Effects of Anesthesia Changes During Maintenance ECT: A Longitudinal Comparison of Seizure Quality Under Anesthesia Using Propofol/Esketamine Versus Methohexital

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ABSTRACT

Introduction The effectiveness of ECT relies on the induction of a generalized cerebral seizure. Among others, seizure quality (SQ) is potentially influenced by the anesthetic drug used. Commonly used anesthetics comprise barbiturates, etomidate, propofol, and esketamine, with different characteristics and impacts on seizure parameters. So far, no studies have compared the influence of methohexital vs. a combination of propofol/esketamine on established SQ parameters.

Methods This retrospective longitudinal study compared eight established SQ parameters (PSI, ASEI, MSC, midictal amplitude, motor and electroencephalography (EEG) seizure duration, concordance, PHR) before and after the change from propofol/esketamine to methohexital in 34 patients under maintenance ECT. Each patient contributed four measurements, two before and two after the anesthesia change. Anesthesia dose, stimulus dose, electrode placement, and concomitant medication remained unchanged throughout the analyzed treatments.

Results Under methohexital ($M = 88.97$ mg), ASEI ($p = 0.039$ to 0.013) and midictal amplitude ($p = 0.022$ to < 0.001) were significantly lower, whereas seizure duration (motor and EEG) was significantly longer when compared to propofol/esketamine (M = 64.26 mg/51.18 mg; $p = 0.012$ to < 0.001). PSI, MSC, seizure concordance, and PHR were not affected by the anesthetic used.

Discussion Although to what extent these parameters correlate with the therapeutic effectiveness remains ambiguous, a decision for or against a particular anesthetic could be considered if a specific SQ parameter needs optimization. However, no general superiority for one specific substance or combination was found in this study. In the next step, anesthetic effects on treatment response and tolerability should be focused on.

Introduction

Electroconvulsive therapy (ECT) is an effective treatment for depressive and psychotic disorders [1–3]. It relies on the induction of a generalized cerebral seizure under anesthesia and muscle relaxation. To measure the quality of this seizure, multiple seizure quality (SQ) parameters have been defined and studied, such as postictal suppression index (PSI), maximum sustained coherence (MSC), midictal amplitude (miA), average seizure energy index (ASEI), seizure duration (electroencephalography, EEG/motor), and peak heart rate (PHR) [4–6]. In literature, these parameters are generally described as being related to the therapeutic response [4–10]. Multiple factors influence the seizure quality, including stimulus dose, electrode placement, patients' age, and concomitant medication like benzodiazepines [11–13]. Among these factors,

seizure quality is potentially influenced by the anesthetic drug used [14]. Until today, there is no (inter-)national consensus on which drugs should be used for induction and maintenance of general anesthesia for ECT. The most frequently used anesthetics are barbiturates, etomidate, propofol, and esketamine [15], each having different characteristics and an impact on seizure quality.

Advantages and disadvantages of different anesthetics used under ECT

Several studies have investigated the effects of different anesthetics on ECT seizure quality and tolerability. Propofol is an ultrashort-acting anesthetic but has anticonvulsive characteristics and was found to cause a shortened EEG seizure [16, 17]. (Es-)ketamine is commonly used in ECT due to its pro-convulsive properties [18], but side effects like nausea, dizziness, and psychotic symptoms appear more frequently than under other anesthetics during ECT [19]. Esketamine – as an enantiomer of ketamine – has both a higher anesthetic effect and fewer side effects compared with equally dosed ketamine [20]. In spite of a mild anticonvulsive effect, methohexital is a short-acting barbiturate that has multiple helpful characteristics for use in ECT: it leads rapidly to a short-lasting narcotic effect, it is not known to have a negative impact on the length of EEG seizure and has a moderating effect on hemodynamic parameters like increase of blood pressure or cardiac arrhythmias [14, 17]. Under etomidate, myoclonies and a longer wake-up time occur more often as a side effect than under other anesthetics [21]. Besides these findings, a systematic review of anesthetic agents from 2016 found no difference in the tolerability of common anesthetics in ECT [22]. While it described ketamine and methohexital to potentially facilitate a higher antidepressant effect – due to a longer seizure duration than propofol or thiopental – other reviews and studies could not find differences in the reduction of depression scores [23, 24] despite the inherent antidepressant effect of ketamine in other treatments. Until now, no study suggests a significant superiority for one of the mentioned anesthetics or their combinations.

