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Vibration Anesthesia for Propofol-Rocuronium Injection Pain

Propofol ve Rokuronyum Enjeksiyon Ağrısı İçin Vibrasyon Anestezisi

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ABSTRACT

Objective: Despite numerous strategies for preventing or alleviating pain associated with propofol and rocuronium injections, it remains common and distressing for patients. Application of vibration is an effective method of reducing pain during facial cosmetic injections and some venipuncture procedures. But it has been studied in limited trials for the context of propofol or rocuronium injection pain. This randomized study aims to evaluate the effect of vibration anesthesia on the incidence and severity of propofol and rocuronium injection pain.

Methods: Fifty-one patients who underwent elective gynecologic operations under general anesthesia, were randomized, into two groups. On the dorsal side of the hand, a 20 G intravenous cannula was inserted. In Group V (n=25), propofol and rocuronium was administered following 1 minute of pre-treatment with the vibration device on the intravenous catheter trace. In Group C (n=26) vibration was not applied before drug administration. Propofol pain was recorded according to McCrirrick and Hunter scale and rocuronium injection pain response was evaluated with a four-point scale.

Results: The number of patients who experienced propofol injection pain, in the vibration group was significantly lower than in the control group (p=0.007). The percentage of pain free patients in Group V was 88%, whereas 46% in Group C. The incidence of withdrawal movements associated with rocuronium injection pain was also significantly lower in Group V (p=0.043). Percentage of pain free patients in Group V was 28% whereas 3.8% in Group C.

Conclusion: Vibration anesthesia before propofol and rocuronium injection significantly reduced the injection pain.

Keywords: Injection pain, propofol, rocuronium, vibration

ÖZ

Amaç: Propofol ve roküronyum enjeksiyon ağrısını önlemek veya azaltmak için birçok strateji üzerinde çalışılmış ise de halen hastalar için stres kaynağı olmaya devam etmektedir. Vibrasyon uygulanması fasiyal kozmetik enjeksiyonlarda ve bazı damar yolu açma prosedürlerinde ağrıyı kesmek veya azaltmak için kullanılan etkili bir yöntemdir. Ancak propofol ve roküronyum enjeksiyon ağrılarına etkisi üzerinde yeterli çalışma yapılmamıştır. Çalışmamızda amaç, vibrasyon anestezisinin propofol ve roküronyum enjeksiyon ağrılarına etkisini değerlendirmektir.

Yöntem: Genel anestezi altında elektif jinekolojik operasyon planlanan 51 hasta çalışmaya dahil edilmiştir. El üstünden, 20 G intravenöz kanül ile damar yolu açılmasını takiben Grup V'de (n=25 hasta) intravenöz kateter trasesi üzerine 1 dakikalık vibrasyon uygulanmasından sonra, Grup C'de (n=26 hasta) ise hiçbir işlem uygulanmadan propofol ve roküronyum enjeksiyonu yapılmıştır. Propofol ağrısı, McCrirrick ve Hunter skalası, roküronyum enjeksiyon ağrısı ise dört nokta skalası ile değerlendirilmiştir.

Bulgular: Propofol enjeksiyon ağrısı vibrasyon uygulanan grupta, kontrol grubundan istatistiksel olarak daha düşük bulunmuştur (p=0,007). Ağrı hissetmeyen hasta yüzdesi Grup V'de %88, Grup C'de %46 olarak bulunmuştur. Roküronyuma bağlı istemsiz hareket insidansı Grup V'de istatistiksel olarak daha düşük olup (p=0,043), ağrı hissetmeyen hasta yüzdesi Grup V'de %28, Grup C'de ise %3,8'dir.

Sonuç: Propofol ve roküronyum enjeksiyonundan önce uygulanan vibrasyon anestezisi enjeksiyon ağrısını anlamlı olarak azaltmaktadır.

Anahtar sözcükler: Enjeksiyon ağrısı, propofol, roküronyum, vibrasyon

INTRODUCTION

Propofol and rocuronium are frequently used together in anesthesia practice and for rapid-sequence intubation due to their rapid onset and short duration of action, ease of titration, recovery, and favorable side effect profile (1,2). However, both cause severe discomfort due to pain during injection. Patients define the induction of anesthesia to be the most painful part, and without treatment, approximately 70% of patients experience pain during propofol administration (3).

Many methods and medications have been used to prevent injection pain due to propofol and rocuronium. These include adding lidocaine to propofol or lidocaine in conjunction with

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venous occlusion, changing the pH of propofol, administration of opioids, gabapentin, dexmedetomidine, magnesium sulfate, ondansetron, ketamine, fentanyl, remifentanil, and antipyretic agents before injection (1,4-10).

