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ACID–BASE BALANCE AND GAS EXCHANGE IN PATIENTS WITH DRUG-RESISTANT EPILEPSY DURING THE PERIOPERATIVE PERIOD: THE ROLE OF CLINICAL CHARACTERISTICS AND THERAPY

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Abstract

Objective: To evaluate the impact of epilepsy duration and type of antiepileptic therapy on acid–base balance and oxygenation parameters in patients with pharmacoresistant focal epilepsy during the perioperative period.

Methods: A retrospective cohort study included 93 adult patients who underwent neurosurgical treatment for pharmacoresistant focal epilepsy between 2019 and 2024. Demographic data, intraoperative fluid therapy, acid–base balance, gas exchange, and respiratory outcomes were analyzed. Patients were stratified by epilepsy duration (≤15 years, >15 years) and therapy type (monotherapy, polytherapy).

Results: Neither epilepsy duration nor therapy type significantly affected acid–base balance or gas exchange. Patients with epilepsy duration >15 years required longer mechanical ventilation. Polytherapy was associated with a higher positive fluid balance (p=0.02). Early postoperative seizures occurred in 9.7% of patients and were linked to increased pH and HCO_3^- without gas exchange deterioration.

Conclusions: Epilepsy duration and type of antiepileptic therapy did not significantly influence acid–base balance or oxygenation in the early postoperative period but were related to fluid balance and ventilation duration. A personalized approach to perioperative fluid and respiratory management is recommended.

***Keywords**: pharmacoresistant epilepsy, antiepileptic therapy, acid–base balance, gas exchange, fluid therapy.*

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Резюме

КИСЛОТНО-ЩЕЛОЧНОЕ РАВНОВЕСИЕ И ГАЗООБМЕН У ПАЦИЕНТОВ С ФАРМАКОРЕЗИСТЕНТНОЙ ЭПИЛЕПСИЕЙ В ПЕРИОПЕРАЦИОННОМ ПЕРИОДЕ: РОЛЬ КЛИНИЧЕСКИХ ХАРАКТЕРИСТИК И ТЕРАПИИ

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Цель: Оценить влияние длительности заболевания и типа противоэпилептической терапии на показатели кислотно-щелочного состояния и оксигенации у пациентов с фармакорезистентной фокальной эпилепсией в периоперационном периоде.

Методы: Проведено ретроспективное когортное исследование у 93 взрослых пациентов, перенесших нейрохирургическое лечение фармакорезистентной фокальной эпилепсии в 2019–2024 гг. Анализировались демографические данные, показатели инфузионной терапии, параметры кислотно-щелочного состояния, газообмена и дыхательные исходы. Пациенты стратифицированы по длительности заболевания (≤15 лет, >15 лет) и типу противоэпилептической терапии (монотерапия, политерапия).

Результаты: Длительность заболевания и тип терапии не оказали статистически значимого влияния на показатели кислотно-щелочного состояния и газообмена. У пациентов с длительностью заболевания более 15 лет отмечена тенденция к увеличению времени искусственной вентиляции легких. Политерапия сопровождалась более высоким положительным гидробалансом (p=0,02). Судороги в раннем послеоперационном периоде наблюдались у 9,7% пациентов и ассоциировались с повышением pH и HCO_3^- без нарушений газообмена.

Выводы: Длительность заболевания и характер противоэпилептической терапии не определяют выраженных изменений кислотно-щелочного состояния и оксигенации в раннем послеоперационном периоде, однако связаны с инфузионным балансом и длительностью искусственной вентиляции легких. Необходим персонализированный подход к инфузионной и респираторной терапии у данной категории пациентов.

***Ключевые слова**: фармакорезистентная эпилепсия, противоэпилептическая терапия, кислотно-щелочное состояние, газообмен, инфузионная терапия.*

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Түйіндеме

ФАРМАКОРЕЗИСТЕНТТІ ЭПИЛЕПСИЯСЫ БАР НАУҚАСТАРДА ПЕРИОПЕРАЦИЯЛЫҚ КЕЗЕҢДЕГІ ҚЫШҚЫЛ-СІЛТІЛІК ТҰРАҚТЫЛЫҚ ПЕН ГАЗ АЛМАСУ: КЛИНИКАЛЫҚ СИПАТТАМАЛАР МЕН ТЕРАПИЯНЫҢ РӨЛІ

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Мақсат: Дәріге төзімді ошақты эпилепсиясы бар науқастарда ауру ұзақтығы мен антиепилептикалық терапия түрінің қышқыл-сілтілік тұрақтылық пен оксигенация көрсеткіштеріне периоперациялық кезеңде әсерін бағалау.

Әдістер: 2019–2024 жж. дәріге төзімді ошақты эпилепсия бойынша нейрохирургиялық операция жасалған 93 ересек науқас талданды. Демографиялық деректер, инфузиялық терапия, қышқыл-сілтілік тұрақтылық, газ алмасу көрсеткіштері және тыныс алу нәтижелері қаралды. Пациенттер ауру ұзақтығына (≤15 жыл, >15 жыл) және терапия түріне (монотерапия, политерапия) бөлінді.