At the University Medical Center Göttingen, methohexital was used for ECT anesthesia in most patients until 2019. In 2019 anesthetic drugs in ECT treatment had to be changed due to unavailability. A combination of propofol/esketamine was chosen to combine the advantages and reduce the disadvantages of the two substances as single applications: poor EEG seizures may improve with lower propofol doses, which can be realized by the addition of (es-) ketamine [25]. Due to renewed availability, methohexital has been used again since 2022. So far, four studies compared methohexital with propofol and detected a shorter seizure duration under the latter [23]. Three studies compared ketamine with methohexital but did not find significant differences in seizure quality or antidepressant effectiveness [19, 24, 26].

To our knowledge, no direct comparisons of methohexital vs. a combination of propofol/esketamine have been made regarding their effects on SQ parameters in ECT so far. The current retrospective longitudinal study aims to close this gap by comparing established SQ parameters before and after the change from propofol/esketamine to methohexital. To minimize other factors which may influence the seizure threshold or seizure quality, only patients undergoing maintenance ECT (mECT) were included. Thus, stimulus dose, electrode placement, and concomitant medication remained completely stable throughout the analyzed treatments.

Materials and Methods

Subjects

The following inclusion criteria were applied: (1) patients receiving mECT at our department irrespective of diagnosis, (2) availability of four consecutive mECTs, two directly before and two directly after the change from propofol/esketamine to methohexital, (3) age ≥ 18 years, (4) mECT within the data collection period from 11/2021 to 04/2022.

We identified 52 patients undergoing mECT, of which 10 were excluded due to discontinuation of mECT, the necessity of a new ECT series, or intolerability regarding change of anesthetics. Eight were excluded due to changes in anesthetics dose, stimulus dose, or electrode placement. Finally, 34 patients were included in the study (age: 20 to 85 years, means (*M*) = 60.29, *SD* = 16.09; 64.7 % female), diagnosed with unipolar depressive disorder (*n* = 24; ICD-10: F32.2, F32.3 and F33.1 to F33.4), schizophrenia spectrum (*n* = 7; ICD-10: F20.0, F20.2, F25.1), bipolar depressive disorder (*n* = 2; ICD-10: F31.3 and F31.8) and dementia with psychotic symptoms (*n* = 1; ICD-10: F02.8). All patients had shown a treatment response to the ECT series beforehand. They received regular mECT for relapse prevention at the Department of Psychiatry and Psychotherapy, University Medical Center Göttingen.

Concomitant medication (see ▶ **Tab. 1**) was kept stable during the course of this study. The study was approved by the local ethics committee (2/5/22).

Study Design

For each patient, data from four mECT treatments was gathered, pre- (T_1 and T_2) and post-change (T_3 and T_4) from propofol/esketamine to methohexital (see above). A total of eight established SQ parameters (see ▶ **Tab. 2**) were measured: (1) PSI, (2) ASEI, (3) MSC, (4) miA, (5/6) seizure duration (motor, cuff method), and EEG, (7) seizure concordance ($\frac{motor}{EEG} * 100$), (8) peak heart rate (PHR). Five missing values due to technical deficits occurred exclusively for the PSI (valid cases for PSI: T_1: *n* = 33, T_2: *N* = 34, T_3: *n* = 33, T_4: *n* = 31).

