Succinylcholine Use in Adult Anesthesia – A Multinational Questionnaire Survey

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ABSTRACT

There are no definitive evidence based standards regarding use of succinylcholine (SCh) for anesthesia induction. However, there is a global trend toward eliminating SCh not only in elective, but also in emergency surgery in adults. The aim of the study was to survey the use of SCh in adult elective and emergency anesthesia practice in several European countries and the United States by questionnaire. One hundred and seventy anesthesiologists out of 201 possible, from six institutions in five countries (Croatia, Bosnia and Herzegovina, Hungary, United Kingdom, and the United States) anonymously completed the questionnaire about their use of SCh. The questionnaire was structured to assess the respondents’ frequency of use of SCh in adult surgery (elective and emergency), reasons for use or rejection of SCh, positive and negative attributes of SCh, and observed side effects in their practice. Differences in use were tested using χ²-test when appropriate. There was a significant difference in the use of SCh between countries for elective surgery with the lower use in UK and Hungary (χ²=45.8, p<0.001). One hundred and seventeen (69%) use it regularly. In emergency surgery 165 (97%) anesthesiologists use it without any significant difference among countries (χ²=2.13, p<0.711). The top indications for SCh use were anticipated difficult intubation/ventilation (74%), caesarean section (54%), and obesity and/or hiatus hernia (49%). The top reasons against SCh use were adequate substitutes (87%), fear of arrhythmias (45%), and anaphylaxis (19%). The most desirable reported drug features were: rapid onset (88%), short duration (64%), and effective relaxation (61%). Forty-six per cent of the surveyed anesthesiologists stated they had never experienced a complication with its use. The most frequently reported side effects were myalgias (47%), bradycardias (42%), and prolonged blockade (39%). Allergic reactions were reported by 13%, and asystole by 12% of physicians. From our survey it is possible to conclude that succinylcholine is still regularly used, at least by surveyed anesthesiologists in Europe and USA, in adult anesthesia practice, especially in elective surgery for which it may be least suited. This reflects the discrepancies between the international guidelines for the use of SCh and the clinical practice of many anesthesiologists in different countries. The regional differences in SCh usage may be considered through anesthesia cultures and practice variations depending on country.

Key words: neuromuscular blocking agents, neuromuscular depolarizing agents, succinylcholine, side effects, contraindications

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**Introduction**

Succinylcholine (SCh) is the only depolarizing muscle relaxant that is still in clinical use after many decades. Its unique clinical features allow a rapid onset of profound muscle relaxation combined with a short duration of action. This makes it particularly suitable for patients with full stomach requiring rapid sequence induction (RSI, expedient intubation of the trachea)\(^1\). However, the drug has significant contraindications and side effects that can be troublesome and potentially life-threatening\(^2\). In particular, the drug manufacturers recommend that it should not be used in elective surgery for children and adolescents, because of the risk of rhabdomyolysis and hyperkalemic cardiac arrest in patients with undiagnosed myopathies\(^3\).

Many serious adverse events have been reported with use of SCh: cardiovascular (bradycardia, nodal rhythms, ectopy, sinus arrest with asystole), muscular (fasciculations, myalgias, malignant hyperthermia), transient increases in intragastric, intraocular and intracranial pressures, myalgias, malignant hyperthermia), transient intracranial pressure increases, rhabdomyolysis and hyperkalemic cardiac arrest in patients with undiagnosed myopathies\(^4\)–\(^6\).

There are no standards based on the available scientific evidence regarding use of SCh. However, there is a worldwide trend toward eliminating SCh not only in elective, but also for emergency surgery. Based on the recent meta-analysis of 52 randomized controlled trials\(^7\), we hypothesized that SCh may still be used more widely in many routine surgeries. Moreover, the question rises regarding abandoning it at all in the near future, especially after the Food and Drugs Administration rejected Sugammadex a new neuromuscular reversal agent\(^8\).

Therefore, we performed an international questionnaire survey of current patterns of use of SCh in five countries – four European (Croatia, Bosnia and Herzegovina, Hungary, the United Kingdom (UK)), and the United States of America (USA) – to test whether there is regional differences in SCh usage that may be considered through anesthesia cultures and practice variations depending on country.

