ONE OF THE COMPLICATIONS OF SPINAL ANESTHESIA: POSTSPINAL BACK-ACHE AND PREEMPTIVE USAGE OF THE TOPICAL DICLOFENAC

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Abstract

Objectives: Pre-emptive analgesic drugs have an important role in the diminish of post-operative pain and some interventions' pain. Present study was to examine the effect of the topical application of diclofenac diethylammonium on the prevention of backache after spinal anaesthesia. **Methods:** This randomized, controlled clinical study consisted of 210 knee arthroscopy patients aged 18–70 years who were scheduled to undergo elective surgery. The patients were randomly assigned to a diclofenac diethylammonium group (Group D) or a placebo group (Group P). Before administration of spinal anaesthesia, diclofenac diethylammonium gel for Group D, plasebo gel for Group P was rubbed onto the skin in the lumbar region where the spinal anaesthetic was to be applied. When the Bromage motor scale (BMS) was 3, an adductor canal catheter was inserted. Using the Visual Analog Scale (VAS), the patients were asked about pain in the area where the spinal anaesthetic had been administered. VAS values were recorded 1, 2, 4, 8, 16 and 24 h after the surgery. **Results:** There wasn't statistically difference between the groups' demographic datas, some datas about spinal anesthesia, duration of the operation and ratios of perioperative analgesia. But there was a statistically differences between the groups' postoperative analgesia. When the groups' 1, 2, 4, 8, 16 and 24-h VAS values and VAS values one week and six months after the surgery were evaluated, there was a statistically significant difference between the two groups in rest and dynamic. **Conclusion:** The use of topical diclofenac after spinal anaesthesia can significantly reduce the incidence of backache.

Keywords: Analgesia, Anesthesia, Spinal, Backache, NSAIDs, Nerve block

Özet

Giriş: Pre-emptive analjezik ilaçlar post-operatif ve anestetik müdahale ağrısının yönetiminde önemlidir. Bu çalışmada, diklofenak dietilamonyumun spinal anesteziden sonra sırt ağrısının önlenmesinde topik uygulanmasının etkisini araştırmak amaçlandı. **Metod:** Bu randomize kontrollü klinik çalışma, elektif cerrahi girişim planlanan 18-70 yaş arasındaki 210 diz artroskopi hastasından oluşmaktadır. Hastalar rasgele seçilerek bir kısmı diklofenak dietilamonyum grubuna (Grup D) bir kısmı plasebo grubu (Grup P) olarak tayin edildi. Spinal anestezi uygulanmadan önce, Grup D için topikal diklofenak dietilamonyum jel, Grup P için topikal placebo jel, spinal anestezik uygulanacak lumbar bölgede cilt üzerine sürüldü. Bromage motor skalası (BMS) 3 olduğunda, tüm hastalara addüktor kanal kateteri takıldı. Visual Analog Skala (VAS) kullanılarak hastalara spinal anestezi uygulanan alanda bulunan ağrı sorgulandı. 1, 2, 4, 8, 16 and 24. saatlerde cerrahi sonrası hastaların VAS skorları not edildi. **Bulgular:** Grupların demografik verileri, spinal anestezi ile ilgili bazı veriler, operasyon süresi ve perioperatif analjezi oranları arasında istatistiksel olarak fark yoktu. Ancak, grupların postoperatif analjezi kullanımları arasında istatistiksel olarak anlamlı farklılık vardı. Operasyondan sonra 1, 2, 4, 8, 16 ve 24 saatlerde, bir hafta ve altı ay sonra tüm grupların VAS değerlerine bakıldığında, istirahat ve hareket halinde Grup D'nin VAS değerlerinin daha düşük olduğu görülmüştür ve her iki grup arasında istatistiksel olarak anlamlı fark vardır. **Sonuç:** Spinal anesteziden sonra topikal diklofenak kullanılması sırt ağrısı sıklığını azaltabilir.

Anahtar kelimeler: Preemptif analjezi, Topikal analjezi, post spinal baş ağrısı, Nonsteroid inflamatuar ilaçlar.