Maintenance (m-) electroconvulsive therapy

MECT was performed with a Thymatron IV device (Somatics, LLC., Lake Bluff, IL, USA). The double-dose program and brief pulse technique were used (maximum dose of 1008mC; 200 %). Initially, the stimulus dose for the first ECT treatments was determined age-based. Both dosing and electrode placement had been previously adjusted depending on clinical response, tolerability, and seizure quality during acute ECT. To eliminate potential intra-individual confounding, only patients with constant stimulus dose and electrode placement were included. All patients received a combination of propofol/esketamine with constant dosage for the first two sessions (T_1 and T_2). In most of the cases, the proportion of propofol was higher (*M* = 0.88 mg/kg) when compared to esketamine (*M* = 0.68 mg/kg). The dosages had been initially adjusted over the

▶ **Tab. 1** Medication examined in this study.

	Antidepressant	Antipsychotic	Anticonvulsants	Lithium	Benzodiazepine
SSNRI	8	–	–	–	–
SSRI	4	–	–	–	–
Tricyclic	1	–	–	–	–
Mirtazapine	2	–	–	–	–
MAO-Inhibitors	2	–	–	–	–
Other	1	–	–	–	–
Combination	12	–	–	–	–
None	4	–	–	–	–
Atypical	–	17	–	–	–
Combination	–	8	–	–	–
None	–	9	–	–	–
Pregabalin	–	–	2	–	–
Lamotrigine	–	–	1	–	–
None	–	–	31	–	–
Lithium	–	–	–	8	–
None	–	–	–	26	–
Benzodiazepine	–	–	–	–	5
None	–	–	–	–	29

Notes. Medication for $N = 34$ patients; SSNRI, selective serotonin norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitor; MAO-Inhibitors, monoamine oxidase inhibitors.

▶ **Tab. 2** Definition of SQ parameters.

1. Postictal suppression index (PSI)	Measures the decrease of the EEG amplitude directly at the end of the seizure in %
2. Average seizure energy index (ASEI)	Is the integral of the seizure amplitude over time divided by the duration of the seizure $\frac{\mu V^2}{1000}$
3. Maximum sustained coherence (MSC)	Measures the synchronization of convulsions between the hemispheres in %
4. Midictal amplitude (miA)	Describes the maximal ictal amplitude in a seizure in µV
5. Motor seizure duration	Is defined by the length of motoric convulsions, here measured by the cuff method in seconds
6. EEG seizure duration	Is measured by EEG and shows the total length of the seizure in seconds
7. Seizure concordance	Calculates the concordance between motor and EEG seizure $(\frac{motor}{EEG} * 100)$
8. Peak heart rate (PHR)	Describes the maximum heart rate during the seizure, measured in beats per minute

Notes. Source: Instruction manual from the Thymatron IV device (Somatics, LLC., Lake Bluff, IL, USA; [44]); EEG, electroencephalography; SQ, seizure quality.

course of treatment before mECT: At the beginning, most patients had received a dosage of 1 mg propofol/kg body weight and 0.5 mg esketamine/kg body weight.

For the second two mECT sessions (T_3 and T_4), all patients received a constant dosage of methohexital. Here, the initial dosage before mECT was 1 mg methohexital/kg body weight, and $M = 1.21$ mg/kg during mECT.

Statistical analyses

IBM SPSS Statistics 29 (IBM Corp. Armonk, NY) was used to analyze data. For descriptive representation, means (M) and standard deviations (SD) were created for numeric variables, as well as Pearson correlations (r). To analyze the main outcome (change of SQ parameters), eight general linear models (GLM) for repeated measures were used. Measurements were included as a four-staged within-subjects factor (mECT sessions: T_1 to T_4). Pairwise comparisons could be calculated both within a constant condition of anesthesia (propofol/esketamine: T_1 vs. T_2; methohexital: T_3 vs. T_4) and between two conditions of anesthesia (T_1/T_2 vs. T_3/T_4), enabling us to control for intrapersonal variations independently of anesthesia changes. For multiple comparisons, p-values were corrected within each model (Bonferroni method; initial significance at $p < 0.05$ before correction, two-tailed). Exploratory models controlled for age (see results section for details). For all SQ parameters except for PSI (see above), $N = 34$ patients provided complete datasets.