We hypothesized that succinylcholine was still regularly used by many anesthesiologists in Europe and the USA for adult surgery. This may reflect the discrepancy between the recommendations for avoiding the use of SCh due to its serious side effects, and the clinical practice of many anesthesiologists in different countries.

**Subjects and Methods**

Out of 201, a total of 170 anesthesiologists from Croatia, Bosnia and Herzegovina, Hungary, UK, and USA completed an anonymous questionnaire about the use of SCh for surgery (Table 1).

The questionnaire was composed by the authors themselves, and validated with senior colleagues who were not any more in anesthesia service, and in the previous study among anesthesiologists in different Croatian hospitals\(^9\). In this study the questionnaire was distributed to possible respondents in person by authors themselves, during morning anesthesia meetings and sessions. There was no preference to survey only staff anesthesiologists, the residents were also included in the study. The questionnaire was distributed in: Split University Hospital Center (Croatia), University Hospital of Sarajevo, and General Hospital of Sarajevo (Bosnia and Herzegovina), Kent & Canterbury General Hospital (UK), Department of the Cardiovascular Anaesthetics and ICU, Semmelweis University, Budapest (Hungary), and St Joseph Regional Medical Center in Milwaukee, and Veteran Affairs (VA) Hospital, Palo Alto (USA).

The questionnaire explored four areas of the clinical use of SCh by the respondents (see Appendix 1): 1) Their use of SCh in adult elective and emergency surgery; 2) Reasons for using/not using SCh in adult anesthesia; 3) Positive and negative attributes of SCh; 4) Side effects of SCh they observed in their clinical practice.

The questionnaire consisted of four sections A-D; section A: personal data, section B: use of SCh in adult elective surgery, section C: use of SCh in adult emergency surgery, and section D: side effects of the drug based on personal observations by the surveyed.

The data were analyzed using Statistica 8.0 (StatSoft, Tulsa, OK, USA) software package. The difference in regional use, gender, working experience, and position was tested using chi-squared test. p<0.05 was considered significant.

**Results**

The response rates were as follows: Croatia 84.1%, Bosnia and Herzegovina 89.5%, Hungary 82.5%, USA 82.5%, and UK 86.4%. Overall response rate was 84.6% (170/201).

**Adult elective surgery**

Almost 69% (117/170) of all anesthesiologists in the whole sample use SCh in the adult elective surgery with the lower use in UK (18/31), and especially in Hungary

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**Table 1:** NUMBER OF PARTICIPANTS BY COUNTRY, GENDER AND POSITION

<table>
<thead>
<tr>
<th>Country</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Staff</th>
<th>Resident</th>
</tr>
</thead>
<tbody>
<tr>
<td>Croatia</td>
<td>37</td>
<td>18</td>
<td>19</td>
<td>32</td>
<td>5</td>
</tr>
<tr>
<td>Bosnia and Herzegovina</td>
<td>34</td>
<td>7</td>
<td>27</td>
<td>32</td>
<td>2</td>
</tr>
<tr>
<td>Hungary</td>
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<td>11</td>
<td>22</td>
<td>27</td>
<td>6</td>
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<td>USA</td>
<td>33</td>
<td>25</td>
<td>8</td>
<td>29</td>
<td>4</td>
</tr>
</tbody>
</table>
| **Total (N, %)**    | 170   | 87   | 83     | 140   | 30       | 18
The anesthesiologists who use SCh for elective cases (31%) do it routinely (6%), often (18%), occasionally (20%), and rarely (25%) (Figure 1). There were no significant differences regarding use of SCh by gender, position, or working experience (Table 3).

The top indications for use were: anticipated difficult intubation/ventilation (74%), caesarean section (54%), patients with obesity and/or hiatus hernia (49%), uncertainty of patient’s preoperative fasting (45%), short anaesthesia times (37%), and ear, nose and throat (ENT) surgery (27%). The top reasons for not using SCh were availability of adequate substitutes (87%), fear of arrhythmias (45%), anaphylaxis (19%), and muscle fasciculations (17%).

**Adult emergency surgery**

SCh was used in adult emergency surgery by 97% (165/170) of physicians if there were no obvious contraindications such as known myopathy, burns, renal failure, history of malignant hyperthermia or central core disease. There was no significant difference among countries ($\chi^2=2.13$, $p=0.711$). The most frequent indications were: full stomach (78%), rapid sequence induction of anaesthesia (68%), anticipated difficult intubation/ventilation (66%), ileus (57%), emergency cesarean section (53%), and laryngospasm (51%). Multiple indications were frequently provided by the surveyed.