1. INTRODUCTION

Among anaesthesia practices, regional anaesthesia, such as epidural, spinal and spinal-epidural (combined), is usually preferred over general anaesthesia. A number of factors explain this preference. With regional anaesthesia, the patient is conscious, and pulmonary functions are maintained. In addition, regional anaesthesia does not require intubation, it reduces operational bleeding and thromboembolic complications, and it is more cost effective then general anaesthesia(1).

After regional anaesthesia, a patient usually starts to feel pain in the surgical area after the effects of analgesic drugs have worn off. Although the pain that develops in the surgical area is usually primary, patients may also experience secondary pain in the regional anesthesia intervention area. Various studies have highlighted the role of backache following post-spinal anaesthesia as a cause of patient discomfort after surgery(2-5). Several studies shows that postspinal backache incidance in early period of the surgery varies from 4,95% to 29% (6, 7). According to one study, the incidence of backache after spinal anaesthesia was 2.3% (6). In another study, post-spinal backache was reported by 29.3% of patients on one day after spinal anaesthesia (1). In a study, evaluate 3 months period after surgery, showed that postspinal backache incidance was found 12,3% at the end of the 3th months (5).

Pre-emptive analgesic drugs, which are administered to reduce the need for analgesic agents during the post-operative period, are important in the management of post-operative pain and the prevention of the stress response caused by surgery (3).Analgesia administered prior to surgery can prevent hyperalgesia by inhibiting cyclooxygenase (COX) enzyme activity, thereby reducing the production of prostaglandin, which increases in response to surgery-related tissue damage. It can also reduce inflammation and the sensation of pain. The inhibition of COX enzyme activity and prostaglandin synthesis has anti-inflammatory and analgesic effects (8). The use of topical analgesic drugs has various advantages. For example, the effects of the drug are targeted to a specific area. As a result, the effects on the entire body are minimized (9). A previous study showed that topical drugs reduced post-spinal related pain in cutaneous interventions (10).

The aim of the present study was to examine the effect of the topical application of diclofenac diethylammonium as a non-steroidal inflammatory drug (NSAID) on the prevention of backache after spinal anaesthesia.

2. METHODS

This randomized, controlled clinical trial was conducted in the anaesthesia clinic operating room service department of a state hospital located in eastern of Turkey. The local ethics committee approved the study. The study consisted of 106 knee arthroscopy patients aged 18–70 years who underwent spinal anaesthesia during a pre-surgery examination prior to elective surgery. All the patients had normal physical examination and laboratory results and were status I-II, according to the American Society of Anesthesiologists (ASA). Patients who had prostaglandin inhibitor sensitivity and bleeding problems and were in ASA III-IV group, as well as pregnant women and breastfeeding mothers, and take an analgesic treatment were excluded from the study. On the day before the surgery, the patients were informed in detail about the planned procedure, and written consent was obtained.

Thirty minutes before the surgery, 53 patients were selected by the sealed envelope method. In this group (Group D), diclofenac diethylammonium (Dikloron®, Deva Holding, İstanbul) gel was applied in the amount recommended by the manufacturer (4 g per 400 cm^2 area, 46.4 mg). The gel was rubbed onto the skin in the lumbar region where the spinal anaesthesia was to be applied. The other 53 patients served as the placebo group (Group P). The colour and texture of the gel applied in Group P were similar to the colour and texture of that applied in Group D.

At the time of the surgery, each patient was placed in a supine position on the operating table. In all the patients, vascular access was established through a vein. Using an 18-gauge (G) cannula, a 0.9% NACl infusion was initiated at a rate of 5–8 ml/kg/h. The region where the spinal anaesthesia injection was to be applied was sterilized with povidone iodine. Sterile sheets were placed around the site, and the spinal anaesthesia was administered using a 27-G spinal needle. After cerebrospinal fluid was observed, a 2–2.5 ml dose of bupivacaine hydrochloride and dextrose monophosphate (Marcain Spinal Heavy®, AstraZeneca, İstanbul) was administered. Spinal drug doses were administered taking into account the physical features of the patients such as age, weight, height etc. When the Bromage motor scale (BMS) was 3, and heat desensitization was observed, an adductor canal catheter was inserted into the patient via ultrasound guidance. The surgical incision was then made. The following parameters were recorded: the patient's age, weight, and height, sites of spinal anesthesia, prior history of spinal anaesthesia, number of spinal anesthesia interventions in the current surgery, presence of perioperative analgesia, presence of post-operative analgesia, and duration of the surgery.