Нәтижелер: Ауру ұзақтығы мен терапия түрі қышқыл-сілтілік тұрақтылық пен газ алмасуға айтарлықтай әсер етпеді. >15 жылдық анамнезі бар науқастарда өкпенің жасанды желдету ұзақтығы ұзарды. Политерапия оң гидробаланс жоғарылауымен байланысты болды (p=0,02). Ерте операциядан кейінгі құрысу 9,7% науқаста байқалды, ол pH мен HCO_3^- жоғарылауымен, бірақ газ алмасу бұзылуымен сипатталмады.

Қорытындылар: Ауру ұзақтығы мен антиепилептикалық терапия түрі ерте операциядан кейінгі кезеңде қышқыл-сілтілік тұрақтылық пен оксигенацияға айқын әсер етпейді, бірақ инфузиялық баланс пен өкпені жасанды желдету ұзақтығымен байланысты. Бұл топтағы науқастарда инфузиялық және тыныс алу терапиясына жекеленген көзқарас қажет.

***Түйінді сөздер**: дәріге төзімді эпилепсия, антиепилептикалық терапия, қышқыл-сілтілік тұрақтылық, газ алмасу, инфузиялық терапия.*

Дәйексөз үшін:

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Introduction

Pharmacoresistant focal epilepsy (PRFE) represents a severe disease phenotype, as up to 30% of patients fail to achieve adequate seizure control with conventional therapy [1]. In this group, surgical treatment remains the most effective option, significantly reducing seizure frequency and improving quality of life [2]. However, prolonged disease duration, chronic antiepileptic drug (AED) exposure, and the complexity of surgical procedures create an unfavorable perioperative setting, often associated with respiratory complications and impaired gas exchange [3].

Epilepsy-related disturbances in central respiratory control, including apnea, hypoventilation, and oxygen desaturation, have been described even during focal

seizures [4,5]. The postictal state is marked by reduced sensitivity to hypercapnia, which compromises compensatory mechanisms and contributes to acute respiratory risk [6,7]. Respiratory dysfunction is also implicated in the pathogenesis of sudden unexpected death in epilepsy (SUDEP) [7]. Although the direct link between epilepsy duration and severity of respiratory impairment remains unclear, cumulative subclinical disturbances are likely to accrue over time [3,5].

AED therapy further complicates perioperative management by influencing central nervous system function, acid–base balance, and metabolic regulation [1,2]. While some drugs such as levetiracetam demonstrate favorable safety profiles [8], others, including valproate, carbamazepine, and topiramate, may induce adverse metabolic or respiratory effects [10–14]. Polytherapy and prolonged AED use can exacerbate these risks, particularly when combined with anesthetics and opioids, whereas drug withdrawal increases seizure likelihood [2,9,13]. Comorbidities such as obesity, OSA, and COPD further elevate the risk of perioperative hypoxemia and respiratory failure [9,14,15]. In selected cases, extended mechanical ventilation or ICU monitoring within the first 24 postoperative hours is required [9,13].

Neurosurgical procedures for PRFE are often prolonged, associated with blood loss, and necessitate high anesthetic doses. More than half of patients undergoing extensive resections require postoperative ventilatory support due to hypoxemia, aspiration, hypoventilation, or impaired consciousness, particularly in the context of polytherapy and metabolic imbalance [2,7,13].

Despite clinical experience, several gaps remain unresolved. Specifically, the effect of epilepsy duration on perioperative respiratory function, the cumulative impact of long-term AED exposure, and the interplay between therapy regimen (monotherapy vs. polytherapy) and postoperative outcomes are poorly characterized. Given the heterogeneity of PRFE patients—ranging from decades-long disease to adult-onset epilepsy—an individualized risk assessment approach is required to optimize anesthetic and perioperative strategies.

Purpose: To investigate the relationship between epilepsy tenure and antiepileptic drug regimen characteristics with regard to acid-base equilibrium and oxygenation parameters during the perioperative course among adult patients receiving neurosurgical management of pharmacoresistant focal epilepsy.

Materials and Methods

This retrospective cohort study was conducted at the Hospital of the Medical Center of the Administration of Affairs of the President of the Republic of Kazakhstan. We analyzed 93 adult patients who underwent surgery for pharmacoresistant focal epilepsy between 2019 and 2024.

Inclusion criteria: age ≥18 years, confirmed diagnosis of pharmacoresistant focal epilepsy, documented neurosurgical procedure with complete records, and perioperative observation up to 48 hours.

Exclusion criteria: generalized epilepsy, insufficient data, severe comorbidities (decompensated pulmonary disease, respiratory failure, end-stage cardiac insufficiency, neoplasia, stage IV hepatorenal dysfunction), major intraoperative hemorrhage, or reoperation.

Parameters recorded:

Demographics: age, sex, body mass index.

Surgical variables: anesthetic technique, duration.

Hemodynamics: arterial pressure, heart rate, oxygen saturation, fluid balance (administration, blood loss, urine output).

Respiratory and oxygenation: minute ventilation, fresh gas flow, ABG values (pH, pCO_2, pO_2, HCO_3^-, base excess, oxyhemoglobin, ctO_2, FiO_2, PaO_2/FiO_2, A–a gradient, a/A ratio) intraoperatively, at completion, on ICU admission, and 12 h post-op.

Clinical outcomes: duration of mechanical ventilation, RASS scores, ICU stay, need for non-invasive ventilation, postoperative seizures.

