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Nötrofil/Lenfosit Oranının Postoperatif Ağrı İçin Öngörücü Rolü
Predictive Role of Neutrophil/Lymphocyte Ratio for Postoperative Pain

Vildan Kölükçü, Mürsel Kahveci[2]

[1]Tokat State Hospital, Tokat, Turkey

[2]Amasya University, Medical Faculty, Department of Anesthesiology and Reanimation, Amasya, Turkey

Sorumlu Yazar

Vildan Kölükçü

Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı. Merkez/Tokat

E-mail:
vildankolukcu@gmail.com

Özet

Amaç: Ameliyat sonrası ağrı, cerrahi işlemin neden olduğu akut inflamasyon ile yakından ilişkilidir. Çalışmamızda, sistemik bir inflamasyon belirteci olarak nötrofil/lenfosit oranı (NLR) ile postoperatif ağrının belirteci olarak postoperatif analjezik tüketimi arasındaki ilişkiyi araştırmak amaçlandı.
Gereç ve Yöntem: Çalışmada 18-55 yaşları arasında genel anestezi altında septorinoplasti uygulanan olguların verileri analiz edildi ve American Society of Anesthesiologists (ASA) sınıflamasına göre sınıf I-II olarak değerlendirildi. Hastaların demografik verileri, ASA skorları, operasyon süresi ve postoperatif dönemdeki toplam analjezik tüketimi kaydedildi. Hastalar preoperatif NLO'ya göre iki gruba ayrıldı. Buna göre NLO <2 olan hastalar Grup 1, NLO ≥2 olan hastalar Grup 2 idi.
Bulgular: Çalışmaya toplam 116 vaka dahil edildi. Demografik veriler ve operasyon süreleri açısından iki grup arasında istatistiksel olarak anlamlı fark yoktu ($p>0.05$). Grup 1 ve 2'de ortalama NLR sırasıyla 1,46±0,29 ve 2,64±0,74 idi. Grup 2'nin, Grup 1'e göre istatistiksel olarak anlamlı derecede yüksek postoperatif analjezik tüketimine sahip olduğu belirlendi ($p=0,006$).
Sonuç: Çalışmamızda elde edilen veriler ışığında ameliyat öncesi NLR'nın ameliyat sonrası ağrıyı öngörerek uygun tedavi stratejilerinin belirlenmesinde yol gösterici bir belirteç olarak değerlendirilebileceği sonucuna varıldı.

Anahtar Kelimeler: Nötrofil/lenfosit oranı, postoperatif ağrı, analjezik tüketimi, septorinoplasti

Abstract

Aim: Postoperative pain is closely associated with acute inflammation caused by the surgical procedure. In our study, the aim was to investigate the correlation between neutrophil/lymphocyte ratio (NLR) as a systemic inflammation markerwith postoperative analgesic consumption as a marker of postoperative pain.

Material and Method: The study analysed data from cases undergoing septorhinoplasty under general anaesthesia aged from 18-55 years and assessed as class I-II according to American Society of Anesthesiologists (ASA) classification. The demographic data of patients, ASA scores, operation duration and total analgesic consumptionin the postoperative period were recorded. Patients were divided into two groups according to preoperative NLR. Accordingly, patients with NLR <2 were Group 1, while patients with NLR ≥2 were Group 2.

Results: The study included a total of 116 cases. There were no statistically significant differences between the two groups in terms of demographic data and operation durations ($p>0.05$). The mean NLR in Groups 1 and 2 were 1.46±0.29 and 2.64±0.74, respectively. Group 2 were identified to have statistically significantly higher postoperative analgesic consumption compared to Group 1 ($p=0.006$).

Conclusion: In light of data obtained in our study, it was concluded that preoperative NLR may be assessed as a guiding marker for determination of appropriate treatment strategies by predicting postoperative pain.

Keywords: Neutrophil/lymphocyte ratio, postoperative pain, analgesic consumption, septorhinoplasty

Introduction

Postoperative pain is an acute pain beginning with the surgical incision and ameliorating with tissue healing. The surgical procedure and resulting postoperative pain affect metabolic, endocrine and inflammatory systems and may cause increases in morbidity and mortality if not treated (1). If sufficient analgesia is not provided in the peroperative period, pain may become chronic, and may cause unwanted situations like increased cardiac and thromboembolic complications, lengthened wound healing and mobilization durations, lengthened hospital stay and increased costs (2). Inflammation triggered by surgical trauma is a predictive factor for postoperative pain occurrence (3). Many cytokines and hormones are released as a result of the neuroendocrine and inflammatory response developing during the surgical procedure and anaesthesia. These include relatively expensive mediators used to assess the neuroendocrine response like interleukin 6 (IL-6), tumour necrosis factor alpha (TNF-α), cortisol, c-reactive protein (CRP) and leptin (4). With the systemic inflammatory response, as a result of increased lymphocyte apoptosis and neutrophil apoptosis inhibition, systemic leukocyte changes like neutrophilia, lymphopenia and leucocytosis may be observed (5,6). The neutrophil/lymphocyte ratio (NLR) is an easily measured and cheap inflammation marker that is frequently used to assess the inflammatory response in recent years (7). Currently, NLR is used as a predictive factor for morbidity, mortality and