Results

Descriptive results

Please see ▶ **Tab. 3** for an overview. Electrodes were placed left anterior right temporal ($n = 15$), right unilateral ($n = 10$), and bitemporal ($n = 9$). The mean stimulus dose was $M = 109.12$ % (SD = 54.57; 100 % = 504mC). The mean PSI in percent reached $M = 75.59$ % (SD = 15.10), ASEI was $M = 13.14$ $\frac{\mu V^2}{1000}$ (SD = 9.06), MSC (0 % to

▲ **Tab. 3** Correlations, means, standard deviations, and frequencies.

Variable	1	2	3	4	5	6	7	8	9	10	*M* ± *SD*/*Freq.*
1. Age	–										60.29 ± 16.09
2. Gender	-.153	–									f: 22, m: 12
3. Stim. dose	.458**	-.172	–								109.12 ± 54.57
4. PSI	-.514**	.325	-.412*	–							75.59 ± 15.10
5. ASEI	-.503**	.128	-.637**	.484**	–						13.14 ± 9.06
6. MSC	-.119	-.018	-.384*	.027	.096	–					95.71 ± 5.63
7. Midictal amplitude	-.468**	.125	-.668**	.478**	.966**	.167	–				190.25 ± 57.65
8. Seiz. dur. (motor)	-.240	.224	-.409*	.355*	.067	.458**	.059	–			35.51 ± 12.93
9. Seiz. dur. (EEG)	-.022	.006	-.190	-.039	-.221	.370*	-.222	.840**	–		52.26 ± 17.33
10. Seiz. concordance	-.379*	.351*	-.372*	.721**	.485**	.237	.467**	.430*	-.103	–	69.12 ± 15.79
11. Peak heart rate	-.438**	.336	-.458**	.421*	.211	.443**	.234	.521**	.359*	.372*	126.24 ± 19.08

Notes. *$p < .05$. **$p < .01$. Captions: *Gender* (f = female/1, m = male/2); *stimulus dose* (0 % to 200 %; 100 % = 504mC); *postictal suppression index* (PSI; 0 % to 100 %); *ASEI* ($\frac{\mu V^2}{1000}$); *seizure duration in seconds* (motor and EEG); *seizure concordance* ($\frac{motor}{EEG} * 100$); *maximum sustained coherence* (MSC; 0 % to 100 %); *midictal amplitude* (μV) (*N* = 34); PSI, postictal suppression index; ASEI, average seizure energy index; MSC, maximum sustained coherence; EEG, electroencephalography; Seiz. dur. seizure duration.