Perioperative fluid therapy targeted: MAP ≥70 mmHg, CVP 6–12 mmHg, urine output >0.5 mL/kg/h, lactate <2.0 mmol/L. Management used 0.9% saline, switching to Sterofundin (B.Braun, Switzerland) with high-volume needs or hyperchloremic acidosis; Gelofusine was applied as colloid support. Norepinephrine was administered if MAP <65 mmHg despite adequate volume expansion.

Ventilation and oxygenation strategies were titrated to arterial blood gases and acid-base status, with SpO_2 maintained ≥93% via continuous monitoring.

Stratification:

By disease duration: Group 1 (≤15 years) and Group 2 (>15 years).

By antiepileptic regimen: monotherapy vs. polytherapy.

Statistical Analysis: We analyzed data utilizing SPSS version 26.0 and JASP statistical software. Descriptive statistics for continuous variables included means with standard deviations, supplemented by medians and interquartile ranges where indicated. Categorical variables were expressed as absolute frequencies and proportions. We employed nonparametric Friedman and Wilcoxon tests for temporal comparisons of acid-base status parameters, given the non-normal distribution of quantitative data (Kolmogorov-Smirnov test, $p<0.05$). When statistical significance was established, we conducted post-hoc pairwise analyses via Wilcoxon signed-rank test.

Results

A total of 93 patients underwent neurosurgical treatment for pharmacoresistant focal epilepsy. The mean age was 33.2±8.2 years; 59.8% were male and 40.2% female. The mean body mass index (BMI) was 23.9 kg/m². Nutritional status assessment revealed malnutrition in 7.8%, overweight in 15.7% (16 patients), class I obesity in 10.8% (11 patients), and class II obesity in 0.98% (1 patient).

Antiepileptic therapy. Carbamazepine was the most frequently used agent, prescribed as monotherapy in 28 of 37 patients and incorporated as either primary or adjunctive therapy in polytherapy regimens. Levetiracetam was frequently administered in patients with longer disease duration (n=30), either as monotherapy (n=4) or adjunctive therapy (n=23). Lamotrigine, oxcarbazepine, and topiramate were exclusively prescribed in polytherapy. Valproic acid showed slightly greater prevalence in long-standing disease, always as part of polytherapy.

Stratification. Patients were grouped according to disease duration (≤15 vs. >15 years) and treatment regimen (monotherapy vs. polytherapy). Patients with epilepsy >15 years were older than those with shorter

disease duration (34.1 vs. 30.7 years, p<0.05). No significant differences were observed in BMI or sex distribution. Mean ages by treatment regimen were comparable (32.3 vs. 32.4 years), with male predominance in both groups.

Intraoperative course. Minute ventilation, fresh gas flow, and anesthetic exposure time did not differ between groups. Richmond Agitation-Sedation Scale (RASS) scores post-extubation clustered around –1 (drowsy but arousable), without group differences. All patients remained in ICU for >12 hours. Postoperative mechanical ventilation duration was significantly longer in patients with chronic epilepsy (>15 years, p<0.05), but did not differ between therapy regimens.

Table 1.

Clinical and demographic characteristics of patients depending on type of therapy and disease duration

Variables		Disease duration			Type of antiepileptic therapy		
		≤15 years (n=45)	>15 years (n=48)	p	Monotherapy (n=33)	Polytherapy (n=60)	p
Mean age (M, 95% CI)		30.7 (28.4-33.0)	34.1 (31.9-36.3)	0.01	32.3 (29.5-34.0)	32.4 (30.4-34.4)	0.51
Body mass index		24.92±4.02	23.31±4.69	0.85	24.11±4.8	23.68±4.2	0.97
Sex	Female	18 (40%)	20 (41.7%)		11 (33.3%)	26 (43.3%)	
	Male	27 (60%)	28 (58.3%)		22 (66.7%)	34 (56.7%)	
Minute ventilation during surgery, l/min.		6.73±0.79	7.0±0.89	0.1	6.81±0.90	6.89±0.81	0.5
Fresh gas flow during surgery l/min.		3.01±1.03	2.86±0.95	0.4	2.98±1.06	2,90±0.93	0.8
Anesthesia duration, min. (M ± SD)		552.29 ±120.9	559.8 ±112.3	0.16	536.3 ±116.6	579.59 ±109.9	0.07
Extubation time, min. (M ± SD)		81.66 ±44.16	111.93 ±70.5	0.03	93.45 ±58.30	97,76 ±61,35	0.38
RASS score (M ± SD)		-0.96±0.19	-0.93±0.24	0.57	-0.94±0.22	-0.95±0.21	0.59
ICU length of stay, h (M ± SD)		14.47±3.34	14.06±2.54	0.19	14.37±2.8	14.22±3.11	0.71
M ± SD – mean ± standard deviation; CI – confidence interval; RASS – Richmond Agitation-Sedation Scale; ICU – intensive care unit							

Hemodynamics. Systolic, diastolic, and mean arterial pressure, heart rate, and peripheral oxygen saturation remained stable and within reference ranges throughout the perioperative period. No intergroup differences were observed.

Infusion therapy. Analysis of infusion parameters (Table 2) revealed significantly higher intraoperative fluid administration and net fluid balance in the polytherapy cohort, with increased variability. Patients with epilepsy ≤15 years demonstrated a trend toward more favorable fluid balance, though not statistically significant. Blood loss was comparable between groups, and no transfusions were required. Urine output was slightly greater in polytherapy patients, without statistical significance.

