Osmangazi Tıp Dergisi
Osmangazi Journal of Medicine 2021; 157-163

Research Article / Araştırma Makalesi

Risk of Methemoglobinemia in Scalp Block and İnfiltration Anesthesia in Patients Undergoing Deep Brain Stimulation

Derin Beyin Stimulatörü Uygulanan Hastalarda Skalp Bloğu ve İnfiltrasyon Anestezisinde Methemoglobinemi Riski

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Abstract

The application of local anesthetics in areas with a high blood supply, such as scalp block, is more susceptible to systemic effects of local anesthetics such as methemoglobinemia because of the high absorption rate and the risk of intravascular injection. In this study, we aimed to evaluate the risk of methemoglobinemia by reviewing methemoglobin values after scalp block in patients with a deep brain stimulation (DBS) due to neurological diseases, especially Parkinson's.The study included 41 patients aged >18 years who were admitted between January 2017 and December 2018 for DBS and underwent regional anesthesia (n = 41). Patients were administered scalp block (n = 10) and infiltration anesthesia (n = 31). Using data from the patients' medical records, we statistically analyzed the patients' age, American Society of Anesthesiologists (ASA) status, gender, DBS indication, scalp block/infiltration anesthesia, highest methemoglobin level in arterial blood gas, pH, pO2, SpO2, and clinical symptoms.The indications for DBS were Parkinson's disease in 29 patients hyperreactivity, dystonia and tremor in the remaining patients. Furthermore, 33 patients were classified as ASA class II. The methemoglobinemia level was >2% in two patients who underwent scalp block and six patients who underwent infiltration anesthesia. However, there was no statistically significant difference in methemoglobin levels between scalp and infiltration anesthesia.In areas with high blood flow, such as the scalp, caution should be exercised in administering local anesthesia because of the patient's risk of developing methemoglobinemia, although there are no clinical findings on this topic.

Keywords: deep brain stimulator, methemoglobinemia, scalp block, infiltration anesthesia

Özet

Skalp bloğu gibi kanlanması yüksek olan bölgelerde lokal anesteziklerin uygulanması, emilim hızının ve intravasküler enjeksiyon riskinin yüksekliği nedeniyle methemoglobinemi gibi lokal anesteziklerin sistemik etkilerine karşı daha hassastır. Çalışmamızda, özellikle Parkinson olmak üzere nörolojik hastalıklara bağlı derin beyin stimülatörü (DBS) yerleştirilen hastalarda skalp bloğu sonrası methemoglobin değerlerini retrospektif inceleyerek methemoglobinemi riskini değerlendirmeyi amaçladık.Çalışmaya DBS için Ocak 2017 ve Aralık 2018 tarihleri arasında başvuran, 18 yaş üstü ve rejyonel anestezi uygulanan 41 hasta dahil edildi. Hastalara skalp bloğu (n: 10) ve infiltrasyon anestezisi (n: 31) uygulandı. Hastaların yaş, Amerikan Anesteziyologlar Derneği fiziksel sınıflaması (ASA), cinsiyet, DBS endikasyonu, skalp bloğu / infiltrasyon anestezisi, arteriyel kan gazında pH, pO2, Spo2, en yüksek methemoglobin düzeyleri ve klinik semptomlar istatistiksel olarak analiz edildi.DBS endikasyonları 29 hastada Parkinson hastalığı, diğerleri hiper-reaktivite, distoni ve titremeydi. Ayrıca 33 hasta ASA Sınıf II olarak sınıflandırıldı. Skalp bloğu yapılan 2 hastada ve infiltrasyon anestezisi uygulanan 6 hastada MeHb düzeyi% 2'nin üzerindeydi. Ancak skalp bloğu ve infiltrasyon anestezisi arasında methemoglobin düzeylerinde istatiksel olarak anlamlı bir fark gözlenmedi.Skalp gibi kanlanmanın yüksek olduğu bölgelerde klinik bulgu olmadan, lokal anestezi uygulamalarında methemoglobinemia gelişme riski nedeniyle dikkatli olunmalıdır.

Anahtar Kelimeler: Derin beyin stimulatörü, methemoglobinemi, skalp block, infiltrasyon anestezisi

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Received 04.08.2020 ***Accepted*** 05.10.2020 ***Online published*** 06.10.2020

Cite this article as:
Onay M, Harbelioglu MA, Vural M, Ekemen S, Risk of Methemoglobinemia in Scalp Block and İnfiltration Anesthesia in Patients Undergoing Deep Brain Stimulation, Osmangazi Journal of Medicine, 2021; Doi: 10.20515/otd.776960

1. Introduction

In Turkey, deep brain stimulation (DBS) is used in the treatment of neurological diseases such as essential tremor, dystonia, and Parkinson's disease (1,2). Parkinson's disease is a chronic, progressive, neurodegenerative disease characterized by postural instability, rigidity, bradykinesia, resting tremor, anxiety, depression, and cognitive and autonomic dysfunction. Initial treatment is medical, and DBS can be planned when medical treatment is insufficient (3). The prominent features of DBS are that it is effective, nondestructive, easy to adapt, and reversible (4).

Anesthesia management is important for intraoperative neurophysiological target validation, clinical evaluation, and patient comfort (5). Appropriate anesthesia conditions can be provided using scalp block or infiltration anesthesia accompanied by conscious sedation, and general anesthesia can be used in patients with anxiety and intolerance or in pediatric patients (1,5).

Methemoglobinemia (MetHb) occurs when the Fe^{++} in the hemoglobin is oxidized to Fe^{+++}. During this process, the Fe^{++} affinity to oxygen increases and leads to tissue hypoxemia (6). This leads to a leftward shift in the oxyhemoglobin dissociation curve (7). MetHb is a rare condition that may be acquired or congenital (8). Dapsone, sulfonamides, benzocaine, primaquine, and some local anesthetics have been reported as causes of acquired MetHb. (9,10). In clinical practice, it occurs mostly as a result of the use of local anesthetics (6). Patients with MetHb levels >10% may present with symptoms of cyanosis, and individuals with levels >30% may present with respiratory distress, nausea vomiting, lethargy and coma (11,12).

In our clinic, we perform DBS under scalp block or infiltration anesthesia. Because we recently encountered a case with a MetHb level of 5.9%, we conducted a retrospective study to examine the relationship between regional techniques and MetHb in a region with high blood supply, such as the scalp. The aim of this study is to evaluate complications, particularly possible MetHb risk, in patients receiving scalp and infiltration anesthesia.

2. Materials and Methods

Ethical approval was obtained from Eskişehir Osmangazi University Ethics Committee (decision No. 2019-125). We retrospectively reviewed the records of 41 patients aged >18 years who were admitted to the Medical Faculty Hospital between January 2017 and December 2018 and underwent scalp block (n = 10) and infiltration anesthesia (n = 31). Age, American Society of Anesthesiologists (ASA) physical status classification, gender, DBS indication, scalp block/infiltration anesthesia, highest methemoglobin levels in arterial blood gas, pH, pO_2, SpO_2, and clinical symptoms (cyanosis, respiratory distress, nausea vomiting, lethargy, and coma) were recorded. Noninvasive monitoring (electrocardiogram, blood pressure, and peripheral oxygen saturation) and invasive radial arterial monitoring were performed routinely after patients who did not receive premedication were brought to the operating table. Using an infusion dose of 0.2–0.7 $\mu g\ kg^{-1}\ h^{-1}$ of low-dose dexmedetomidine, sedation was achieved so that patients could easily be awakened and cooperate. When necessary, nitroglycerin infusion was initiated as an antihypertensive treatment. DBS surgery has been performed in our clinic since 2012, but because of the lack of access to previous records, only patients treated in the past two years were included in the current study.

Scalp block

Scalp block was performed in sterile conditions. Local anesthesia was applied to the supraorbital, supratrochlear, auriculotemporal, zygomaticotemporal, and major and minor occipital nerves using a 22-gauge needle. Local anesthesia doses were calculated based on 2 mg kg^{-1} 0.5% bupivacaine and were administered in a total volume of 40 mL after completing with saline. Anesthesia was administered in equal doses to the specified areas.

Infiltration anesthesia

Infiltration anesthesia was performed in sterile conditions. Using a 23-gauge needle, local anesthesia was administered to the head holder entry points (two occipital and two frontal), and the head frame was placed. After the coordinates were determined and the lead placement was ready to be initiated, local anesthesia infiltration was applied to the incision area. Bupivacaine 0.5% 20 mL was used at the head holder entry points (two occipital and two frontal), and 10–12 mL 2% prilocaine was administered at the incision site.

Anesthesia was performed by a specialist (anesthesiologist or neurosurgeon), and in both blocks, local anesthesia was applied to the scalp using the infiltration technique. All surgical procedures were performed by an experienced team. After sufficient anesthesia was provided under operating room conditions, a stereotaxic frame was placed for microelectrode recording, and the target coordinates were marked using magnetic resonance and computed tomography fusion. The Brain LAB software planning system (St. Jude Medical Infinity DBS System, Abbott, USA) was used for direct targeting. Brain penetration was performed only when systolic blood pressure was ≤130 mm Hg. Clinical and neurophysiological evaluations were performed by an experienced neurologist during MER, and the permanent leads were subsequently placed by a neurosurgeon under regional anesthesia. A permanent pulse generator was placed on the pectoral muscle of all patients by switching to general anesthesia in the same session. Because of the risk of aspiration under standard general anesthesia, airway safety was ensured by tracheal intubation. For anesthesia induction, we used 4–7 mg kg^{-1} thiopental, 0.6 mg kg^{-1} rocuronium, and 0.1–0.3 µg kg^{-1} remifentanil; for anesthesia maintenance, 2%–3% sevoflurane, 0.1–0.3 µg/kg remifentanil infusion, 40% oxygen, and 60% air were used. However, pulse generators were activated after an average of three weeks postoperatively. For postoperative analgesia, 1 g paracetamol and 1 mg/kg tramadol were administered.

Statistical analysis

Continuous data are presented as mean ± standard deviation. Categorical data are presented as percentage (%). We used Shapiro–Wilk's test to evaluate whether the data were normally distributed. Independent-samples *t* test was used to compare two groups with normal distribution. Pearson's exact chi-square analysis was used to analyze the crosstabs. The data were analyzed statistically using IBM SPSS Statistics 17.0 (IBM Corp., released 2012, IBM SPSS Statistics for Windows, version 17.0, Armonk, NY). A P value of <0.05 was considered statistically significant.

3. Results

A total of 42 patients underwent DBS surgery in our clinic between January 2017 and December 2018. One patient was excluded because he was younger than 18 years. A total of 41 patients (10 receiving scalp block and 31 receiving infiltration anesthesia) were included.

Table 1 presents the demographic data of the patients. Overall, 80% of the patients were classified as ASA II, and most patients had concomitant hypertension. No significant difference was observed between the groups in terms of age; 70% of the indications for DBS were Parkinson's disease, and the remaining indications were hyperreactivity, dystonia, and tremor (Table 1).

The MetHb level was greater than 2% in two patients who underwent scalp block and six patients who underwent infiltration anesthesia. No significant difference was observed in MetHb, Ph, pO_2, and SpO_2 levels between the blocks. A suspicious gray-blue nail fold was clinically observed in one patient (MetHb: 5.8) who underwent infiltration anesthesia for MetHb symptoms (Table 2).

Table 1. Patient demographic data

	Scalp block	Infiltration anesthesia	*P* value
Gender			
Male	5	17	0.789
Female	5	14	
Age, years	45.20 ± 16.49	53.84 ± 11.78	0.075
ASA			
I	0 (0.00%)	2 (6.45%)	0.641
II	8 (80.00%)	25 (80.60%)	
III	2 (20.00%)	4 (12.90%)	
Diagnosis	3 (30.00%)	4 (12.90%)	0.607
Dystonia	0 (00.00%)	1 (3.23%)	
Hyperreactivity	6 (60.00%)	23 (74.19%)	
Parkinson’s	1 (10.00%)	3 (9.68%)	
Tremor			

ASA, American society of Anesthesiologist physical status classification.
**$P < 0.05$ indicates statistical significance.*

Table 2. MetHb, Ph, pO_2, and SpO_2 levels and symptoms

	Scalp block	Infiltration anesthesia	*P* value
MetHb level	2.11 ± 1.84	1.95 ± 1.56	0.795
Ph	7.41 (SD: 0.03)	7.42 (SD: 0.05)	0.494
pO_2	138.60 (SD: 47.35)	151.74 (42.83)	0.415
SpO_2	96.90 (SD: 2.81)	96.55 (SD: 2.00)	0.664
Symptoms	0 (00.00%)	1 (3.23%)	0.565
Yes	10 (100.00%)	30 (96.77%)	
No			

*$P < 0.05$ indicates statistical significance.

4. Discussion

DBS is a minimally invasive surgical method that has become popular as a treatment for movement disorders, particularly Parkinson’s disease (3,12). It is a two-stage procedure: a head frame is placed in the first stage for localization, followed by placement of electrodes in the deep and small target nuclei in the brain. The placement of the frame and the pins on the scalp causes an intense nociceptive stimulant, resulting in an increase in heart rate and blood pressure. These reactions may lead to brain edema, increased intracranial pressure, and intracranial hemorrhage (13). Scalp block and infiltration anesthesia are regional anesthesia techniques that enable neurologic examination with sufficient analgesia and fewer systemic side effects in neurosurgery patients (12). Most DBS patients have comorbidities. Attention should be paid to situations of overdose in terms of difficult airway due to sedation and frame fixed with spiked head. Most DBS patients have Parkinson’s disease. In patients with long-term Parkinson’s disease, autonomic dysfunction, impaired lung reserve, decreased cough reflex, and sleep apnea increase the risk of aspiration. Dystonia patients are hypovolemic because of malnutrition, which may result in hemodynamic instability. It is difficult to position these patients because of accompanying skeletal deformities. In addition, developmental delay, dementia, behavioral disorders, and communication problems may prevent the evaluation of symptoms in patients with DBS (14).

Postoperative pain is common in neurosurgery patients, and hemodynamic stability should be achieved by suppressing surgical stress with optimal pain treatment (15,16). Because a single analgesic method cannot provide adequate pain relief, we use multimodal analgesia to avoid the undesired effects of opiates (16). In addition, opiates may provide excellent analgesia but can cause respiratory depression, hypercarbia, and consequently an increase in intracranial pressure, thus hindering neurological examination (12). Therefore, in these patients, regional anesthesia techniques might be the right choice. In areas with high blood supply, such as the scalp, the blockade time is prolonged by the addition of epinephrine to long-acting local anesthetics, and a minimal increase is observed in the plasma concentration of local anesthetics (5,15,17).

In patients undergoing elective craniotomy under general anesthesia, Vallapu et al performed infiltration anesthesia with bupivacaine (group I), infiltration anesthesia with bupivacaine plus dexmedetomidine (group II), and scalp block with bupivacaine plus dexmedetomidine (group III) for postoperative analgesia management. The researchers found that the pain-free period was longer in group III, and pain control was better in the dexmedetomidine treated groups. They concluded that the pain-free period was prolonged with dexmedetomidine (1 µg/kg) added to bupivacaine and that scalp block was a superior technique to infiltration anesthesia (12).

Awake DBS is stressful for patients. In cases in which the patient's comfort is affected because of a prolonged operation and sufficient analgesia cannot be achieved, the patient's heart rate and blood pressure increase. Complications such as intracerebral hematoma, hypertension, dyskinesia, seizures, and ischemic stroke may occur during this procedure. The risk of intracerebral hemorrhage is further increased in patients with preexisting hypertension and may cause permanent neurological sequelae and is vital. Although this was a retrospective study, adequate hemodynamic records could not be obtained; however, no neurological complications were observed.

Short-acting agents that affect neurocognitive functions to a lesser extent, such as propofol, remifentanil, and dexmedetomidine, are frequently used for sedation (3, 5). The administration of all agents is stopped 15–30 minutes before microelectrode recording (5). Dexmedetomidine is an alpha-2 agonist that has a sedative, analgesic, and anxiolytic effect without causing respiratory depression. It suppresses the reactions to surgical incision and reduces the need for antihypertensive treatment (14). Dexmedetomidine has become popular in DBS applications and is successfully used as an adjuvant in regional anesthesia (5, 12). In their retrospective study, Rozet et al reported that in DBS implantation cases, dexmedetomidine provides hemodynamic stability, patient comfort, and surgeon satisfaction and also does not affect electrophysiological monitoring (18). In our practice, we prefer dexmedetomidine, which is a sedative, analgesic, and anxiolytic agent that has also been shown to have adjuvant properties in regional anesthesia.

In their study, Bala et al showed that postoperative complications increased in patients aged >60 years as well as in ASA II patients. Patient tolerance to long-term and stressful tasks decreases with age, whereas their morbidity increases (13). In the present study, 80% of patients were classified as ASA II, and the mean age was <60 years in both groups; perioperative complications were rare.

Combinations of local anesthetics are commonly used in peripheral nerve blocks to enable rapid onset and long-term analgesia. Several studies have recommended the use of scalp block with long-acting local anesthetics for awake craniotomies. However, little is known about the pharmacokinetic and pharmacodynamic effects of different mixtures of local anesthetics, their effect on scalp block, and their safety. The reduction in blood concentrations of long-acting local anesthetics such as bupivacaine may potentially contribute to the prevention of cardiotoxicity and neurotoxicity (19). In the present study, 0.5% bupivacaine was preferred for use in scalp blocks, and 2% prilocaine and 0.5% bupivacaine were preferred for different sites at different times in infiltration anesthesia. Combined local anesthetics, especially in blocks applied to regions with a high blood supply, such as the scalp, should be used in therapeutic doses. MetHb is likely to occur in patients receiving prilocaine; therefore, clinicians must remain aware of this issue.

In healthy individuals, the NADH cytochrome b5 reductase enzyme maintains the MetHb level at <2%. However, some studies have shown that the nitroglycerin MetHb level >2% used during general anesthesia in antihypertensive treatment is as the only cause (10). In our study, the MetHb level was >2% in two patients (20%) who underwent scalp block and in six patients (19.3%) who underwent infiltration anesthesia. The MetHb levels were not different between groups (scalp block mean MetHb: 2.11 ± 1.84, infiltration anesthesia mean MetHb: 1.95 ±1.56). However, in two of our patients in the scalp block group, high MetHb values (5.2% and 5.9%) were attributed to the injection of prilocaine into the incision site due to insufficient block.

The risk of MetHb increases when therapeutic doses are increased or combinations of local anesthetics are used. Then the MetHb level reaches <20%, clinical improvement is observed after cessation of the drug (2,6). In patients with high concentrations of MetHb (>20%), treatment with methylene blue and ascorbic acid is recommended (11). MetHb levels of >70% are fatal (15).

In case report by Sarsu et al of a one-year-old boy with 20% second-degree burns, the patient's MetHb level after the use of prilocaine cream was 10.9%. The peripheral oxygen saturation was 60%, and the patient had cyanosis in the lip, hands and feet, and nail folds. However, because of the patient's poor general condition, he was intubated and followed up in intensive care conditions. In addition to burn treatment, a single dose of 1 mg kg^{-1} methylene blue and 100 mg ascorbic acid treatment was used (11). In the present study, a 59-year-old patient who underwent infiltration anesthesia developed clinical symptoms of MetHb, including gray-blue nail fold. In this patient, 20 mL of 0.5% bupivacaine and 30 mL of 2% prilocaine were applied to the stereotaxic frame entry points. The use of combined local anesthetics exceeding theropathic doses triggered MetHb. Peripheral oxygen saturation of the patient decreased from 94% to 89% while receiving 2 L/ min^{-1} oxygen by mask. No known respiratory disease was reported. The MetHb level measured was 5.9%; 100% oxygen therapy was administered, and the patient was closely followed. The patient's MetHb level regressed after 24 hours postoperatively, and clinical improvement was achieved.

In the case report presented by Yamaji et al, in which a 67-year-old male patient experienced decreased saturation during gastrointestinal endoscopy, PaO_2 and SaO_2 levels in the studied blood gas were normal, and the MetHb level was 26.2%. During the procedure, 8% lidocaine spray was used as a local anesthetic. The MetHb level reduced to 1.6% after treatment with 1 mg/kg methylene, and dyspnea and cyanosis improved. However, the MetHb level gradually increased to 18% over 15 days. Congenital type 1 hemoglobinemia was considered, and treatment with 60 mg riboflavin and 600 mg/day ascorbic acid was initiated. DNA gene analysis identified a new variant CYB5R3 gene. The patient's MetHb level dropped dramatically to 5.6%, and the patient was discharged without complications (20). Although clinically acquired MetHb is commonly observed, congenital MetHb should be considered in cases of elevated MetHb despite methylene treatment. Each patient can present different methb levels with different clinical signs. The treatment of MetHb is usually presented in only case reports. Therefore, treatment arrangements should be planned according to the patient's clinic and methb level.

The study has some limitations. The data were from a single center and collected retrospectively, and the distribution between groups was uneven. MetHb is not only associated with local anesthetics but can also be affected by drugs such as antibiotics and nitroglycerin. The reported literature on MetHb consists of only case reports; therefore, multicenter and prospective studies are needed.

5. Conclusion

As a result, it was seen that the two techniques were not different in terms of metHb risk in this study. Although the increase in the current methb level does not show clinical signs, we think that this increase risk should be aware of.

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