3.4	4.8
5	5	3.9	3.9	4.8
6	6	3.5	3.6	3.9
7	7	4.8	4.8	4.2
8	8	3.3	3.0	3.2
9	9	4.0	3.8	4.0
10	10	3.6	3.7	4.4
11	11	3.6	3.8	4.0
12	12	3.2	3.4	3.9
13	13	3.6	3.7	4.1
14	14	4.4	3.7	3.7
15	15	3.7	3.7	4.1
16	16	4.2	4.6	4.2
17	17	3.9	3.8	4.0
18	18	3.7	3.7	4.9
19	19	4.0	4.0	4.8
20	20	3.4	3.8	5.0
21	21	3.6	4.2	4.4

Discussion

Compared with the increases in serum potassium produced by suxamethonium in healthy humans (11-13), the average increase in serum potassium observed in the patients of our study could not be considered as abnormal. Thus, our study can disprove the hypothesis that an anomalous and menacing increase in potassium would be a typical and frequent response to suxamethonium in FAP Met 30 patients.

A possible explanation for our findings may be found in the mechanisms by which suxamethonium produces a potassium increase in neurological diseases. Although there are some doubts about the complete mechanisms, the currently accepted theory is that the suppression of nervous stimulation to a muscle produces an increase in the number of cholinergic receptors and the development of extra-junctional chemosensitivity, leading to abnormal liberation of potassium in the presence of suxamethonium (14).

The abnormal increase of serum potassium after suxamethonium may have a time-related distribution, or in other words, it varies with the time elapsed from the start of the neurological disease. Some differences exist between animal (15, 16) and human studies (17, 18) but it is accepted that, in lesions with an abrupt onset, no abnormal increase in potassium is observed when suxamethonium is administered more than 3 months after trauma (14) or 6 months after upper motor lesions (3, 14). In familial amyloid polyneuropathy type I, the motor neuropathy and muscle atrophy have an insidious course, advancing for more than 10 years from initial symptoms in the feet until lower limb paralysis and upper limb involvement. The disease progresses from nerve to nerve and muscle to muscle, in a slow way, and the conditions leading to hyperkalaemia presumably do not exist simultaneously in extensive areas of the patient. Probably, in the muscular masses of the body of FAP patients, three phases exist concerning the evolution of the neuropathy and subsequent motor involvement: an initial phase in which there is no involvement and the liberation of potassium after suxamethonium is similar to the muscle of a normal population; a second one, with recent motor involvement, in which suxamethonium produces an abnormal increase in the liberation of potassium; a third one, where motor involvement appeared several months or years ago and where the liberation of potassium is no longer anomalous. The possible explanation for the absence of hyperkalaemia in our patients is that, probably, the second phase is never an extensive one.

However, our study of 21 patients cannot exclude that a dangerous rise in serum potassium may occur in certain patients or at certain times of the evolution of the disease, and three points must be stressed:

First: It is important to consider that 4 patients (19.0%) had increases in plasma concentrations of potassium higher than 1.0 mmol/L with a maximal value of 1.6 mmol/L. This rise was not dangerous because the initial value was 3.4 mmol/L but it would be a problem if the pre-operative potassium was in the upper limits of the normal range. It should be noted that in our study several patients had baseline potassium concentrations under the normal levels.

Second: We used only 1 mg/kg of suxamethonium. With the use of higher doses higher increases in potassium may be expected.

Third: it is important to notice that, independent of the number of measurements done in a study, potassium measurements are always serial measurements and not continuous measurements. Consequently, it is possible that there could exist higher values than those measured. Previous studies indicate that 5 min after the administration of suxamethonium would be the point where the maximal increase in potassium or values near the maximal increase might be observed (11, 18, 19) but also, looking at the individual data of these studies, that individual variations were observed. If, in some of our patients, the maximal increase occurred before or after the 5-min sample, the design of our study would not reveal this increase.

These three points of concern suggest that the use of suxamethonium in FAP type I patients should be done with a certain degree of caution. One specific reason supports its use in this particular pathology. Slow gastric emptying as a consequence of neuropathy is invariably present in these patients even during the initial phases of the disease (20), with gastric residues observed frequently in their stomachs 24 hours after the last meal. This fact makes it imperative that these patients should always be considered by the anaesthesiologist as patients with a full stomach (21). Suxamethonium is still by far the most frequently used drug in such circumstances (22, 23) but the introduction in clinical practice of new muscle relaxants probably will soon change this aspect.

In conclusion, the use or non-use of suxamethonium in FAP is probably an individual decision after weighing the risks and advantages. Pre-operative potassium levels, the dose of suxamethonium to be used and the degree of motor involvement and muscle atrophy must be considered in this decision.

Acknowledgements

The study was supported by a grant from the Medical Research Council of the Minister of Health, the Portuguese Government. The authors appreciate the contribution of Antónia Pereira da Silva, Maria do Céu Lapa and Valentina Pinho for manuscript preparation.

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