Acid–base balance. Dynamic assessment (Table 3) demonstrated pH values within the physiological range, approaching significance (p=0.05). Arterial carbon dioxide tension remained stable with a trend toward normocapnia (p=0.06). Base excess and bicarbonate concentrations improved significantly from deficit to near-compensated values (p<0.001).

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	Disease duration			Type of antiepileptic therapy		
	≤15 years (n=45)	>15 years (n=48)	p	Monotherapy (n=33)	Polytherapy (n=60)	p
Total infusion volume, ml (Me, Q1–Q3)	2800.0 (2400.0–3000.0)	500.0 (2300.0–3400.0)	0.79	2500.0 (2200.0–2900.0)	2800.0 (2400.0–3400.0)	0.05
Urine output, ml (Me, Q1–Q3)	000.0 (650.0–1650.0)	900.0 (525.0–1250.0)	0.27	900.0 (550.0–1500.0)	1425.0 (650–2040.0)	0.89
Blood loss, ml (Me, Q1–Q3)	100.0 (100.0–200.0)	100.0 (100.0–200.0)	0.16	100.0 (100.0–200.0)	100.0 (100.0–200.0)	0.72
Fluid balance, ml (Me, Q1–Q3)	400.0 (960.0–1825.0)	600.0 (1100.0–2025.0)	0.11	1250.0 (950.0–1650.0)	1700.0 (1150.0–2000.0)	0.02
Norepinephrine dose, mcg/kg/min (Me, Q1–Q3)	0.040 (0.040–0.050)	0.050 (0.030–0.050)	0.60	0.050 (0.040–0.050)	0.040 (0.040–0.050)	0.69
Me – median; Q1–Q3 – interquartile range; p – Mann–Whitney test.						

Acid–base balance indicators over time.

Indicators	During surgery	At the end of surgery	On ICU admission	12 h post-op	p
pH (Me, Q1–Q3)	7.39 (7.35–7.42)	7.38 (7.35–7.41)	7.38 (7.35–7.41)	7.40 (7.37–7.42)	0.05
pO_2 (Me, Q1–Q3)	232.0 (183.5–261.0)	173.0 (147.0–236.0)	157.0 (122.0–212.0)	100.0 (89.0–138.0)	<0.001
pCO_2 (Me, Q1–Q3)	36.8 (32.7–40.1)	38.0 (34.7–41.0)	38.1 (34.5–38.9)	37.0 (34.3–40.3)	0.06
BE (Me, Q1–Q3)	3.20 (–4.85 – –1.50)	-2.80 (–4.60 – –1.00)	-2.50 (–4.30 – –0.80)	-1.40 (–2.95 – 0.35)	<0.001
HCO_3^- (Me, Q1–Q3)	22.3 (21.0–23.5)	22.1 (21.1–23.2)	22.5 (21.2–23.6)	23.4 (22.2–24.6)	<0.001
Hb (Me, Q1–Q3)	128.0 (110.0–139.5)	124.0 (109.0–138.0)	124.0 (110.0–138.0)	125.0 (108.0–136.5)	0.71
Ht (Me, Q1–Q3)	38.0 (32.0–41.0)	36.0 (32.0–41.0)	36.0 (32.0–41.0)	37.0 (32.0–40.0)	0.28
SO_2 (Me, Q1–Q3)	98.3 (97.7–98.8)	98.0 (97.3–98.4)	97.6 (96.1–98.2)	96.7 (94.1–97.6)	<0.001
PaO_2/FiO_2 (Me, Q1–Q3)	520 (460–596)	490 (397–570)	434 (367–537)	390 (314–470)	<0.001
A–a gradient (Me, Q1–Q3)	41.0 (23.9–71.0)	34.3 (22.8–44.9)	41.0 (25.2–55.6)	39.4 (32.0–56.2)	0.08
a/A ratio (Me, Q1–Q3)	84.0 (73.0–89.0)	74.0 (57.5–85.5)	72.0 (56.0–84.0)	73.0 (56.0–80.0)	<0.001
ctO_2 (Me, Q1–Q3)	18.5 (16.0–20.4)	17.4 (15.6–19.4)	17.1 (15.4–19.0)	16.2 (14.5–17.9)	<0.001
Lactate (Me, Q1–Q3)	1.02 (0.89–1.70)	1.25 (1.02–1.90)	1.30 (0.99–1.85)	1.06 (0.88–1.60)	0.004
FiO_2 (Me, Q1–Q3)	50.0 (50.0–50.0)	50.0 (45.0–50.0)	45.0 (40.0–45.0)	30.0 (30.0–31.0)	<0.001
Me – median; Q1–Q3 – interquartile range; p – Mann–Whitney test.					

Oxygenation. Oxygen tension (pO_2) declined significantly from intraoperative hyperoxia (232 mmHg) to physiological levels during recovery (p<0.001), paralleling FiO_2 reduction and restoration of spontaneous respiration. Hemoglobin oxygen saturation (SO_2) decreased modestly but remained within normal limits (p<0.001). The PaO_2/FiO_2 ratio declined significantly across the perioperative course (p<0.001). The alveolar–arterial (A–a) gradient trended toward higher values (p=0.08), whereas the arterial-to-alveolar ratio (a/A) and total oxygen content (ctO_2) decreased significantly (both p<0.001). Hemoglobin and hematocrit declined slightly but without significance (p=0.71 and p=0.28). Lactate rose mildly at the end of surgery and on ICU admission (1.25–1.30 mmol/L), with subsequent normalization (p=0.004).