After the surgery, the patients were moved to the recovery room. Patients displaying no haemodynamic problems and having sensory block at the level of the 10th thoracic dermatome or lower were transferred to the relevant services. A positive pinprick test was used to determine the cessation of the effect of spinal anaesthesia after the surgery, as well as the presence of heat sensitization and a BMS value of 0. Then, as is routine practice in our clinic, 10 ml of 0.5% bupivacaine (Marcaine®) were administered as post-operative analgesia.

After the pain surrounding the surgical area had receded to a tolerable level with 10 ml of 0.5% bupivacaine via adductor canal catheter, the Visual Analog Scale (VAS) was used to assess the pain in the area of the spinal anaesthesia intervention. The patients were asked to score the pain from 0 (minimum) to 10 (maximum), and these values were recorded. The number of patients with a score of 4 or higher on the VAS was recorded. In case of VAS>4, 10 mg/kg Paracetamol infusion was applied to patients Starting from the moment that the BMS value was the 0, VAS values were recorded 1, 2, 4, 8, 16 and 24 h after the surgery. Post-surgery VAS values were also recorded one week and six months later. The one-week VAS evaluations were performed in the orthopaedics outpatient clinic, and the six-month VAS evaluations were determined via a telephone call

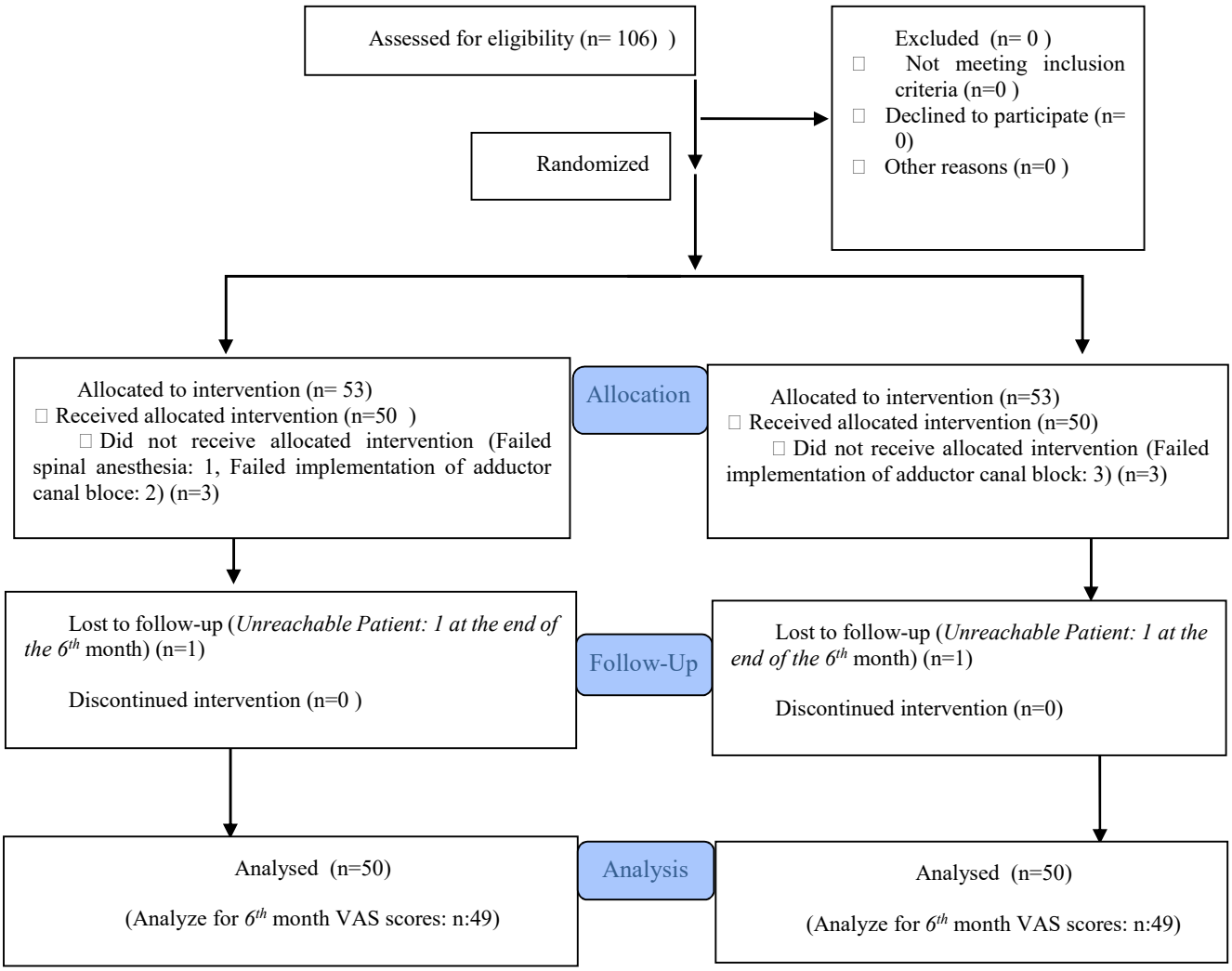
2.1 Sample Size

In the power analysis performed with VAS assessment with dynamic at the sixth months, it was determined that the power was 0.91 in the 95% confidence interval with 0.05 α error by G Power power analyzer calculator. This result indicates that the study sample is sufficient.

2.2 Statistical Analysis

The SPSS (Statistical Package for Social Sciences) (Chicago, USA) for Windows 20.0 program was used for the evaluation of all the data. Categorical data between the two groups were compared using Pearson' chi-square test and expressed as counts (percentages). The Kolmogorov–Smirnov test was used to evaluate the data distribution. The Mann–Whitney *U* test was applied for non-normally distributed continuous variables. Continuous variables were expressed as the mean and standard

Figure 1: Progress diagram of the study showing all groups



