Timing of blood sampling for butyrylcholinesterase (BChE) phenotyping in patients with prolonged recovery after mivacurium or suxamethonium.

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Background and Goal of Study: About 76% of the population is homozygous for usual BChE, while 24% carries at least one genetic variant allele. Most of these variants have reduced BChE activity ([BChE]) that can lead to prolonged neuromuscular block (NMB) after suxamethonium (SUX) or mivacurium (MIV). BChE can be characterized by phenotyping and by determination of genotype. Inappropriate timing of blood sampling can interfere with results of BChE assay. However, guidelines regarding desirable delay between exposure to anaesthesia/neuromuscular blocker and testing are not clearly defined. We therefore compared BChE phenotype based on blood samples collected during or shortly (<6h) after recovery from NMB (T1) with that assessed on blood drawn after >1 week (T2).

Materials and Methods: After ethical committee approval and written informed consent 19 patients with a prolonged NMB after MIV and SUX were selected. Screening at T1 and T2 was done in all patients. [BChE] was assayed using benzoylcholine as a substrate. Phenotyping was based on dibucaine and fluoride inhibition. Genotyping was done by the Centre of Medical Genetics (University of Ghent). [BChE] at T1 and T2 were compared using a paired t-test. The effect of neostigmine on [BChE] was assessed by analysis of co-variance.

Results and Discussion: We included 19 patients with prolonged NMB following MIV (18) and SUX (1). MIV dose was 0.17 (0.1) mg·kg⁻¹ and NMB duration (TOF90) was 184 (42) min. [BChE] were significantly different at T1 and T2, i.e. 2459 (1905) U·L⁻¹ and 4287 (2636) U·L⁻¹, respectively (p<0.002). Values are mean (SD). Neostigmine did not significantly decrease [BChE] at T1. In 3 patients at T1 and 2 patients at T2, [BChE] was too low to determine phenotype. In all other patients phenotyping yielded identical results at T1 and T2. The presumed presence of at least one allele for the atypical variant on phenotypic characterization was confirmed by sequence analysis of patient's DNA. Phenotyping failed to identify one new variant (p.Tyr146Cys) and in detecting the K variant in 14 out of 15 patients.

Conclusion(s): Anaesthesia interfered with [BChE], but not with phenotyping. Phenotyping can be performed on blood drawn during or immediately after recovery of NMB to screen for clinically relevant variants of BChE. However, accurate diagnosis of BChE deficiency needs further confirmation by determination of genotype [1].

Patient	Phenotype		Genotype		
	T1	T2	A-variant	K-variant	Other
1	U,U	U,U	-/-	-/-	
2	A,A	A,A	+/-	+/-	
3	U,A	U,A	+/-	+/+	
4	A,A	A,A	+/+	+/+	
5	Nm	U,A	-/-	+/-	F1, §
6	A,K	A,K	+/-	+/+	
7	U,A	U,A	+/-	+/+	
8	U,U	Nm	-/-	+/+	
9	A,A	A,A	+/+	+/+	
10	U,A	U,A	+/-	+/-	
11	Nm	Nm	+/+	+/+	
12	U,U	U,U	-/-	-/-	
13	A,A	A,A	+/+	+/+	
14	Nm	U,U	-/-	+/-	
15	Na	U,U	-/-	-/-	
16	A,A	A,A	+/+	+/+	
17	U,A	U,A	+/-	+/-	
18	A,K or A,J	A,K or A,J	+/+	+/-	
19	U,U	U,U	-/-	-/-	

Table 1. Phenotype (at T1 and T2) and genotype of BChE.
Nm: not measurable; Na: not available
-/-: no variant; +/-: heterozygote; +/+: homozygote.
§: new variant of BChE; p.Tyr146Cys.