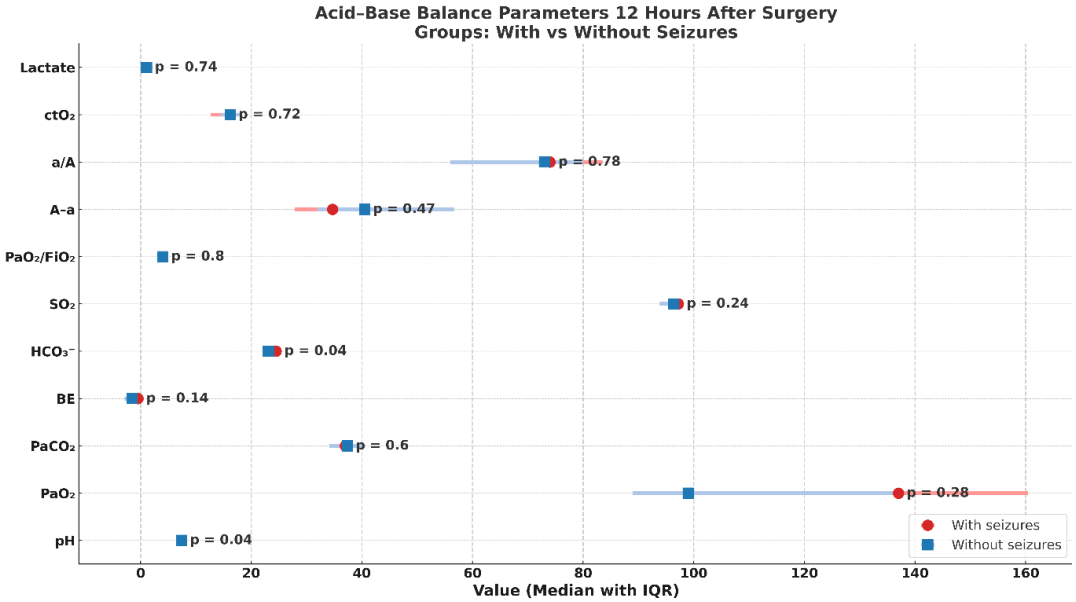
Stratified oxygenation analysis (Table 4).

Oxygenation parameters	Disease duration			Type of antiepileptic therapy		
	≤15 years (n=45)	>15 years (n=48)	p	Monotherapy (n=33)	Polytherapy (n=60)	p
SO_2 (Me, Q1–Q3)	96.8 (94.3–97.8)	96.2 (93.6–98.0)	0.8	96.3 (94.3–97.6)	96.8 (93.0-93.8)	0.7
A–a gradient (Me, Q1–Q3)	37.8 (30.1–50.4)	42.0 (32.4–58.4)	0.9	37.6 (28.4–53.5)	42.0 (32.0–56.8)	0.4
a/A ratio (Me, Q1–Q3)	74.0 (56.0–84.8)	71.0 (54.5–78.0)	0.3	73.0 (54.0–82.0)	74.0 (56.0–80.0)	0.4
ctO_2 (Me, Q1–Q3)	16.3 (14.1–18.3)	16.2 (14.6–17.8)	0.5	16.2 (14.6–18.2)	16.1 (14.4–17.7)	0.7
PaO_2/FiO_2 (Me, Q1–Q3)	4.01 (3.71–4.35)	3.85 (3.68–4.39)	0.9	4.07 (3.66–4.48)	3.85 (3.69–4.30)	0.6
Lactate (Me, Q1–Q3)	1.01 (0.83–1.26)	1.10 (0.90–1.60)	0.8	1.04 (0.89–1.60)	1.07 (0.87–1.59)	0.4
Mechanical ventilation duration, minute (Me, Q1–Q3)	70.0 (46.3–135.0)	100.0 (60.0–127.5)	0.7	90.0 (50.0–142.0)	77.5 (51.3–125.0)	0.3
Me – median; Q1–Q3 – interquartile range; p – Mann–Whitney test.						

By disease duration: SO_2 values were equivalent between ≤15 years and >15 years cohorts (p=0.8). The A–a gradient was higher in patients with epilepsy >15 years, but not significant (p=0.9). The reduced a/A ratio in chronic cases suggested modest impairment of gas exchange, though not clinically or statistically relevant. ctO_2 and lactate values were similar. Prolonged postoperative ventilation was more frequent in the >15 years cohort, without significance (p=0.7).

By treatment regimen: SO_2 values were comparable (p=0.7). The A–a gradient was slightly higher in polytherapy patients, without significance (p=0.4). The a/A ratio and ctO_2 did not differ. Lactate was similar between groups (p=0.4). Ventilation duration was longer in monotherapy patients (90 vs. 77.5 h), though not significant (p=0.3).