Roughly 50-80% of the patients experience rocuronium injection pain. Withdrawal of the forearm (flexion-extension activity of wrists and elbows) may soon extend to the whole-body movements after rocuronium injection (11).

Vibration anesthesia has been shown to be an effective and safe way to relieve pain. A vibration device is intended to reduce pain in patients during minor procedures such as medication injection, suture or staple removal, phlebotomy, and venipuncture (12). The low cost, lack of side effects, and simplicity of use are all advantages of this device. It has been demonstrated to lessen pain by a mechanism based on the gate control theory, which states that vibrations activate the dorsal horn neurons, which are the places where pain signals are modified, and therefore prevent full transmission of the pain (13).

We proposed this randomized controlled trial to examine the effectiveness of a vibration device for propofol and rocuronium injection pain relief during general anesthesia induction.

MATERIAL and METHODS

The study protocol was conducted at the Ankara City Hospital, Ankara, Turkey; from May 1 to 30, 2021, in accordance with the Declaration of Helsinki. The study was approved by the hospital's research ethics committee protocol E1-21-1740, April 14, 2021, and the registration number of clinical trials is NCT04987866. The principal investigator had no financial conflicts or managing interest in a company or other entity related to the results of this study. Written informed consent was obtained from all participants in this study.

This was a prospective randomized clinical trial conducted at a single site. For this study, 51 patients were recruited who were American Society of Anesthesiologists (ASA) I-II, aged 18-65, and scheduled to undergo gynecological surgeries. Participants who were pregnant or had a recent history of a severe allergy or hypersensitive reaction to propofol or rocuronium were excluded.

Patients were not medicated before surgery. On arrival to the gynecologic operation room, routine monitoring, including non-invasive blood pressure, electrocardiography, and peripheral oxygen saturation (SpO_2) monitoring, was performed. In addition, we placed a 20 G intravenous catheter in the largest vein on the back of the patients' hands and a 0.9% sodium chloride infusion was started. The patients were oxygenated before anesthesia induction.

The participants were randomly assigned to one of two groups based on whether they chose an opaque envelope with red or yellow paper. The yellow paper denoted the vibration group (Group V), while the red paper denoted anesthesia induction without vibration - control (Group C).

In Group V (n=25), the vibration device was placed against the dorsal hand intravenous catheter track 1 minute before and during the propofol-rocuronium injection. The vibration device is a reusable, handheld device with a battery-powered motor and a vibration frequency of about 6000 times per minute (Figure 1) (Beauty bar facial massaging device, T-Shape Electric Sign Face Massage Tools, Dangshan, China). Group C (n=26) received only propofol and rocuronium injections without vibration anesthesia.

In both groups, 1% propofol (Propofol 1%, Fresenius 20 mL flacon, Germany) was delivered over 15 seconds at a dose of 2-2.5 mg kg^{-1}. The patients were observed for 20 seconds after the propofol administration. The severity of propofol injection was assessed using McCrirrick and Hunter's four-point pain response scale (Table I) (14,15).

Following the propofol administration, 0.6 mg kg^{-1} rocuronium (Esmeron® 50 mg $5mL^{-1}$ N.V. Organon, Oss, Holland) was injected over a 10-second period. The same observer rated

Figure 1. Beauty bar facial massaging device, T-Shape Electric Sign Face Massage Tools, Dangshan, China.

the movement reaction to rocuronium injection pain on a four-point scale (FPS) (16). The scale was 0: no movement, 1: movement only the wrist, 2: movement of only the arm (elbow-shoulder) and, 3: general response, movement more than one extremity. Intubation was perfomed 2 minutes after induction.

Statistical Analysis

We studied 10 individuals whose anesthesia was induced with propofol and rocuronium to estimate sample size prior to the start of the trial. Six patients out of 10 had pain (60%). When a 50% reduction in the number of patients experiencing pain was accepted clinically significant with 95% significance and 90% power, the sample size, was calculated to be 26. For the calculation of sample size MedCalc Statistical Software version 19.2 (MedCalc Software Ltd, Ostend, Belgium) was used.

Statistical analysis was performed using SPSS 17.0 program (SPSS Inc, Chicago, IL, USA). Continuous variables were presented as mean±standard deviation and median (min-max), and categorical variables were expressed as number (percentage). Conformity to normal distribution was tested using Kolmogorov–Smirnov test. Student's t-test was used for comparing normally distributed data, Mann–Whitney U test was used for comparing non normally distributed data, and Pearson's chi-square or Fisher's test was used for comparing categorical variables. $p<0.05$ was considered statistically significant for all tests.