**Opinion of surveyed anesthesiologists about the properties of SCh**

The most desirable properties of SCh cited were rapid onset (88%), short duration (64%), and reliable relaxation (60%). The major drawbacks reported were potential for hyperkalemia (76%), myalgia (71%), and brady-cardia/bradyarrhythmia (68%).

**Adverse events observed by the surveyed anesthesiologists**

Forty-six per cent (92/170) of respondents stated they had never observed any adverse event with SCh. The most frequently reported adverse events were severe myalgias (47%), bradycardia/bradyarrhythmia (42%), and prolonged blockade (39%) (Table 4). Asystole was reported by 21 physicians (12%). It should be emphasized that these percentages do not refer to the incidence of the various side effects, but to proportion of physicians who have observed the side effect themselves at least once in their clinical practice.
**TABLE 4**

<table>
<thead>
<tr>
<th>Rank</th>
<th>Side effect</th>
<th>Percentage (%) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe myalgias</td>
<td>47</td>
</tr>
<tr>
<td>2</td>
<td>Resistant bradyarrhythmias</td>
<td>42</td>
</tr>
<tr>
<td>3</td>
<td>Prolonged blockade</td>
<td>39</td>
</tr>
<tr>
<td>4/5</td>
<td>Asystole</td>
<td>23</td>
</tr>
<tr>
<td>4/5</td>
<td>Trismus-masseter spasm</td>
<td>23</td>
</tr>
<tr>
<td>6</td>
<td>Allergic reaction</td>
<td>13</td>
</tr>
<tr>
<td>7</td>
<td>Other answers ‡</td>
<td>8</td>
</tr>
</tbody>
</table>

*Multiple answers were allowed; it should be emphasized that percentages do not refer to the incidence of the various side effects, but the proportion of physicians who have seen the side effect at least once in their clinical practice.

‡no answer, premature ventricular complexes, hyperkalemia, pulmonary aspiration after fasciculations

**Discussion**

Many anesthesiologists still appear to use SCh in a variety of clinical situations. Our survey suggested that 69% (117/170) of all anesthesiologists in this study use SCh in the adult elective surgery with the lower use in UK (18/31), and especially in Hungary (9/33). The vast majority of respondents reported use of SCh in adult emergency surgery (165/170) with no difference among countries.

This survey was limited to a few institutions in a few countries and therefore we cannot reliably assess the national use patterns. Nonetheless, the survey suggests that SCh is still widely used for elective or emergency endotracheal intubations. The survey also strongly suggests that SCh is still the first choice in adult emergency surgery, although newer agents were introduced into clinical practice, such as rocuronium.

**Adult elective surgery**

Surprisingly large number of respondents claimed to use SCh in adult elective surgery in many countries. The finding of regional difference regarding usage in adult elective surgery is an interesting and important issue, but hard to explain it at the level of this study. Anesthesiologists in UK, and especially those in Hungary, use SCh relatively less than others. This may reflect the anesthesiology culture and practice variations from country to country, which may address to some form of different national strategies, but may be an accidental finding, as well, since anesthesiologists in UK and Hungary were tested in only one hospital. It would be interesting to further explore the issue of national strategies especially since we did not find significant difference in SCh use in different hospitals in Croatia in our previous study.

Despite potential life-threatening side-effects of SCh, the surveyed anesthesiologists consider it indispensable, especially in patients with unreliable information about their appropriate fasting status, as well as the possibility of difficult intubation. The use of SCh for expected difficult intubation is particularly concerning, since the difficult airway algorithm by the American Society of Anesthesiologists (ASA) states that no muscle relaxant should be given in this scenario.

**Adult emergency surgery**

Undoubtedly, there is a greater and more consistent use of SCh in adult emergency surgery, than in adult elective surgery. The main indication in an emergency surgery is facilitation of endotracheal intubation in patients considered to be at an increased risk of aspiration of gastric contents. This was confirmed in our survey. Regarding rapid-sequence induction, 68% of our respondents used SCh, rather similar to Hofmockel report of 56.5%. Moreover, in the same report, as many as 87% of departments in Germany used SCh for RSI of anesthesia. The availability and increasing experience with an adequate alternative (e.g., rocuronium) may reduce the routine use of SCh for this indication which has been questioned in emergency settings.