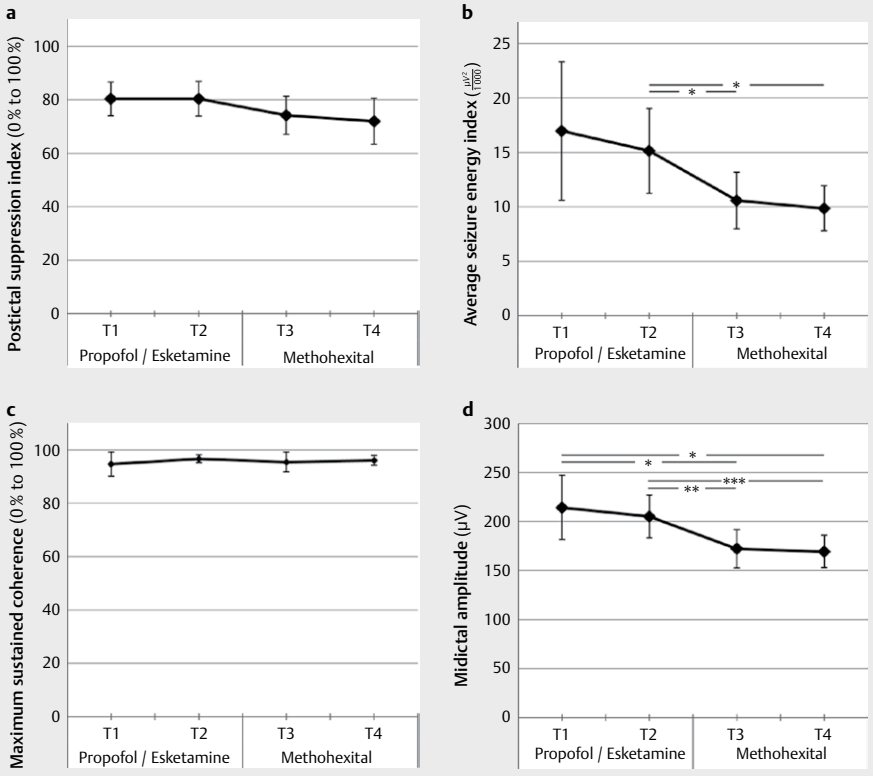
100 %) was *M* = 95.71 % (*SD* = 5.63), and midictal amplitude was *M* = 190.25 (SD = 57.65). The patients showed *M* = 35.51 s (SD = 12.93) motor seizure duration and *M* = 52.26 s (SD = 17.33) EEG seizure duration. Seizure concordance was *M* = 69.12 % (SD = 15.79). The mean peak heart rate was *M* = 126.24 beats/minute (*SD* = 19.08). Significant correlations were found between SQ parameters (see ▶ **Tab. 3**; variables 4 to 11). A higher stimulus dose was applied to older patients ($r = 0.458$, $p < 0.01$). Both increasing age and higher stimulus dose were negatively correlated with SQ parameters (age: *r* between -0.022 and -0.514, $p < 0.05/0.01$ in 5 out of 8 SQ parameters; stimulus dose: *r* between -0.190 and -0.668, $p < 0.05/.01$ in 7 out of 8 SQ parameters).

For the first two mECT sessions (T_1 and T_2), the mean dosage of propofol was *M* = 64.26 mg (SD = 20.04, min = 40 mg, max = 120 mg, *M* = 0.88 mg/kg), and the mean dosage of esketamine was *M* = 51.18 mg (SD = 16.65, min = 20 mg, max = 80 mg, *M* = 0.68 mg/kg). For the second two mECT sessions (T_3 and T_4), the mean dosage of methohexital was *M* = 88.97 mg (SD = 22.99, min = 50 mg, max = 140 mg, *M* = 1.21 mg/kg). The mean interval between the two mECTs was *M* = 4.28 weeks (SD = 2.44). After the change to methohexital, two patients required prophylactic antiemetic medication and one patient needed prophylactic analgesic medication to prevent headaches in further treatments.

Longitudinal analysis of seizure quality parameters

▶ **Fig. 1** and ▶ **Fig. 2** present graphical summaries of all SQ parameters. The (1) PSI did not vary significantly between the four mECT sessions ($F(3, 87) = 2.29$, $p = 0.084$, partial $\eta^2 = 0.07$; see ▶ **Fig. 1a**). For the (2) ASEI, a general variation was found ($F(3, 99) = 4.66$, $p = 0.004$, partial $\eta^2 = 0.12$; see ▶ **Fig. 1b**). Corrected pairwise comparisons showed a significant decline of the ASEI from T_2 (*M* = 11.56) compared to T_3 (*M* = 7.75, $p = 0.039$) and T_4 (*M* = 6.12, $p = 0.013$). Numerically, the difference between T_1 and T_3/T_4 was even higher but did not reach significance due to a higher variance at T_1 ($p = 0.181/0.106$; see ▶ **Fig. 1b**). The (3) MSC did not vary significantly between the ECT sessions ($F(3, 99) = 0.338$, $p = 0.80$, partial $\eta^2 = 0.01$; see ▶ **Fig. 1c)**, in contrast to the (4) midictal amplitude ($F(3, 99) = 8.52$, $p < 0.001$, partial $\eta^2 = 0.01$; see ▶ **Fig. 1d**): Pairwise comparisons showed a significant decline from T_1 (*M* = 214.28)/T_2 (*M* = 205.05) to T_3 (*M* = 172.25) and T_4 (*M* = 169.42; $p = 0.022$ to < 0.001). In sum, a significant decrease with the use of methohexital could be found exclusively for ASEI and midictal amplitude.