RESULTS

There was no statistically significant difference between the groups in terms of demographic data and propofol doses used (Table II). Mean propofol dose was 186.2±21.6 mg in Group C while the dose was 171.6±29.4 mg in Group V. [Median (min-max) 200 mg (150-200) vs 150 mg (120-200), in Group C and Group V respectively, (p=0.06)]. From the point of view of hemodynamic data, there was no significant difference between the groups at the measurement times. Neither bradycardia nor hypotension observed in any patient. Peripheral oxygen saturation in all groups during the study period was ≥ 96%.

The number of patients who experienced propofol injection pain, in the vibration group was significantly lower than in control group (Chi square: 12.126, DF: 3, p=0.007). Percentage of pain free patients in Group V was 88% (22/25) whereas

Table I. Four-Point Pain Response Scale*

Level 0: No pain	No verbal/ facial/ motor reaction to the injection
Level 1: Mild pain	A minor verbal/ facial/ motor reaction to the injection but no physical activity or wrist joint movements
Level 2: Moderate pain	Pain when asked by the anesthesiologist, or complaint of pain during the injection accompanied by physical activity- facial grimacing or withdrawal of the arm (elbow-shoulder)
Level 3: Severe pain	A response accompanied by a facial expression of pain, or a strong vocal response, tears, arm withdrawal, and full body reaction (including other body movements)

* by McCrirrick and Hunter (14,15).

Table II. Demographic Properties and Total Propofol Doses of the Groups

	Group C (mean ± SD)	Group V (mean ± SD)	p
Age (years)	44.9 ± 8.9	40.1 ± 8.9	0.06
Body weight (kg)	77.4 ± 14.6	71.5 ± 15.8	0.17
Height (cm)	161.2 ± 5.1	160.4 ± 6.1	0.60
Propofol dose (mg)	186.2 ± 21.6	171.6 ± 29.4	0.06

Table III. Distribution of Patients for Propofol Injection Pain Scores according to McCrirrick and Hunter's Four-Point Pain Response Scale

	Pain Score				
	0	1	2	3	
Group C n (%)	12 (46.2)	3 (11.5)	8 (30.8)	3 (11.5)	26 (100)
Group V n (%)	22 (88.0)	2 (8.0)	0 (0.0)	1 (4.0)	25 (100)
Chi square: 12.126, DF: 3, p=0.007					

Table IV. Distribution of Patients for Movement Reaction to Rocuronium Injection Pain with a Four-Point Scale

	Pain Score				
	0	1	2	3	
Group C n (%)	1 (3.9)	6 (23.1)	8 (30.8)	11 (42.3)	26 (100)
Group V n (%)	7 (28.0)	2 (8.0)	10 (40.0)	6 (24.0)	25 (100)
Chi square: 8.18, DF:3, p=0.043					

46% (12/26) in Group C with McCrirrick and Hunter's four-point pain response scale (Table III).

The incidence of withdrawal movements assessed with FPS due to rocuronium injection was also significantly lower in Group V (Chi square: 8.18, DF:3, p=0.043). The percentage of pain free patients in Group V was 28% (7/25) whereas 3,8% (1/26) in Group C (Table IV).

No complications such as edema, or allergic reactions were observed due to study drugs.

DISCUSSION

We demonstrated that applying vibration on venous access track before propofol and rocuronium injections significantly reduced injection pain.

The etiology of pain caused by propofol and rocuronium administration is not clear. The most painful part of the perioperative period, according to some patients, was the induction of anesthesia (2). In the absence of other treatments, approximately 70% of patients experience pain after propofol injection (3).

It has been proposed that propofol injection pain may be linked to chemo nociceptor activation directly linked to the solution pH, osmolality and amount of free agents in the emulsion aqueous phase, indirect activation of histamine, bradykinin and other substances mediating inflammation (17).

Propofol is an alkylphenol and highly lipid soluble emulsion with a pH of 7.0. Another reason for the injection pain is this formulation. Many studies have been performed in the literature to lower the pH of propofol and hence the pain it induces (8,15-17).

Propofol injection pain may start immediately or soon after the injection. Delayed pain, described as coldness, numbness, or serious burning pain proximal to the injection site, occurs 10-20 seconds after the injection and ceases when the injection ends. While sudden pain is probably linked to direct irritant effects, pain which starts soon after is due to the indirect effect resulting from the kinin cascade. Propofol has the potential to irritate the skin, venous intima, and mucous membranes, as well as to activate the kallikrein-kinin system, which is involved in inflammation, blood pressure control, coagulation, and pain. Propofol appears to be linked to the release of bradykinin, histamine, and other inflammatory mediators (18). These cause venous dilation and hyperpermeability, which increases the contact between free propofol in the blood and peripheral nerve endings, resulting in pain upon injection. Despite this discomfort, the incidence of venous complications such as phlebitis is less than 1% (19).

The mechanism of rocuronium-induced injection pain remains unclear as propofol. The mechanisms of pain caused by rocuronium injection include activation of C-nociceptors by the solution's low pH (pH=4), as well as the release of various mediators such as bradykinin and histamine (2,17-20).

Melzack and Wall's "gate control" theory of pain suggests that the intensity of pain perception can be reduced by concurrent non-noxious stimulation, which explains the analgesic capability of a vibration stimulus (21). According to this theory, non-noxious spinal cord stimulation via somatic sensation closes the "gate" for pain. Skin mechanoreceptors, primarily Meissner's corpuscles in the superficial dermis, but also Pacinian corpuscles in the deep dermis and primary endings of muscle spindles, are activated by a vibration stimulus. The small fibers transmit pain stimuli to the brain, whereas the large fibers fired by vibration inhibit the transmission at small fibers (13,21). Although the "gate control" theory is inadequate, increasing scientific evidence suggests that vibration is an effective local anesthetic (22,23). Vibration activates skin mechanoreceptors and with this effect it reduces injection pain which is due to direct irritant effect.

Also, in a previous study, Choi et al. studied lidocaine for rocuronium injection pain and they found that time between lidocaine and rocuronium injection is important (2). They concluded that lidocaine may have a short-term peripheral analgesic effect. Therefore, lidocaine must be used just before injection of rocuronium.

A lot of pharmacological methods have been tried for injection pain pretreatment; lidocaine, magnesium, ondansetron, meperidine, morphine, or ketamine may prevent pain associated with propofol. These medications, which are used to prevent pain, may have some side effects.

A previous study by Pang et al. compared the effect of morphine and meperidine on propofol injection pain (24). They reduced pain severity but also caused significantly more incidence of skin reactions than placebo. Meperidine and morphine released histamine, causing skin erythema/wheals distal to the tourniquet. The erythematous skin reactions had a distinct margin, indicating that the drug was indeed held in the peripheral veins. In our study, we found statistically effective pain relief with no adverse effect, and this is important for people who cannot use or tolerate the other pain treatment methods before the propofol injection.

In a previous study, adding lidocaine to prevent propofol injection pain changed the stability of propofol emulsions, which may cause pulmonary embolism (25).

Picard and Tramer stated that the best method for preventing propofol-associated pain is to administer intravenous lidocaine 0.5 mg kg^{-1} while a tourniquet is applied for 30 to 120 seconds prior to injection (26). However, the failure rate was 40% and the technique failed, possibly due to the time required to apply the tourniquet. In our study percentage of pain free patients was 88% (22/25) in vibration pretreated group.

In a previous study to prevent pain linked to propofol and rocuronium, gabapentin was compared with placebo (1). Gabapentin administered 2 hours before the operation reduced the injection pain of propofol and rocuronium. However, compared to vibration anesthesia, which can be utilized just one minute prior to the induction of anesthesia, the slow onset effect may not be practicable.

Many studies have found that vibration can help to reduce the pain associated with dental and cosmetic procedures, as well as incision and drainage; it can also help to reduce needle phobia (22,27,28). Furthermore, vibration has been used to treat diabetic peripheral neuropathy and during venipuncture in infants (12,29). Similarly, to our study, Baxter et al. combined vibration and cold to alleviate venipuncture pain and found that it reduced pain scores in patients aged 4 to 18 (30).

Lately in 2021 a manuscript was published about vibration anesthesia before propofol injection and like us they found the same results. However, our study was the first in the literature to evaluate the impact of vibration on both propofol and rocuronium injection pain (31).

Unfortunately, inequivalent number of patients (26 vs 25) in study groups is the limitation of this study.

CONCLUSION

In this study, we demonstrated that vibrating devices are effective for reducing propofol and rocuronium injection pain without any adverse effects. This impact is especially noticeable for propofol injection pain. The efficacy, safety, ease of use, and cost of vibration make it a good alternative for reducing injection pain, and future research may show vibration devices to be an effective adjunctive anesthetic for many painful procedures.

AUTHOR CONTRIBUTIONS

Conception or design of the work: AG, NNO

Data collection: AG, NNO

Data analysis and interpretation: AG, NNO

Drafting the article: AG, NNO

Critical revision of the article: AG, NNO

Other (study supervision, fundings, materials, etc): AG, NNO

All authors (AG, NNO) reviewed the results and approved the final version of the manuscript.

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