Although it is frequently put in the second place (after rocuronium) as a SCh »substitution« agent, it seems that mivacurium is readily used in emergency situations by anesthesiologists. The very recent case report describes its usage in emergency caesarean section in primigravida suffering from torsion dystonia. Rapid sequence induction was achieved as described by Ali and colleagues. The authors suggested that mivacurium seemed a suitable alternative to SCh for rapid sequence induction since it had a quick onset and offset action with minimal residual effects.

**Opinions of surveyed anesthesiologists about the properties of SCh**

According to the respondents in this study, rapid onset and short duration are major advantages, and hyperkalemia is a major drawback of SCh use. There are many case reports of dangerous hyperkalemia and rhabdomyolysis after succinylcholine, associated with various clinical situations – burns, massive trauma, severe intraabdominal infection, brain trauma, spinal cord injury, Guillain-Barre syndrome, prolonged immobilization, polyneuropathy, myopathy, etc. The hyperkalemic cardiac arrest after SCh is usually refractory to routine cardiopulmonary resuscitation and often requires the use of calcium, glucose and insulin, bicarbonate and dantrolene and prolonged resuscitation. A recent review highlights some molecular mechanism of SCh – induced hyperkalemia.

**Adverse events observed by surveyed anesthesiologists**

A significant number of surveyed anesthesiologists claimed they never experienced any complication from SCh use. Anaphylactic or anaphylactoid reactions occurring during anesthesia are estimated to be between 1 in 1,000 and 1 in 25,000 anesthetic procedures, with the...
neuromuscular blockers being involved in as many as 50–80% of cases. The reported mortality from such serious reactions is 3.4–6%. The highly immunogenic SCh, was found to be the most frequently involved agent\(^{19}\). Two fatal anaphylactic reactions, officially attributed to SCh by the local Hospital Committee, occurred in the Split University Hospital Center in Croatia during anesthesia induction for ENT surgery, which was a trigger for this and similar studies.

There was also a continuing search for other SCh replacements (e.g., rapacuronium, GW280430A), but with disappointing results\(^{19}\). The non-depolarizing muscle relaxant curorium is considered by many to be an adequate substitute, because of a rapid onset at 2–4 times ED\(_5\). Unfortunately, such doses result in a minimum duration of neuromuscular block of 30–60 minutes\(^{20,21}\). Nevertheless, according to the Cochrane Database of Systematic Reviews, SCh creates excellent intubation conditions more reliably than curorium. Only if used with propofol, rocuronium creates intubating conditions more reliably than rocuronium. Only if used with propofol, rocuronium creates intubating conditions equivalent to those with succinylcholine\(^{22}\).

However, it seems that rocuronium is currently the best alternative, especially after introduction of sugammadex. This agent could dramatically change our clinical administration of muscle relaxants. Sugammadex is a novel selective relaxant-binding drug which antagonizes or reverses steroid non-depolarizing neuromuscular blocking agents, especially rocuronium, and is likely the most exciting drug in clinical neuromuscular pharmacology\(^{23}\). However, it must be emphasized that FDA rejected it for registration due to hypersensitivity or allergic reactions\(^{8}\).

Ronald Miller wrote in a recent editorial\(^{24}\) that after more than 50 years of dramatic advances in anesthesia, a pharmacologically dirty and dangerous drug (SCh) is still "the golden standard" for producing paralysis during RSI. A replacement for SCh does not appear to be imminent. We, therefore, have an obligation to keep trying to improve the safety of SCh. The same author’s question in the most recent editorial is, if sugammadex can reliably reverse the neuromuscular block of a large dose of rocuronium 10–15 min (or sooner) after its administration, will SCh finally begin its ultimate demise?\(^{25}\) Nevertheless, recent studies suggest there may be a renewed interest in the use of SCh for routine intubation in adult patients in a reduced dose of 0.5–0.6 mg kg\(^{-1}\)\(^{26,27}\).

**Limitations of the study**

The principal limitation is the fact that the sample of respondents does not allow the representative overview of the opinion of all anesthesiologists in particular country. As mentioned above, this survey was limited to a few institutions in a few countries and therefore we cannot reliably assess the national use patterns. However, our previous research on anesthesiologists from different hospitals in different towns of Croatia suggested rather uniform behavior within the country\(^{9}\). This survey, as well as some other reports, deals with rather important issue about discrepancies between international official recommendations and present clinical practice with regard to routine usage of succinylcholine\(^{28}\).