Seizure outcomes. Postoperative seizures occurred in 9 patients (9.7%) within 2–48 hours after surgery. Comparative analysis (Figure 1) demonstrated higher pH values in seizure patients (p=0.04), trending toward alkalosis. Bicarbonate concentrations were also higher (24.5 vs. 23.1 mmol/L, p=0.04). Base excess did not differ significantly (p=0.14). pO_2 and SO_2 were higher in seizure patients but without significance (p=0.28 and p=0.24). Neither the A–a gradient nor the a/A ratio differed (p=0.47 and p=0.78). Arterial oxygen content was identical in both groups (16.2, p=0.72). pCO_2 and lactate were essentially unchanged (p=0.60 and p=0.74).



Discussion

Pharmacotherapy patterns. This investigation evaluated the perioperative trajectory of acid–base equilibrium, oxygenation indices, and related clinical parameters, with particular emphasis on epilepsy chronicity and antiepileptic drug (AED) regimens. The findings are broadly consistent with existing literature [11,17], confirming carbamazepine and levetiracetam as the most frequently prescribed AEDs. Carbamazepine maintained its position as the predominant monotherapeutic agent, whereas levetiracetam and lamotrigine were preferentially administered within polytherapy regimens rather than as monotherapy. The use of polytherapy increased with disease duration, reflecting the necessity for comprehensive pharmacological strategies to manage pharmacoresistant epilepsy. The observed age differential is explained by the overrepresentation of older patients in the group with epilepsy exceeding 15 years in duration.

Fluid management implications. One of the most clinically relevant findings concerns fluid management. Patients on polytherapy exhibited greater positive fluid balance and higher intraoperative infusion volumes, despite comparable blood loss, urine output, and vasopressor use. Several explanations may account for this observation. First, polytherapy patients may have undergone technically complex or prolonged procedures, even though mean anesthesia duration was similar across groups. Second, confounders such as body composition, latent hypovolemia, or increased electrolyte requirements may have influenced perioperative fluid strategy. Third, cumulative metabolic disturbances associated with AEDs may alter water–electrolyte homeostasis and renal regulatory mechanisms, as previously suggested [18,19,25,28]. These findings highlight the need for cautious fluid administration, particularly in patients on polytherapy, where excessive positive balance may increase the risk of edema and pulmonary complications [20].

Respiratory and gas exchange dynamics. Intraoperative and postoperative courses demonstrated the expected transition from controlled surgical ventilation to spontaneous breathing under intensive care conditions. Stepwise FiO_2 reduction was associated with decreases in PaO_2 and SO_2, while pH remained within physiological limits, $PaCO_2$ trended toward normocapnia, and BE and HCO_3^- shifted toward compensated values, reflecting restoration of buffering capacity. Prior studies report that topiramate may contribute to perioperative metabolic acidosis [21], and *Türe H. et al.* recommend close acid–base monitoring in patients on long-term AED therapy [18].

The decline in PaO_2/FiO_2 ratio was primarily attributable to FiO_2 reduction and transition to spontaneous ventilation. Although values decreased significantly, median levels remained above 300 mmHg, excluding acute respiratory failure. No major intergroup differences were observed, suggesting preserved alveolar–capillary gas exchange. The alveolar–arterial gradient remained stable, while reductions in a/A ratio and ctO_2 at 12 hours reflected moderate impairment of oxygen transfer efficiency during oxygen weaning, likely due to decreased PaO_2 and hemoglobin concentration. Nevertheless, these changes did not compromise global oxygen delivery. Consistent with Kennedy J. and Seyal M., approximately one-third of epilepsy patients demonstrate respiratory disturbances and ventilation–perfusion mismatch [15,22]. Lactate normalization over time may indicate transient stress-induced hypermetabolism with subsequent recovery.

Impact of disease duration. Patients with epilepsy duration >15 years required longer postoperative mechanical ventilation. This finding is consistent with anticipated outcomes: age-related decline, cumulative sedative–hypnotic exposure, reduced pharyngeal muscle tone, occult sleep-disordered breathing, and altered central respiratory control may collectively hinder extubation and spontaneous breathing. Kanth K. et al. reported delayed recovery of respiratory function in patients with long-standing epilepsy [5]. However, the absence of differences in RASS scores (~−1), hemodynamic stability, and primary oxygenation parameters suggests that extended ventilation requirements were related to functional limitations (arousal, airway protection, reflex integrity) rather than overt respiratory failure. Previous investigations have

documented the potential for AEDs to impair brainstem respiratory centers [23], though no severe complications were observed in this cohort.

Although the >15-year group exhibited trends toward increased alveolar–arterial gradients, lower a/A ratios, and longer ventilatory support, no significant differences in core oxygenation or acid–base variables were demonstrated. Kouchi H. et al. described variable respiratory dysfunction in patients with pharmacoresistant epilepsy [3], supporting the plausibility of these findings as cumulative sequelae of chronic disease and comorbidities. Conversely, Kanth K. et al. reported no clear association between epilepsy duration and respiratory dysfunction severity [5]. Dereli A. et al. highlighted hypoventilation and respiratory instability as major determinants of postoperative complications [24]. Clinically, these results underscore the importance of enhanced respiratory monitoring in patients with prolonged disease, even though chronicity itself did not determine early postoperative gas exchange outcomes. Hampel et al. noted that hemodynamic and respiratory dysregulation during focal seizures is not directly correlated with oxygenation [25], while Blum A. et al. suggested that oxygenation status may serve as an adjunctive predictor of complications [26].