Seizure duration varied significantly between measurements, both for (5) motor ($F(3, 99) = 13.90$, $p < 0.001$, partial $\eta^2 = 0.30$; see ▶ **Fig. 2e**) and (6) EEG ($F(3, 99) = 22.11$, $p < .001$, partial $\eta^2 = 0.40$; see ▶ **Fig. 2f**). Motor seizure duration raised from T_1 (*M* = 30.76)/T_2 (*M* = 30.35) to T_3 (*M* = 39.26) and T_4 (*M* = 41.65; $p = 0.012$ to < 0.001). Likewise, the EEG seizure duration raised from T_1 (*M* = 44.29)/T_2 (*M* = 44.00) to T_3 (*M* = 59.15) and T_4 (*M* = 61.62; all $p < 0.001$). Seizure concordance (7) did not vary significantly between the measurements ($F(3, 99) = 0.60$, $p = 0.615$, partial $\eta^2 = 0.02$; see ▶ **Fig. 2g**). There was no significant variation for the (8) PHR between measurements ($F(3, 99) = 0.367$, $p = 0.777$, partial $\eta^2 = 0.01$; see ▶ **Fig. 2h**). In sum, seizure duration was significantly longer with the use of methohexital, both for motor (approx. + 10 s) and for EEG (approx. + 15 s).



▶ **Fig. 1** Course of seizure quality parameters in psychiatric patients during four maintenance electroconvulsive therapy (mECT) sessions, pre- (T_1/T_2) and post- (T_3/T_4) anesthesia change. $p<0.05$ *, $p<0.01$ **, $p<0.001$ ***. Mean values with 95 %-CIs and Bonferroni corrected pairwise comparisons; **(a)** postictal suppression index (PSI); **(b)** average seizure energy index (ASEI); **(c)** maximum sustained coherence (MSC); **(d)** midictal amplitude.

Influence of age on seizure quality parameters

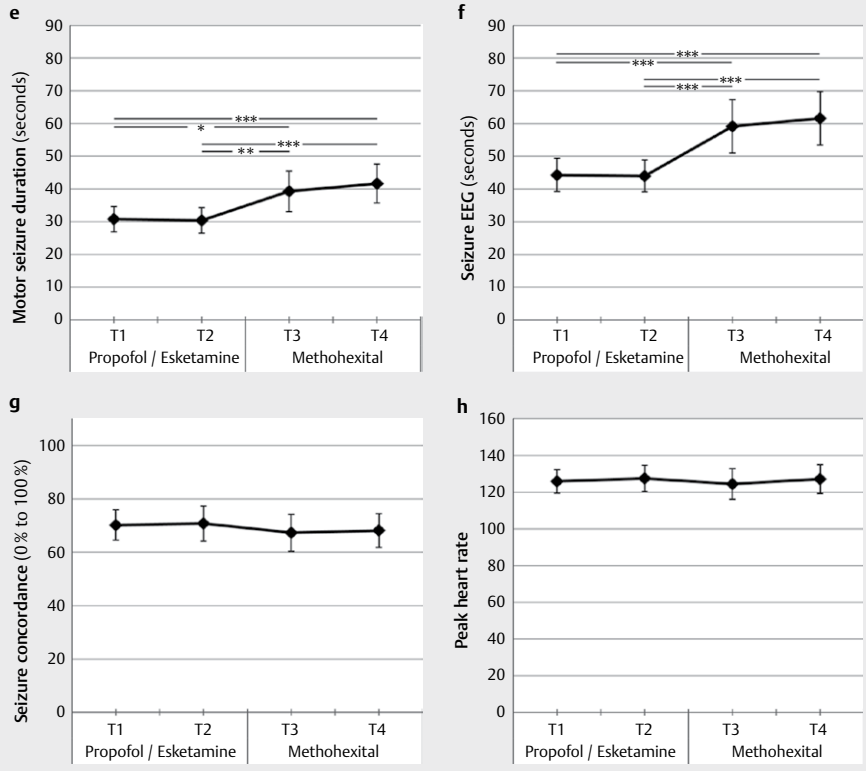
Numerous studies have found that elderly patients show inferior SQ parameters [11–13], which may lead to treating them with higher stimulus doses (see ▶ **Tab. 3**). We created two subgroups of patients based on the median age (63 + years vs. < 63 years; each group $n = 17$). A two-staged between-subjects factor was then added to each of the eight GLMs reported above to analyze general differences between both groups (main effect: between groups) or different possible trajectories between older vs. younger patients depending on the anesthetic used (interaction effect). In sum, we did not find a significant effect between both groups ($p = 0.094$ to 0.619) or an interaction effect ($p = 0.176$ to 0.771) for any GLM. Numerically, older patients showed worse SQ parameters, but differences were too small to reach significance and remained constant over the anesthesia changes for all parameters.