Best to our knowledge, at the time of this survey sugammadex was not approved in tested countries. It is possible that the data raised from this survey would be different if this neuromuscular reversal agent was introduced into clinical practice. This could be a topic for future research.

According to our results, indications and contraindications for SCh use deserve further work on developing standard international expert consensus guidelines. The majority of surveyed physicians was aware of its potential risks, but still used it for specific indications. Therefore, it would be desirable that large prospective databases are established to accurately assess the true risk profile of the rapid onset and short acting muscle relaxants currently available.

The data from this survey demonstrate that succinylcholine is still regularly used by many surveyed anesthesiologists in Europe and the USA for adult surgery. This reflects the discrepancies between the international guidelines for the use of SCh and the clinical practice of many anesthesiologists in different countries. The regional differences in SCh usage may be considered through anesthesia cultures and practice variations depending on country.

**Acknowledgements**

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**References**

UPORABA SUKCINILKOLINA U ANESTEZIJI ODRASLIH – MULTINACIONALNO ISTRAŽIVANJE S POMOĆU UPITNIKA

S A Z Ė T A K

Standardi temeljeni na dokazima ne postoje za uporabu sukcinilkolina pri uvodu u anesteziju. Međutim, postoji globalni trend prema eliminaciji sukcinilkolina, ne samo u elektivnoj, već i u hitnoj kirurgiji. Cilj studije bio je pregled uporabe sukcinilkolina u elektivnoj i hitnoj kirurgiji odraslih, u anesteziološkoj praksi nekoliko europskih država i Sjedinjenih Američkih Država. Sto sedamdeset anesteziologa, od mogućih 201, iz petišest bolnica u pet država (Hrvatska, Bosna i Hercegovina, Mađarska, Velika Britanija i Sjedinjene Američke Države) anonimno je ispunilo upitnik o vlastitoj uporabi sukcinilkolina. Upitnik je strukturiran u cilju ustanovljavanja učestalosti uporabe sukcinilkolina u elektivnoj i hitnoj kirurgiji odraslih, zatim razloge uporabe ili odbijanja uporabe sukcinilkolina, kao i mišljenje anesteziologa o pozitivnim i negativnim značajkama SCh te prikupljanje podataka o nuspojavama ili komplikacijama iz njihove prakse.

Razlike u uporabi testirane su $c^2$-testom kada je to bilo primjereno. Nađena je značajna razlika u uporabi sukcinilkolina u elektivnoj kirurgiji s manjim udjelom uporabe u Velikoj Britaniji i posebice u Mađarskoj ($c^2=45.8$, $p<0.001$). U hitnoj kirurgiji $165/170$ (97%) ih rabi SCh bez značajnih razlika ovisno o državi rada ($c^2=2.13$, $p<0.711$). Glavne indikacije za uporabu bile su očekivana teška intubacija/ventilacija (74%), carski rez (54%) i debljina i/ili hijatalna hernija (49%). Najvažniji razlozi protiv uporabe sukcinilkolina bili su: primjerena zamjena (87%), strah od aritmija (45%) te anafilaktska (19%). Najpoželjnije karakteristike medicamenta bile su: brz početak (88%), kratko trajanje (64%) i učinkovita relaksacija (61%). Jednadeset i pet posto anesteziologa uključenih u studiju izjavilo je da nikad nisu imali komplikaciju pri uporabi toga lijeka. Najčešće nuspojave bile su mijalgije (47%), bradikardije (42%) i produljena relaksacija (39%). Alergijske reakcije prijavilo je 13% te asistolije 12% anesteziologa. Iz našeg pregleda moguće je zaključiti da sukcinilkolin u anesteziji odraslih redovito rabe anesteziologi iz Europe i SAD uključeni u istraživanje, posebno u elektivnoj kirurgiji za koju je taj lijek najmanje primijenjen. To ukazuje na nesklad između međunarodnih smjernica o uporabi SCh i kliničke prakse velikog broja anesteziologa u različitim zemljama. Razlog značajne regionalne razlike u uporabi sukcinilkolina mogao bi se promatrati kroz varijacije anesteziološke prakse i kulture ovisno o državama.