Seizures and acid–base balance. Postoperative seizures occurred in 9.7% of patients, consistent with prior reports documenting early seizures in >5% of cases [27]. Patients who experienced seizures exhibited modest but statistically significant increases in pH and HCO_3^- at 12 hours. This pattern likely reflects postictal hyperventilation combined with perioperative alkalosis induced by fluid administration and electrolyte correction. These findings are in line with Forsyth R., who postulated that seizures initiate under alkalotic conditions and terminate in acidic environments [28]. While other studies emphasize hypoxia and respiratory acidosis as seizure precipitants [29,30], neither hypoxemia nor acidosis was identified in our cohort. The lack of intergroup variation in PaO_2, $PaCO_2$, SO_2, A–a gradient, and lactate suggests that seizures primarily influenced acid–base balance without significant impact on tissue perfusion or ventilation.

Clinical implications. Taken together, the findings indicate no major association between disease chronicity or pharmacotherapy complexity and perioperative acid–base or oxygenation disturbances. Trends toward longer ventilation and positive fluid balance in certain subgroups highlight areas of potential vulnerability. Clinically, the immediate postoperative trajectory in patients with pharmacoresistant epilepsy appears more strongly determined by intraoperative management and intensive care interventions than by antecedent disease duration or AED regimen.

Study Limitations. Our investigation presents several limitations. First, the single-center retrospective design limits the generalizability of findings. Second, the relatively modest sample size constrains statistical power and increases the risk of type II error in intergroup comparisons. Third, heterogeneity of surgical interventions and antiepileptic therapy regimens precluded more detailed stratification by specific medications and dosages. Fourth, analysis was restricted to the early postoperative period, without assessment of long-term respiratory outcomes and complications. Finally, the potential influence of comorbid conditions (such as obesity, OSA, COPD) was not evaluated independently, which may constitute a confounding factor.

Conclusion. This study revealed that neither epilepsy chronicity nor antiepileptic pharmacotherapy complexity significantly impacts perioperative acid-base homeostasis or oxygenation indices following neurosurgical intervention for pharmacoresistant focal epilepsy. However, extended disease tenure correlated with prolonged ventilatory support duration and subtle oxygenation compromise, whereas polypharmaceutical regimens were characterized by excessive fluid accumulation. These observations emphasize the imperative for personalized perioperative protocols encompassing judicious volume management and vigilant respiratory surveillance. Convulsive episodes predominantly modulate acid-base parameters without inducing oxygen transport deficits or clinically relevant tissue hypoperfusion.

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Literature:

1. *Bindra A., Chouhan R., Prabhakar H. et al.* Perioperative anesthetic implications of epilepsy surgery: a retrospective analysis. J. Anesth 29, 229–234 (2015). https://doi.org/10.1007/s00540-014-1919-2

2. *Larkin C., O'Brien D., Maheshwari D.* Anaesthesia for epilepsy surgery. BJA Educ. 2019 Dec;19(12):383-389. https://doi.org/10.1016/j.bjae.2019.08.001.

3. *Kouchi H., Ogier M. et al.* Respiratory dysfunction in two rodent models of chronic epilepsy and acute seizures and its link with the brainstem serotonin system. Sci Rep 12, 10248 (2022). https://doi.org/10.1038/s41598-022-14153-6

4. *Allen L., Vos S., Kumar R., Ogren J., Harper R., Winston G., et al.* Cerebellar, limbic, and midbrain volume alterations in sudden unexpected death in epilepsy. Epilepsia. (2019) 60:718–29. https://doi.org/10.1111/epi.14689/

5. *Kanth K., Park K., Seyal M.* Severity of Peri-ictal Respiratory Dysfunction With Epilepsy Duration and Patient Age at Epilepsy Onset. Front. Neurol. 11:618841. https://doi.org/10.3389/fneur.2020.618841

6. *McGuire M., Zhang Y., White D., Ling L.* Phrenic long-term facilitation requires NMDA receptors in the phrenic motonucleus in rats. J Physiol. (2005) 567(Pt. 2):599–611. https://doi.org/10.1113/jphysiol.2005.087650

7. *Frida A. et al.* Seizures Cause Prolonged Impairment of Ventilation, CO2 Chemoreception and Thermoregulation. Journal of Neuroscience 5 July 2023, 43 (27) 4959-4971; https://doi.org/10.1523/JNEUROSCI.0450-23.2023

8. *Söylemez E., Öztürk O., Alpaydın S., Ezgi Z., Ataklı D.* Metabolic syndrome and obstructive sleep apnea syndrome among patients with epilepsy on monotherapy.

Epilepsy & Behavior. Volume 111,2020, 107296. https://doi.org/10.1016/j.yebeh.2020.107296.

9. *Eleanor L Carter, Ram M Adapa.* Adult epilepsy and anesthesia. BJA Education, Volume 15, Issue 3, June 2015, Pages 111–117, https://doi.org/10.1093/bjaceaccp/mku014.

10. *Isojärvi J., et al.* Obesity and endocrine disorders in women taking valproate for epilepsy. Ann Neurol. 1996 May;39(5):579-84. https://doi.org/10.1002/ana.410390506.