Discussion

In this retrospective study, we longitudinally analyzed the influence of different anesthetics on SQ parameters. Therefore, data from four mECTs was gathered, pre- and post-change from propofol/esketamine to methohexital for each patient. Both ASEI and midictal amplitude showed a significant decrease under methohexital if compared to propofol/esketamine, whereas seizure duration (motor and EEG) was significantly longer under methohexital. PSI, MSC, seizure concordance, and PHR remained stable.

Before interpreting these findings, it must be noted that uncertainties do still exist regarding SQ parameters. Although the quality of a seizure under ECT is evaluated on the basis of wave amplitudes, seizure duration, PSI, MSC, and PHR [5, 9, 27], to what extent these parameters correlate with the therapeutic efficacy remains ambiguous. For example, elderly patients have higher seizure thresholds but respond more often to ECT [28, 29], and though benzodiazepines may decrease SQ parameters, their use does not seem to reduce the effectiveness of ECT [30]. Also, factors associated with better SQ parameters, like younger age or hyperventilation right before ECT, do not necessarily result in a better therapeutic effect [28, 31]. Furthermore, clinical predictors improving the probability of ECT response like psychotic/catatonic symptoms, fewer previous medication failures, short illness episodes or absence of comorbid personality disorder do not influence seizure quality markers [32–34]. Nonetheless, these parameters represent the best-researched predictors for ECT effectiveness to date [4].

In this study, we found that seizure duration heavily depended on the choice of (combined) anesthetic substances. There is some evidence that notably short seizure duration (depending on the source less than 15 or 24 s) is leading to a poorer clinical outcome [5, 35] – this would argue for the use of methohexital over propofol/esketamine in cases of borderline seizure duration. However,



▶ **Fig. 2** Course of seizure quality parameters in psychiatric patients during four maintenance electroconvulsive therapy (mECT) sessions, pre- (T_1/T_2) and post- (T_3/T_4) anesthesia change. $p<0.05^*$, $p<0.01^{**}$, $p<0.001^{***}$. Mean values with 95 %-CIs and Bonferroni corrected pairwise comparisons; **(e)** motor seizure duration; **(f)** seizure duration electroencephalography; **(g)** seizure concordance (); **(h)** peak heart rate (PHR).

other studies did not show a significant correlation between seizure duration and clinical outcome [9, 36, 37]. Regarding the meaning of ASEI and midictal amplitude for the therapeutic outcome, different studies come to heterogeneous results: some outpoint a correlation between a decrease in depressive symptoms and a higher wave amplitude [4, 5, 27], others do not [7, 10]. Furthermore, as described above, there is a negative correlation between wave amplitude, seizure length, and age [11, 38, 39], with age being considered a positive predictor for ECT response [28, 34, 40]. Our results also show that some of the established SQ parameters listed above (PSI, MSC, seizure concordance, PHR) are not influenced by the change of anesthetics. So far, mostly PSI [7, 10, 27] and MSC [7, 27] have been positively associated with a better therapeutic effect.