APPENDIX 1

Usage of Succinylcholine

The Anonymous Questionnaire

Dear colleagues,

• this questionnaire is an anonymous one
• it is not linked with any investigation of the Ministry of Health or public authorities
• the investigators are interested in the frequency of usage of neuromuscular relaxant succinylcholine among anesthesiologists
• it consists of 4 groups of questions (A-D)
• group A questions involve personal data, while following questions consider use of succinylcholine in elective surgery (group B), emergency surgery (group C). Finally, there are group D questions about side effects of the drug (personal opinions and observations in clinical practice)
• please answer all the questions.

Z. Dogaš

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A. Personal data
A1. Age (yrs)
   a) ≤30 (yrs)
   b) 31–35
   c) 36–40
   d) 41–45
   e) 46–50
   f) 51–55
   g) 56–60
   h) > 60

   a) ≤5
   b) 6–10
   c) 11–15
   d) 16–20
   e) >20

A2. GENDER  
   F  M

A3. Clinical experience in anesthesia

A4. Position held
   1) staff
   2) resident

B1. Do you use succinylcholine IN ELECTIVE SURGERY IN ADULTS?
   1) yes
   2) no

B2. If the B1 answer is YES, how often do you use succinylcholine in ELECTIVE SURGERY IN ADULTS?
   1) always
   2) often
   3) occasionally
   4) very rarely

B3. If the answer B1 is YES, cite the CLINICAL CIRCUMSTANCES (more than 1 answer allowed)
   a) anticipated difficult intubation/ventilation scenario
   b) cesarean section
   c) uncertainty of patient’s preoperative fasting
   d) very short anesthesias
   e) ENT surgery
   f) obesity, hiatal hernia
   g) I always use it in induction of anesthesia
   h) .......... (other answers)

B4. If you never use it (the B1 answer is NO), THE POSSIBLE REASONS are (more than 1 answer allowed)
   a) there is no need, there are other suitable relaxants
   b) possibility of arrhythmias
   c) possibility of allergic reactions
   d) fasciculations
   e) .......... (other answers)

B4a. FOR HOW LONG haven’t you been using succinylcholine?
   Months.....
   Years.....

C1. Do you use succinylcholine IN EMERGENCY SURGERY?
   1) Yes
   2) No

C2. If you use it (C1 answer is YES), HOW OFTEN do you use succinylcholine in EMERGENCY SURGERY:
   1) always
   2) often
   3) occasionally
   4) very rarely

C3. If the C1 answer is YES, the POSSIBLE REASONS are: (more than 1 answer allowed)
   a) a patient is considered to be at risk for aspiration of gastric contents
   b) ileus
c) anticipated difficult intubation/ventilation

d) rapid and safe relaxation

e) emergency cesarean section

f) rapid sequence induction of anesthesia

g) laryngospasm

h) ………. (other answers)

C4. If you NEVER use it (C1 answer is NO), the POSSIBLE REASONS are:

a) there is no need, there are other suitable relaxants

b) possibility of arrhythmias

c) possibility of allergic reactions

d) fasciculations

e) ……….. (other answers)

______________________________________________________________________________________________________

______________________________________________________________________________________________________

D1. In your opinion, what are THE MOST ACCEPTABLE CLINICAL FEATURES of succinylcholine (more than 1 answer allowed)

a) rapid onset

b) short duration, quick recovery

c) effective and reliable relaxation

d) tried in emergency situations

e) ………………..(other answers)

f) there are no positive features

D2. In your opinion, what are THE DRAWBACKS of succinylcholine: (more than 1 answer allowed)

a) myalgias/fasciculations

b) bradycardias/bradyarrhythmias

c) possibility of hyperkalemia in certain circumstances

d) trigger of malignant hyperthermia

e) prolonged duration (low pseudocholinesterase levels)

f) possible allergic reaction

g) …… (other answers)

h) there are no drawbacks

D3. Have you observed any ADVERSE REACTION(S) after usage of succinylcholine in your clinical practice?

1) yes

2) no

D3a. If yes (E3 answer is YES), which one (more than 1 answer allowed)

a) resistant bradyarrhythmias

b) asystole

c) trismus – masseter spasm

d) severe myalgias

e) prolonged blockade

f) allergic reaction

g) ………(other answers)