11. *Kulkarni R., Pandurangi S., Tiwari P.* Carbamazepine-induced Hyperammonemia and Asterixis in Young Adults: Case Series. Indian Journal of Psychological Medicine. 2023;0(0). https://doi.org/10.1177/02537176231205834.

12. *Mirza N., Marson A., Pirmohamed M.* Effect of topiramate on acid-base balance: extent, mechanism and effects. Br J Clin Pharmacol. 2009 Nov;68(5):655-61. https://doi.org/10.1111/j.1365-2125.2009.03521.x.

13. *Perks A. Cheema R Mohanraj.* Anaesthesia and epilepsy. British Journal of Anaesthesia, Volume 108, Issue 4, April 2012, Pages 562–571, https://doi.org/10.1093/bja/aes027

14. *Lisa M. et al.* Ictal hypoxemia in localization-related epilepsy: analysis of incidence, severity and risk factors. Brain, Volume 131, Issue 12, December 2008, Pages 3239–3245, https://doi.org/10.1093/brain/awn277

15. *Kennedy J, Seyal M.* Respiratory pathophysiology with seizures and implications for sudden unexpected death in epilepsy. J Clin Neurophysiol. 2015 Feb;32(1):10-3. https://doi.org/10.1097/WNP.0000000000000142.

16. *Curtis N. Sessler, Mark S. Gosnell, et al.* The Richmond Agitation–Sedation Scale. American Journal of Respiratory and Critical Care Medicine, Vol. 166, No. 10 (2002), pp. 1338-1344. https://doi.org/10.1164/rccm.2107138

17. *Kanner A., Ashman E., et al:* Practice guideline update: Efficacy and tolerability of the new antiepileptic drugs I: Treatment of new-onset epilepsy. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 91 (2):74–81, 2018. https://doi.org/10.1212/WNL.0000000000005755.

18. *Türe H., Keskin Ö., Çakır Ü., Aykut Bingöl C., Türe U.* The frequency and severity of metabolic acidosis related to topiramate. J Int Med Res. 2016 Dec;44(6):1376-1380. https://doi.org/10.1177/0300060516669897.

19. *Badry R.* Changes in Vital Signs During Epileptic and Psychogenic Nonepileptic Attacks: A Video-EEG Study. J Clin Neurophysiol. 2020 Jan;37(1):74-78. https://doi.org/10.1097/WNP.0000000000000614.

20. *Kutum C., Lakhe P., Ghimire N., Bc AK., Begum U., Singh K.* Intraoperative goal-directed fluid therapy in neurosurgical patients: A systematic review. Surg Neurol Int 2024;15:233. https://doi.org/10.25259/SNI_412_2024

21. *Şahin S., Küçük O., Tütüncüler B.* The relationship between anti-seizures medications and metabolic acidosis in craniotomy operations: is topiramate or zonisamide the cause of metabolic acidosis? // BMC Anesthesiol 24, 296 (2024). https://doi.org/10.1186/s12871-024-02677-5

22. *Seyal M. et al.* Postictal generalized EEG suppression is linked to seizure-associated respiratory dysfunction but not postictal apnea. Epilepsia. 2012 May;53(5):825-31. https://doi.org/10.1111/j.1528-1167.2012.03443.x.

23. *Layer N., Brandes J., et al.* The effect of lamotrigine and other antiepileptic drugs on respiratory rhythm generation in the pre-Bötzinger complex. Epilepsia. 2021; 62: 2790–2803. https://doi.org/10.1111/epi.17066

24. *Dereli A., Apaire A., El Tahry R.* Sudden Unexpected Death in Epilepsy: Central Respiratory Chemoreception. Int J Mol Sci. 2025 Feb 13;26(4):1598. https://doi.org/10.3390/ijms26041598.

25. *Hampel K., Jahanbekam A., Elger C., Surges R.* Seizure-related modulation of systemic arterial blood pressure in focal epilepsy. Epilepsia. 2016 Oct;57(10):1709-1718. https://doi.org/10.1111/epi.13504.

26. *Blum A., Ives J., et al.* Oxygen desaturations triggered by partial seizures: implications for cardiopulmonary instability in epilepsy. Epilepsia. 2000 May;41(5):536-41. https://doi.org/10.1111/j.1528-1157.2000.tb00206.x.

27. *Ersoy T., Ridwan S., Grote A., Coras R., Simon M.* Early postoperative seizures (EPS) in patients undergoing brain tumour surgery // Sci Rep. 2020 Aug 13;10(1):13674. https://doi.org/10.1038/s41598-020-70754-z.

28. *Forsyth R., Allen M., et al.* Seizure control via pH manipulation: a phase II double-blind randomised controlled trial of inhaled carbogen as adjunctive treatment of paediatric convulsive status epilepticus (Carbogen for Status Epilepticus in Children Trial (Crescent)). Trials. 2024 May 29;25(1):349. https://doi.org/10.1186/s13063-024-08188-5.

29. *Aydin S., Özdemir C., Gündüz A., Kiziltan M.* Seizures in patients with respiratory disease - a retrospective single center study. Arq Neuropsiquiatr. 2020 May;78(5):247-254. https://doi.org/10.1590/0004-282x20190196.

30. Kuang X., Chen S., Ye Q. The lactate metabolism and protein lactylation in epilepsy. Front Cell Neurosci. 2025 Jan 14;18:1464169. https://doi.org/10.3389/fncel.2024.1464169

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