In conclusion, this study clearly shows differential effects of the anesthetics methohexital vs. propofol/esketamine on four out of eight analyzed SQ parameters: methohexital is associated with a longer seizure duration, whereas propofol/esketamine lead to higher amplitudes. However, it is not possible at this time to make a definitive statement about their relationship – or the relationship of propofol/esketamine vs. methohexital – to treatment response.

From a pharmacological point of view, both the combination of propofol/esketamine as well as the use of methohexital are suitable approaches for inducing general anesthesia for ECT. Both substances show a very quick onset of 10–30 s after infusion with a duration of action of 5–10 min, which makes them suitable for short-lasting procedures. The effects on the central nervous system significantly differ between the two substances. Methohexital application initially leads to biphasic EEG changes with the occurrence of excitatory, proconvulsive symptoms, especially in low to moderate doses. A state of burst-suppression is reached only after high doses. Propofol has a dose-dependent anticonvulsive effect even in low doses, which can be a limitation for its use in ECT patients. It is, therefore, usually combined with a second hypnotic substance such as ketamine, to avoid relevant anticonvulsive concentrations altering ECT quality. Ketamine leads to dissociative anesthesia. It is not known to have relevant anticonvulsive effects.

Regarding the tolerability of propofol/esketamine vs. methohexital, we examined concomitant medication of patients during treatment and found that in two cases, a new medication was started to prevent (1) nausea and (2) headaches after switching to methohexital. Whereas barbiturates are known to cause postanesthetic nausea and vomiting in a relevant proportion of patients, propofol is known to prevent these side effects [41, 42]. As numbers are very small and a direct assessment of symptoms in the patients was missing, so rather mild symptoms might have been overlooked, and at this point, no general statement can be made. Therefore, a future prospective design with a focus on tolerability (and possibly treatment response) would be necessary. In summary, neither methohexital nor propofol/esketamine was clearly superior regarding the influence on seizure parameters, tolerability or clinical applicability.

Limitations and strengths

There are some limitations regarding this study. First, as the study relied on retrospective examination of longitudinal clinical data, possible effects of the different anesthetics on tolerability were not systematically examined. As discussed above, this would facilitate implications for clinical routine and should be focused on in the future, then prospective studies. Second, due to the retrospective design, dosages of anesthetics had been chosen according to clinical standard but without a consistent dosing protocol. Therefore, it cannot be stated with absolute certainty that the depth of anesthesia was equivalent between subjects and may have impacted seizure quality. The same applies to the time interval between anesthetic administration and stimulation: this had also been done according to clinical standard, but timings had not been protocolled during clinical routine and could thus not be analyzed within the framework of this retrospective study. Furthermore, it was not possible to correlate anesthesia with therapeutic implementations, which should be considered in a future prospective design. Third, the generalization of results is limited due to our relatively small sample size, although our sample represented a typical set of stable treated mECT patients. Only larger and prospective, comparative trials focusing on acute ECT could help to ultimately clarify the differential effects of different anesthetic regimens regarding (a) SQ parameters, (b) effectiveness, and (c) tolerability. This would also allow the addition of separate samples, in each of which only propofol or esketamine could be administered as the sole anesthetic, to analyze differential effects. However, we would like to point out that the longitudinal study design presented here largely eliminated interference factors (e. g., changes in stimulus dose, electrode placement, etc.), which is a clear strength of this study.

Ethical approval

This study has been approved by the local ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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