prognosis in a variety of cancer types, systemic and inflammatory diseases (8-10). There are very limited numbers of studies assessing the correlation between postoperative pain developing as a result of acute inflammation caused by surgical stress and preoperative NLR. In our study, the aim was to investigate the correlation between postoperative pain and NLR in patients undergoing septorhinoplasty operations under general anaesthesia.

Material and Method

The study was carried out in accordance with the principles of the Helsinki Declaration.This study with single-centre, retrospective and observational design screened the files of patients undergoing septorhinoplasty operations with the open technique under general anaesthesia from January 2018 to December 2019. A total of 116 cases aged from 18-55 years, with American Society of Anesthesiologists (ASA) risk score I-II were included. Patients with clinical situations that may change NLR like rheumatologic diseases, immune failure, acute infective pathologies, severe endocrinologic disorders and use of steroids, anti-aggregants or anticoagulants were excluded from the study. The patients' age, sex, body mass index (BMI), ASA score, operation duration and analgesic amounts consumed in the postoperative period were recorded. NLR was investigated on routine complete blood counttaken during preoperative anaesthesia consultation. NLR was calculated by dividing the neutrophil count by the lymphocyte count in completeblood counts. All haematological parameters were expressed as $10^3/\mu L$. Based on broad-series studies in previous periods, the cut-off value for NLR was taken as 2 (11,12). Accordingly, those with NLR <2 were Group 1 and those with NLR ≥2 were classified as Group 2. During the operation, all patients had monitoring with electrocardiogram (ECG), peripheral oxygen saturation (SpO_2) and non-invasive blood pressure (NIBP) using a bedside monitor. All patients had standard general anaesthesia protocol applied. Preoxygenation was performed with spontaneous respiration using 100% O_2 and fresh gas flow of 5 L/min with a mask for three minutes. Patients had induction with 1-2 mcg/kg fentanyl and 5-7 mg/kg thiopental. Muscle relaxation was provided by 0.6 mg/kg rocuronium and then patients were intubated with an endotracheal tube with appropriate diameter for the patient. Maintenance anaesthesia used 1 MAC sevoflurane and 50% O_2 – air mixture. The anaesthesia device (Primus® Dräger Medical, Lübeck, Germany) was set to tidal volume 7-10 mL/kg, respiratory rate12/min, I:E ratio 1:2, and PEEP 4-5 cmH_2O for mechanical ventilation in volume-controlled ventilation mode. For postoperative analgesia, every patient was administered 1 mg/kg intravenous tramadol. Patients were decurarised at the end of the operation and then extubated. Patients were not administered non-steroidal anti-inflammatory drugs in the peroperative period. For postoperative pain management, patients were administered paracetamol iv as first choice. If sufficient analgesia was not provided, in the second step, tramadol 50 mg iv was administered and if necessary repeated until total iv tramadol dose was maximum 300 mg per day. The total tramadol consumption of patients in the postoperative first 24 hours were recorded.

Statistical Method

Descriptive analyses were performed with the aim of providing information about the general characteristics of the study groups. Data with quantitative values are given as mean±standard deviation, while data with qualitative values are shown as n (%). Differences between the groups were investigated with the independent samples t test for quantitative values and the chi-square test for qualitative values. When p values smaller than 0.05 were calculated, it was accepted as statistically significant. Correlation between preoperative NLR and total analgesic consumption was assessed with the Pearson correlation test. Calculations used available statistical software (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

Results

In our study, the mean age of analysed cases was 29.21±10.45 years and BMI was 23.85±2.11 kg/m^2. Mean operation duration was recorded as 134.51±23.77 min. There were 68 patients in Group 1 and the demographic data and operation durations were similar in both groups (**Table 1**). For all cases assessed in our study, the neutrophil and lymphocyte values were 4.65±1.40 and 2.54±0.69, respectively. Preoperative NLR was measured as 1.46±0.29 in Group 1 and 2.64±0.74 in Group 2. All cases had mean analgesic amount consumed of 111.21±62.58 mg in the postoperative first 24 hours. When these values were compared, Group 2 was statistically significantly higher than Group 1 (p=0.006) (**Table 2**).