deviation (SD), depending on the normality distribution of the data. A *p* value of less than 0.05 was considered statistically significant.

3. RESULTS

In total, 106 patients were included in the study: 53 in Group D and 53 in Group P. In Group D, one patient was excluded from the study because no spinal anaesthesia was applied, and another two patients were excluded from the study because of failed implementation of the adductor canal block. In Group P, three patients were excluded from the study because of failed implementation of the adductor canal block. One patient in Group D and another in Group P could not be contacted by telephone at the time of the six-month evaluation. Thus, their six-month VAS values were not included in the study (Figure 1).

Table 1: Demographic datas, some datas about intervention, duration of the operation and ratios of peroperative and postoperative analgesia of Group D and Group P

	Group D (n:50)	Group P (n:50)	p value
Age (Years)	46.68 ± 8.81	47.56 ± 8,78	0.629 α
Weight (kg)	65.40± 10,27	66.24 ± 9.77	0.777 α
Height (cm)	172.34 ± 7.13	171.00 ± 5.62	0.847 α
Gender (M/F)	28/22	26/24	0.688 α
Spinal Anesthesia History (0/1/2/3)	28/16/5/1	15/13/5/2	0.763 β
Intervention Area (L5-S1/L4-L5/L3-L4/ 2 levels)	21/25/3/1	26/21/2/1	0.782 β
Count of Intervention (1/2/3/4/5)	34/13/1/1/1	29/17/3/0/1	0.570 β
Bone Contact (Y/N)	10/40	13/37	0.476 β
Duration of the Operation (1/2 hour)	46/4	43/7	0.338 β
Peroperative Analgesia (Y/N)	8/42	6/44	0.564 β
Postoperative Analgesia (Y/N)	12/38	15/35	0.499 β

Values are expressed mean ± standart deviation or number. kg; kilogram, cm; centimeter, M; male, F; female. L: Lumbar, S: Sacral

α p>0,05 Student's T test between groups

β p>0,05 Chi-square test between groups.

Table 2: The Comparison of VAS values in rest between group D and Group P

VAS	Group D (n:50)	Group P (n:50)	p value
VAS 1st hours	3.18 ± 0.71	3.52 ± 0.73	0.021 α
VAS 2nd hours	3.24 ± 0.68	3.56 ± 0.70	0.024 α
VAS 4th hours	3.02 ± 0.71	3.30 ± 0.61	0.038 α
VAS 8th hours	2.66 ± 0.65	2.98 ± 0.76	0.028 α
VAS 16th hours	2.42 ± 0.60	2.70 ± 0.76	0.045 α
VAS 24th hours	1.92 ± 0.69	2.26 ± 0.66	0.014 α
VAS 1st Week	1.64 ± 0.52	1.90 ± 0.46	0.010 α
VAS 6th Month	1.12± 0.43	1.34 ± 0.59	0.037 α

Values are expressed mean ± standart deviation or number.

α p<0,05 Student's T test between groups

Table 3: The Comparison of VAS values with dynamic between group D and Group P

VAS (mean±SD)	Group D (n:50)	Group P (n:50)	p value
VAS 1st hours	5.04 ± 0.75	5.38 ± 0.75	0.026 α
VAS 2nd hours	5.12 ± 0.62	5.40 ± 0.69	0.038 α
VAS 4th hours	4.84 ± 0.73	5.16 ± 0.81	0.043 α
VAS 8th hours	4.50 ± 0.67	4.82 ± 0.84	0.040 α
VAS 16th hours	4.24 ± 0.62	4.56 ± 0.81	0.030 α
VAS 24th hours	3.72 ± 0.72	4.06 ± 0.89	0.039 α
VAS 1st Week	1.90 ± 0.64	2.70 ± 0.95	0.000 α
VAS 6th Month	1.26± 0.63	1.78 ± 1.03	0.003 α

Values are expressed mean ± standart deviation or number.

α p<0,05 Student's T test between groups

Table 4: Number of patients who score 4 or more on the VAS scale

	Group D		Group P	
VAS (%)	**P**	**A**	**P**	**A**
VAS 1st hours	17	48	22	49
VAS 2nd hours	18	48	29	49
VAS 4th hours	10	48	34	49
VAS 8th hours	4	47	18	48
VAS 16th hours	2	47	3	46
VAS 24th hours	2	30	2	38
VAS 1st Week	0	1	0	28
VAS 6th Month	0	1	0	10

Values are expressed as a number P; passive, A; Active

No statistical differences were found between the groups' age ratios, average ages, weights, and heights. There were also no statistical differences in the patients' prior histories of spinal anaesthesia, sites of spinal anaesthesia, numbers of spinal anaesthesia injections, vertebral contact and durations of the operations (Table 1). In addition, there was no statistical differences between groups in perioperative analgesia, whereas there was a significant between-group difference in the use of post-operative analgesia (Tables 2 and 3).

When the post-surgery VAS values (1, 2, 4, 8, 16 and 24 h and one week and six month) of the groups were evaluated, there was a statistically significant difference in rest and dynamic between the two groups (Table 4).

4. DISCUSSION

At the end of the study; In patients, who were rubbed onto diclofenac diethylammonium on spinal anesthesia intervention area, had a low postspinal backache incidence at the end of the 6th months compared with patients weren't applied diclofenac diethylammonium.

Topical NSAIDs are used for pain-related complaints and anti-inflammatory purposes, such as soft tissue damage, minor arthritis injuries and burns (11). Many enteral and parenteral analgesic and anti-inflammatory systemic drugs are available to treat post-surgery related pain (12). However, the use of topical analgesic and anti-inflammatory drugs has been found to be an appropriate treatment for minimizing systemic side effects. As systemic effects were expected to be relatively uncommon in the present study, topical administration was selected as pre-emptive analgesia to prevent backache following spinal anaesthesia. The topical NSAID significantly reduced backache associated with post-spinal anaesthesia.

Various types and sizes of spinal needles are used in lumbar puncture (LP) procedures involving children in paediatric oncology clinics (4). Backache was observed in 6 (11%) of 56 patients after LP using a 22-G Quincke spinal needle, whereas no backache was observed in 43 of 56 patients after LP using a 25-pencil-point spinal needle (4). In the present study, the incidence of backache without topical medication before the intervention was 0% in the rest and %10 dynamic at the end of the six mounths, which was similar to that found in other studies (2, 13).

Apart from NSAIDs, various topical locally applied anaesthetic agents can be used for pre-emptive analgesia. These include creams containing lidocaine and prilocaine, both of which have been tested and found to be successful as pre-emptive analgesia (14-16). Although studies have examined the use of topical NSAIDs as pre-emptive analgesia in eye surgery and surgery involving a laryngeal mask (17, 18), there are no studies in the literature on the use of topical NSAIDs used for spinal backache. In a study in which topical lidocaine- and prilocaine-containing creams and penil block were used for pre-emptive analgesia in circumcision operation, a local anaesthesia mixture was applied to the patients 1 h before the operation, and penile block was compared (19). Although the analgesic effects of the creams were similar during the surgery, the analgesic effect of penile block was better during the post-operative period (19). In another study, post-operative pain was assessed in patients who underwent laparoscopic cholecystectomy and received a topical local anaesthetic before and after insertion of a trocar (20). As compared with a placebo group, the patients who received the topical local anaesthetic reported less pain (20). Another study examined the effect of a local anaesthetic mixture on the prevention of pain associated with injections into the tails of rats (21). Observations of behavioural disturbances and aggressive behaviours after the injections provided indirect evidence that the effect of the pre-emptive analgesia was insufficient (21). A study of the analgesic effect of topical tramadol during invasive third molar dental surgery showed that locally administered tramadol, combined with oral ketorolac, had an effective analgesic effect after the surgery (22). General anaesthetics and local tramadol exhibit only analgesic effects. In contrast, NSAIDs have both analgesic and anti-inflammatory effects, allowing them to effectively prevent inflammation and pain after surgery.

In common with other studies, in the present study, the topical drug was administered at least 30 min before the invasive intervention (15, 16, 19, 23). This provided enough time for the drug to produce the maximum analgesic effect. The BMS and pinprick test were used to determine when the effect of the spinal anaesthesia had worn off after the surgery, and the VAS was used to determine whether the diclofenac diethylammonium-containing drug reduced pain surrounding the surgical area to a tolerable level after the adductor canal block. The effect of the diclofenac diethylammonium-containing gel was statistically significant in comparison to that of the placebo gel. As shown by the VAS values in the hours, weeks and six months after the surgery, the NSAID significantly reduced pain levels in Group D in comparison to those in Group P. The use of the NSAIDs for pre-emptive analgesia significantly reduced backache resulting from the spinal anaesthesia.

In a previous study, throat ache after surgery involving the use of a laryngeal mask was decreased in a group treated with topical benzydamine hydrochloride as compared to a placebo group (23). The degree of severity of backache following post-spinal anaesthesia varies. The use of a topical drug is associated with relatively few side effects and can therefore prevent morbidity associated with post-spinal anaesthesia. It seems that the use of topical drugs in the other methods technically similar to spinal anaesthesia, such as LP, can be a proper option.

The analgesia guidelines recommend the NSAIDs as the first line treatment for preemptive analgesia in order to reduce the potential incidence of any adverse reactions due to the administration of subsequent lines of treatment (24). The use of topical NSAIDs in this study further reduced the possibility of these potential adverse reactions. Furthermore, topical medicine use facilitated the monitorization of the patients by the healthcare personnel due to their simple mode of administration and follow-up. Therefore, topical anesthetics and NSAIDs have been used for many years for superficial tissue traumas and interventions (25).

The study had some limitations. In some of the patients who were interviewed, there might be some other underlying conditions leading to pain in the skin in addition to the spinal anesthesia interventions or to the interventions performed in the past. These underlying conditions might have been overlooked by the patients, raising a possibility to affect the results of the study. Another limitation could be that the study participants were evaluated at the orthopedia and traumatologia clinic end of the 1st week and on the phone at the 6. months after without investigators' observations. In addition, the results of the pain assessment might vary among the individuals and therefore it is a possibility that misleading results might be obtained. Although the assessments are possible using the VAS results reported by the patients themselves, the VAS values still remain to be just a subjective method for assessment.

The use of topical diclofenac significantly reduced the incidence of backache, which is a common occurrence after spinal anaesthesia. NSAIDs have both analgesic and anti-inflammatory effects. Therefore, they can effectively prevent inflammation and pain after surgery. Prior to the administration of spinal anaesthesia, we recommend the administration of topical diclofenac in situations other than emergency surgery, where there is insufficient time for the analgesic agent to take effect.

Conflict of Interest: The authors declare that no conflict of interest.

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REFERENCES

1. Tekgul ZT, