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Local Anesthetic-Related Methemoglobinemia During Cardiac Device Implantation; A Retrospective Registry: The LAMDA Study

Kardiyak Cihaz İmplantasyonu Sırasında Lokal Anesteziye Bağlı Methemoglobinemi; Retrospektif Bir Kayıt: LAMDA Çalışması

ABSTRACT

Objective: This study aimed to determine the frequency of methemoglobin development and identify associated factors in patients undergoing Implantable Cardioverter-Defibrillator (ICD) and Cardiac Resynchronization Therapy (CRT) procedures, with the local anesthetic prilocaine.

Method: The data from 64 patients was analyzed. The patients' methemoglobin levels before and after the procedure were measured and compared. The relationships between the results and factors such as creatinine, hemoglobin, body mass index (BMI) and the amount of prilocaine used were examined. Exclusion criteria included being aged under 18 years, pregnant, breastfeeding, presence of malignancy, undergoing chemotherapy, hemoglobin chain disorders, liver failure and renal failure (glomerular filtration rate (GFR) < 60 ml/min), chronic obstructive pulmonary disease, other hypoxic lung diseases and being a smoker.

Results: Methemoglobin levels were significantly higher in the first hour after the procedure ($P < 0.001$). Oxygen saturation levels were significantly lower during the first hour post-procedure ($P < 0.001$). In the group with elevated methemoglobin levels after the procedure, creatinine levels were significantly higher ($P < 0.001$), while BMI ($P < 0.001$) and hemoglobin levels ($P < 0.001$) were significantly lower. No significant relationship was found with alanine transaminase (ALT) levels ($P = 0.425$).

Conclusion: While significant methemoglobin elevation was observed following ICD/CRT procedures with prilocaine, clinically significant methemoglobinemia cases are rare. A significant relationship was identified between methemoglobin elevation and BMI, hemoglobin and creatinine.

Keywords: Cardiac resynchronization therapy, implantable cardioverter-defibrillator, methemoglobin, methemoglobinemia, prilocaine

ÖZET

Amaç: Bu çalışma, lokal anestezik prilokain ile Implantable Cardioverter-Defibrillator (ICD) ve Cardiac Resynchronization Therapy (CRT) prosedürleri uygulanan hastalarda methemoglobin gelişme sıklığını belirlemeyi ve ilişkili faktörleri tanımlamayı amaçlamıştır.

Yöntem: 64 hastanın verileri analiz edilmiştir. Hastaların işlem öncesi ve sonrası methemoglobin seviyeleri ölçülmüş ve karşılaştırılmıştır. Elde edilen sonuçlarla kreatinin, hemoglobin, BMI ve kullanılan prilokain miktarı gibi faktörler arasındaki ilişkiler incelenmiştir. Çalışmaya dahil edilmeyen kriterler: 18 yaş altı, hamilelik, emzirme, malignite, kemoterapi, hemoglobin zincir hastalıkları, karaciğer yetmezliği ve böbrek yetmezliği (GFR < 60 ml/dak), kronik obstrüktif akciğer hastalığı, diğer hipoksik akciğer hastalıkları ve sigara içen hastalar idi.

Bulgular: İşlem sonrası ilk saatte methemoglobin seviyeleri anlamlı şekilde yüksek bulunmuştur ($P < 0.001$). Oksijen saturasyonu seviyeleri ise işlem sonrası ilk saatte anlamlı şekilde düşük olmuştur ($P < 0.001$). Prosedür sonrası yükselmiş methemoglobin seviyelerine sahip olan grupta, kreatinin seviyeleri anlamlı şekilde yüksek ($P < 0.001$), BMI ($P < 0.001$) ve hemoglobin seviyeleri ise anlamlı şekilde düşük bulunmuştur ($P < 0.001$). ALT seviyeleri ile anlamlı bir ilişki bulunmamıştır ($P = 0.425$).

Sonuç: Prilokain ile gerçekleştirilen ICD/CRT prosedürlerinden sonra önemli methemoglobin yükselmesi gözlemlense de, klinik olarak anlamlı methemoglobinemia vakaları nadirdir. Methemoglobin yükselmesi ile BMI, hemoglobin ve kreatinin arasında anlamlı bir ilişki bulunmuştur.

Anahtar Kelimeler: Kardiyak resenkronizasyon tedavisi, implante edilebilir kardiyoverter-defibrilatör, methemoglobin, methemoglobinemi, prilokain

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

Nazif Yalçın[1]
Fatih Kahraman[2]
Mehmet Ali Astarcıoğlu[2]
Taner Şen[2]

[1]*Department of Internal Medicine, University of Health Sciences, Bursa Sehir Training and Research Hospital, Bursa, Türkiye*
[2]*Department of Cardiology, Kütahya Health Sciences University, Evliya Çelebi Training and Research Hospital, Kütahya, Türkiye*

Corresponding author:
Nazif Yalçın
✉ nazifyalcin16@gmail.com

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Methemoglobinemia, though rare, can be life-threatening if unrecognized.[1] In healthy individuals, the iron in hemoglobin (Hb) remains in the divalent form (Fe^{2+}) to facilitate oxygen binding and delivery. In contrast, methemoglobin (MetHb) contains iron in the trivalent form (Fe^{3+}), which reduces oxygen affinity and impairs binding.[2] Typically, 2–3% of hemoglobin is converted to methemoglobin, but this is kept below 1% through metabolic pathways.[3] Disruption of these pathways leads to elevated MetHb levels. A key clinical sign of methemoglobinemia is blue-gray cyanosis unresponsive to oxygen therapy, although other symptoms, such as cough, dizziness, shortness of breath, dysrhythmias, confusion, circulatory issues and even death, may also occur.[4] Methemoglobinemia can be hereditary or acquired, with the latter being more common. Various drugs and chemicals, including nitrites, nitrates and chlorates, have been implicated in causing this condition.[5]

Local anesthetics are commonly used in cardiovascular procedures such as coronary angiography, transesophageal echocardiography and permanent pacemaker implantation. While methemoglobinemia is rare with local anesthetics, its toxicity can be severe and potentially fatal, necessitating careful monitoring post-procedure. This study aimed to investigate methemoglobinemia and related factors in patients receiving Implantable Cardioverter-Defibrillator (ICD) and Cardiac Resynchronization Therapy (CRT) devices, with local anesthetics.

Methods

Ethical Considerations

The study was approved by the Kütahya Health Sciences University Rectorate Non-Interventional Clinical Research Ethics Committee (Approval Number: 2021/40, Date: 05.03.2021) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Study Design

This retrospective study aimed to investigate methemoglobinemia occurring in the postoperative period due to local anesthetic administration, during ICD and CRT device implantation. The study was conducted at a tertiary facility specializing in advanced cardiovascular care. No artificial intelligence-supported technologies were used in the study.

Study Population

Patients who received ICD and CRT devices were included in the study.

Inclusion criteria:

- Age ≥ 18 years
- Voluntary participation

Exclusion criteria:

- Age < 18 years
- Pregnancy
- Active lactation
- Active malignancy or ongoing chemotherapy
- Hemoglobin chain disorders

ABBREVIATIONS

ALT	Alanine transaminase
BMI	Body mass index
CRT	Cardiac resynchronization therapy
FDA	Food and drug administration
GFR	Glomerular filtration rate
Hb	Hemoglobin
ICD	Implantable cardioverter-defibrillator
MetHb	Methemoglobin
TEE	Transesophageal echocardiography

- Liver failure
- Renal failure with glomerular filtration rate (GFR) < 60 mL/min or dialysis treatment
- Chronic obstructive pulmonary disease and other hypoxic lung diseases (eg: Interstitial lung diseases, asthma, occupational diseases)
- Smoker patients
- Use of other sedative agents

Data Collection and Measurements

Patient data were obtained from the hospital's electronic medical records. Demographic parameters (age, sex, weight, height) were recorded. Body mass index (BMI) was calculated as weight (kg) / height^2 (m^2). Laboratory values, including urea, creatinine, alanine aminotransferase (ALT) and hemoglobin levels, were extracted from the clinical database. Patients with missing data were excluded from the study. No additional procedures were performed; all patients were monitored observationally. Pre-procedural laboratory data were recorded and compared with values obtained one-hour post-procedure. The amount of prilocaine administered was also documented.

Outcomes

The primary outcome was the change in methemoglobin levels post-procedure. Secondary outcomes included identifying factors associated with this change, assessing the impact of methemoglobin levels on oxygen saturation and determining the factors influencing changes in oxygen saturation.

Statistical Analysis

Normality was assessed using the Shapiro-Wilk test. Continuous variables are presented as means±standard deviation (SD) for normally distributed data and as medians (minimum-maximum) for non-normally distributed data. Categorical variables are presented as frequencies and percentages. The Spearman correlation test was used for continuous variables, while the Mann-Whitney U test was applied to compare non-normally distributed variables. The Wilcoxon test was used for dependent variables. A P-value < 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS (version 26.0, IBM Corp., Armonk, NY, USA).

Results

A total of 64 patients were included in the study, consisting of 35 males (54.7%) and 29 females (45.3%), with a mean age of 57.02 ± 6.53 years (Table 1). The average weight of the patients

Table 1. Demographic, anthropometric and clinical data of the study population (n=64)

	Min	Max	Mean	SD
Age (years)	38	69	57.02	6.53
Weight (kg)	50	93	71.41	11.08
Height (cm)	155	180	166.09	8.17
BMI (kg/m^2)	18.37	30.37	25.7	2.82

SD, Standard deviation; BMI, Body mass index.

was 71.41 ± 11.08 kg, the mean height was 166.09 ± 8.17 cm and the average BMI was 25.7 ± 2.82 (Table 1). No significant relationship was found between age and methemoglobin levels (P = 0.059). However, significant associations were observed between elevated methemoglobin levels and both weight (P < 0.001) and BMI (P < 0.001) (Table 2). No significant relationship was found between height and methemoglobin levels (P = 0.611) (Table 2).

Laboratory tests revealed a significant relationship between creatinine levels and methemoglobin levels (P < 0.001) (Table 2), as well as a positive correlation between changes in methemoglobin and creatinine levels (P < 0.001) (Table 3). Additionally, a positive correlation was found between changes in oxygen saturation and methemoglobin levels (P = 0.009) (Table 3). No significant relationship was observed between ALT levels and methemoglobinemia (P = 0.425) (Table 2). Total prilocaine doses greater than 600 mg were used in 51 patients and only one patient developed clinically significant methemoglobinemia.

Prilocaine administration was significantly associated with higher methemoglobin levels (P < 0.001) and lower oxygen saturation (P < 0.001) (Table 2). The amount of prilocaine administered showed a positive correlation with both methemoglobin levels (P = 0.006) and changes in oxygen saturation (P = 0.007) (Table 3).

In our study, post-procedural methemoglobin levels were found to be significantly higher compared to pre-procedural values (P < 0.001), while oxygen exchange was significantly lower (P < 0.001) (Table 4). In the regression analysis, the risk of methemoglobin was found to be high when BMI was low (odds ratio (OR): 6.8), hemoglobin was low (OR: 9.9) and the mg of prilocaine used increased (OR: 0.99). In the multiple regression analysis, low BMI (OR: 5.2) among the variables increased the risk of methemoglobinemia (Table 5).

Discussion

Our study is among the first to investigate the development of methemoglobinemia in patients undergoing ICD and CRT procedures under prilocaine anesthesia and exploring the factors contributing to this condition. The indications and technologies for pacemaker implantation are continuously evolving and these procedures are generally regarded as minor surgeries. Consequently, local anesthesia is the preferred method for performing these procedures.[6] Prilocaine is often the preferred agent in the procedures performed and according to the advice of the US Food and Drug Administration (FDA) the maximum safe dose of prilocaine in normal and healthy individuals is 600 mg. Although these procedures are typically safe, complications can occasionally arise. These include pneumothorax, hemothorax, hematoma, pacemaker system infection, diaphragm stimulation and cardiac or venous perforation. However, methemoglobinemia—a rare complication—occurs infrequently.

Cases of methemoglobinemia induced by prilocaine, a local anesthetic used during pacemaker implantation, are scarce in the literature. Methemoglobin levels increase when oxidative stress within red blood cells overwhelms their mechanisms. This stress causes the iron ion in the heme group (Fe^{2+}) to oxidize to the ferric state (Fe^{3+}), resulting in methemoglobin (MetHb), which is incapable of binding oxygen effectively. Normally, MetHb levels remain below 2%, not causing symptoms. However, these levels can rise due to genetic factors (e.g., enzymatic defects) and/or acquired causes (e.g., drugs, toxins).[7,8] Elevated methemoglobin concentrations often lead to more pronounced symptoms. The metabolic mechanisms

Table 2. Methemoglobinemia and associated factors

	Methemoglobin value < 10 (%)		Methemoglobin value > 10 (%)		p
	Mean ± SD	Median (Min–Max)	Mean ± SD	Median (Min–Max)	
Age (years)	56.54±6.0	56 (44–67)	59.6±8.6	60 (38–69)	0.059
Height (cm)	166.2 ± 8.5	170 (155–180)	165.2 ± 6.2	166 (155–175)	0.611
Weight (kg)	73.9 ± 9.7	76 (50–93)	57.5 ± 6.8	58 (50–68)	**<0.001**
BMI (kg/m^2)	26.6 ± 2.0	27 (20.8–30.3)	21.0 ± 1.3	21.4 (18.3–22.4)	**<0.001**
Delta oxygen saturation	0.66±0.86	1.0 (–1.0–3.0)	3.8±3.6	3.0 (2.0–14.0)	**<0.001**
Total prilocation dose (mg)	728.5 ± 136.6	700 (500–1200)	836.0±60.2	800 (800–960)	**<0.001**
ALT (U/L)	22.1±5.2	21.5 (14–33)	23.4±5.3	25 (12–31)	0.425
Serum creatinine (mg/dl)	0.85±0.11	0.86 (0.60–1.16)	1.18±0.15	1.1 (0.97–1.40)	**<0.001**
Urea (mg/dl)	22±4.7	22 (14–37)	31.6±7.7	32.5 (19–43)	**<0.001**
Hgb (g/dL)	12.8 ± 1.2	12.7 (9.6–15.8)	10.4 ± 0.6	10.4 (9.5–11.4)	**<0.001**

*Mann-Whitney U test; ALT, Alanin amino transferaz; BMI, Body mass index; Hgb, Hemoglobin; SD, Standard deviation.

Table 3. Correlation test of delta methemoglobin and delta oxygen saturation related factors

	Delta methemoglobin		Delta oxygen saturation	
	Factor (rho)	**P**	**Factor (rho)**	**P**
Delta methemoglobin (%)	–	–	0.825	**<0.001**
Delta oxygen saturation	0.825	**<0.001**	–	–
Age (years)	0.046	0.774	-0.185	0.144
BMI (kg/m^2)	-0.642	**<0.001**	-0.388	**0.002**
Total prilocation dose (mg)	0.337	**0.006**	0.337	**0.007**
Prilocaine (mg/kg)	0.617	**<0.001**	0.412	**<0.001**
ALT (U/L)	0.099	0.435	0.066	0.606
Serum creatinine (mg/dl)	0.607	**<0.001**	0.323	**0.009**
Urea (mg/dl)	0.471	**<0.001**	0.260	**0.038**
Hgb (g/dl)	-0.612	**<0.001**	-0.359	**0.004**

*Spearman Correlation Test; ALT, Alanin amino transferaz; BMI, Body mass index; Hgb, Hemoglobin; SD, Standard deviation.

Table 4. Changes in pre- and post-operative parameters

	Before operation		After operation		P
	Mean ± SD	**Min–Max**	**Mean ± SD**	**Min–Max**	
Methemoglobin (%)	0.82±0.138	0.6–1.2	6.2±3.8	2.7–25.1	**<0.001**
Oxygen saturation (So_2)	97±1.0	94–98	95.8±2.1	84–98	**<0.001**

*Wilcoxon test; SD, Standard deviation.

Table 5. Effect of independent variables on methemoglobin change (logistic regression analysis)

	Model 1					Model 2			
	OR	**95% CI**		**P**		**OR**	**95% CI**		**P**
BMI (kg/m^2)	6.8	1.5	31.1	**0.012**	-	5.2	1.0	25.3	**0.04**
Hemoglobin(g/dl)	9.9	2.7	36.7	**<0.001**					
Total prilocation dose (mg)	0.99	0.98	0.99	**0.03**					

CI, Confidence interval; OR, Odd ratios; BMI, Body mass index.

counteracting MetHb primarily involve cytochrome b5 reductase and NADPH meth-Hb reductase enzyme systems in red blood cells, with lesser contributions from ascorbic acid and glutathione enzyme systems. Disruption of these pathways can result in methemoglobinemia.[9]

Guay J. reported a review of 242 methemoglobinemia cases linked to local anesthesia. Of these, 159 (65.7%) patients were anesthetized with benzocaine-containing agents, with 105 (43.4%) receiving benzocaine alone and twelve cases of methemoglobinemia were associated with lidocaine administration.[10] In another study of 24,431 patients undergoing endoscopic procedures, no cases of methemoglobinemia occurred in 22,210 patients anesthetized with 4% lidocaine spray for upper gastrointestinal endoscopy or bronchoscopy. In contrast, in the second group of 2,221 patients who received 20% benzocaine spray prior to transesophageal echocardiography (TEE), nine cases of clinically significant methemoglobinemia were reported.[11] Strzecka DF examined data from 3,354 patients over a 13-year period and reported no cases of methemoglobinemia requiring clinical intervention in anesthesia performed with lidocaine.[12]

Cases of methemoglobinemia related to prilocaine are less common. Cicek et al.[13] reported a case where a patient undergoing an ICD procedure developed low oxygen saturation post-procedure, with high methemoglobin levels detected. Following treatment with methylene blue, methemoglobin levels decreased and the patient's vital signs improved. Similarly, Canpolat et al.[9] described a case where methemoglobinemia developed following prilocaine administration during an ICD procedure.

Our study is pioneering in investigating methemoglobinemia specifically in the context of ICD/CRT procedures under prilocaine anesthesia. The results of our study show a statistically significant increase in methemoglobin levels following prilocaine administration. Furthermore, significant decreases in oxygen saturation values were observed in patients after the procedure. Clinically significant methemoglobinemia (oxygen saturation < 90%) was detected in only one patient. We suggest that caution be exercised in patients with low baseline oxygen saturation or pulmonary comorbidities. Additionally, our study revealed that more significant decreases in oxygen saturation were observed in patients with methemoglobin levels above 10%. In the case of Pay et al.,[14] a 76-year-old patient developed methemoglobinemia

after using 800 mg prilocaine for pacemaker implantation and the patient's methemoglobin levels gradually decreased to the normal range, following methylene blue treatment. One of our patients who developed clinically symptomatic methemoglobinemia (dyspnea, oxygen saturation <90%) was followed up in the intensive care unit for 24 hours. The patient was given oxygen therapy and closely monitored. After 24 hours, our patient, whose clinical complaints improved and whose methemoglobin values dropped below 10%, was transferred from the intensive care unit to the cardiology clinic. Our patient was relieved with symptomatic treatment during the intensive care unit treatment period and methylene blue was not required in the treatment.

A significant relationship was found between the amount of prilocaine administered and higher methemoglobin levels. Elevated methemoglobin levels were also associated with higher creatinine levels, suggesting that caution should be exercised when using prilocaine in patients with renal failure. In a study by Kane et al.,[15] which examined 28,478 cases of local anesthetic administration during TEE, a significantly higher incidence of methemoglobinemia was observed in anaemic patients. In our study, higher methemoglobin levels were found in patients with lower hemoglobin levels. Additionally, while Kane et al.[15] found no relationship between methemoglobinemia and BMI, our study identified a significant correlation between lower BMI and higher methemoglobin levels.

Limitations

The study was conducted in at a single center and the number of cases included was limited. Additionally, the laboratory parameters available for analysis were few, which may have constrained the scope of the findings. The fact that patients do not have comorbidities limits the relationships between other diseases and the results. One of the limitations of the study is the lack of records of the subtypes of operations performed on the patients. The follow-up of the cases was done for a limited time and long-term follow-up is not available. The retrospective, single-center nature of the study affects the potential for case selection and limits its attribution to the entire population.

Conclusion

Methemoglobin levels significantly increased after ICD/CRT procedures with prilocaine. However, clinically significant cases are rare. Methemoglobin elevation is associated with factors such as BMI, creatinine and hemoglobin levels. Further multicenter studies are needed to elucidate these associations more clearly.

Ethics Committee Approval: Ethics committee approval was obtained from the Kütahya Health Sciences University Rectorate Non-Interventional Clinical Research Ethics Committee (Approval Number: 2021/40, Date: 05.03.2021).

Informed Consent: Written informed consent was obtained from all participants.

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References

1. Chander K, Lavie CJ, Ventura HO, Milani RV. Benzocaine induced methemoglobinemia: A potentially fatal complication of transesophageal echocardiography. *Ochsner J*. 2003;5(2):34-35.
2. Guertler AT, Pearce WA. A prospective evaluation of benzocaine-associated methemoglobinemia in human beings. *Ann Emerg Med*. 1994;24(4):626-630. [CrossRef]
3. Darling RC, Roughton FJW. The effect of methemoglobin on the equilibrium between oxygen and hemoglobin. *Am J Physiol*. 1942;137(1):56-68. [CrossRef]
4. Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: Recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26(9):921-964. [CrossRef]
5. Dahshan A, Donovan GK. Severe methemoglobinemia complicating topical benzocaine use during endoscopy in a toddler: A case report and review of the literature. *Pediatrics*. 2006;117(4):e806-e809. [CrossRef]
6. Sarı C, Aslan AN, Baştuğ S, Bayram NA. An unusual complication after permanent pacemaker implantation: Methemoglobinemia. *Arch Turk Soc Cardiol*. 2015;43(5):468-471. [CrossRef]
7. Alter P, Waldhans S, Plachta E, Moosdorf R, Grimm W. Complications of implantable cardioverter defibrillator therapy in 440 consecutive patients. *Pacing Clin Electrophysiol*. 2005;28(9):926-932. [CrossRef]
8. Lata K, Janardhanan R. Methemoglobinemia: A diagnosis not to be missed. *Am J Med*. 2015;128(10):e45-e46. [CrossRef]
9. Canpolat U, Bahadır N, Şahiner L, Aytemir K. A rare cause of cyanosis and hypoxia that should not be forgotten after implantable cardioverter defibrillator implantation. *Turk Kardiyol Dern Ars*. 2017;45(6):560-562. [CrossRef]
10. Guay J. Methemoglobinemia related to local anesthetics: A summary of 242 episodes. *Anesth Analg*. 2009;108(3):837-845. [CrossRef]
11. Vallurupalli S, Manchanda S. Risk of acquired methemoglobinemia with different topical anesthetics during endoscopic procedures. *Local Reg Anesth*. 2011;4:25-28. [CrossRef]
12. Filipiak-Strzecka D, Kasprzak JD, Wiszniewska M, Walusiak-Skorupa J, Lipiec P. The influence of lidocaine topical anesthesia during transesophageal echocardiography on blood methemoglobin level and risk of methemoglobinemia. *Int J Cardiovasc Imaging*. 2015;31(4):727-731. [CrossRef]
13. Cicek Y, Durakoglugil ME, Usta EH. Methemoglobinemia due to local anesthesia: A rare cause of cyanosis and chest pain after placement of implantable cardioverter defibrillator. *J Rural Med*. 2020;15(2):63-64. [CrossRef]
14. Pay L, Arıkan ME, Kolak Z, Hayıroğlu Mİ, Dayı ŞÜ. An unexpected complication of pacemaker implantation: Methemoglobinemia. *Acta Cardiol Sin*. 2021;37(4):449-452.
15. Kane GC, Hoehn SM, Behrenbeck TR, Mulvagh SL. Benzocaine-induced methemoglobinemia based on the Mayo Clinic experience from 28 478 transesophageal echocardiograms: Incidence, outcomes, and predisposing factors. *Arch Intern Med*. 2007;167(18):1977-1982. [CrossRef]