Table 1. Demographic data and operation duration

	GROUP 1 (n=68)	GROUP 2 (n=48)	p
Age (years)	29.66±9.99	28.56±11.13	0.579[a]
Sex			0.767[b]
female	38(56.7)	29(43.3)	
male	30(61.2)	19(38.8)	
BMI (kg/m^2)	23.79±1.97	23.93±2.31	0.738[a]
ASA			0.629[b]
I	47(56.6)	36(43.4)	
II	21(63.6)	12(36.4)	
Operation duration (minute)	136.51±24.62	131.67±22.45	0.281[a]

Data in table shown as Mean±SD and n (%)
[a]Independent samples t test, [b]chi square test
BMI: body mass index

Table 2. Distribution of quantitative values according to groups

	GROUP 1 (n=68)	GROUP 2 (n=48)	p[a]
Preoperative NLR	1.46±0.29	2.64±0.74	<0.001*
Neutrophil (10^3/μL)	4.00±0.94	5.58±1.42	<0.001*
Lymphocyte (10^3/μL)	2.79±0.68	2.17±0.51	<0.001*
Total analgesic consumption (mg)	97.79±56.93	130. 21±65.83	0.006*

Data in table shown as Mean±SD and n (%)
[a]Independent samples t test
*p value 0.05 accepted as significant
NLR: neutrophil/lymphocyte ratio

Discussion

In systemic inflammation, an increase occurs in neutrophil counts and a reduction occurs in lymphocyte counts as the response of leukocytes. NLR is used as a determinant of inflammation alone or in combination with other inflammation mediators and has been included broadly in studies about inflammation in recent years (11). When the literature was investigated deeply,studies in previous periods observed that NLR was used to assess the clinical progression of many chronic diseases like gastrointestinal system pathologies, diabetes mellitus, hypertension, cardiovascular disorders and in evaluating the clinical course of nearly all cancer types(8-11). Additionally, there are limited numbers of studies involving NLR in anaesthesia and algology practice (13-15). A study assessing the effect of anaesthesia technique used on NLR found that postoperative NLR was lower in patients administered spinal anaesthesia compared to those with general anaesthesia (13). A similar study calculated that NLR values were lower in the postoperative second hour for patients with total intravenous anaesthesia using propofol and remifentanil compared to patients with inhalation anaesthesia using sevoflurane (14). Another study investigated the correlation between ASA score and NLR and stated that NLR value may be used as a predictive factor for preoperative assessment in anaesthesia practice (15).

In addition to all of these, NLR as a systemic inflammation markerwas considered to be a predictive factor for postoperative pain due to the inflammatory response occurring as a result of surgical trauma. When the literature is examined, there are limited numbers of studies assessing the correlation of NLR and postoperative pain (11). The first study showing a correlation between postoperative pain and NLR was presented to the literature by Daoudia et al. (16). The study encompassing 60 patients undergoing laparoscopic cholecystectomy operation under general anaesthesia concluded that total analgesic requirements in the first 48 hours postoperative were positively correlated with low preoperative NLR. Contrary to the results of this study, Turgut et al. (11) in a study of a total of 140 patients undergoing orthognathic surgery showed that postoperative analgesic consumption was significantly greater in the preoperative NLR ≥2 group. A similar study investigated the preoperative NLR values of a total of 171 patients with peripheral nerve block due to shoulder arthroscopy operations and found the group with NLR >2 had higher postoperative visual analog scale (VAS) scoresand shorter total analgesic duration (12). In our study, similar to publications in the literature (11,12), in the group with preoperative NLR ≥2, postoperative total analgesic consumption assessed as a marker of postoperative pain was found to be significantly higher compared to the group with NLR <2.

A group of studies investigating the relationship between postoperative pain and NLR showed a significant correlation between postoperative pain and postoperative NLR values. A study by Canbolat et al. (20)administered spinal anaesthesia due to lower extremity surgery and used patient-controlled analgesia for postoperative pain management. They showed there was a statistically significant correlation between NLR in the postoperative first hour and visual analogscores in the postoperative 48th hour in a group undergoing total hip arthroplasty. A study investigating the effects of thoracic epidural analgesia and intravenous

analgesia in thoracotomy surgery on NLRshowed the postoperative NLR values were statistically much increased in the group receiving intravenous analgesia. Additionally, in the postoperative first 2 days, additional analgesia requirements were significantly greater in the group receiving intravenous analgesia. In both groups in the study, postoperative additional analgesia requirements had positive correlation with preoperative NLR values (21).

Currently, postoperative pain management has gained importance with the increase in frequency of surgical procedures. Studies have shown the predictive factors for postoperative pain formation are operation type, obesity, young age, female sex, preoperative anxiety and preoperative pain (22). The results of our study show that preoperative NLR may be an indicator to estimate postoperative pain ahead of time and plan appropriate treatment by taking necessary precautions. Limitations of the study include it being retrospective, single-centre, and documenting a limited number of patients. We think that it is very important to support our results with multi-center, randomised and broad patient series studies in order to contribute to the current literature and find place in clinical practice.

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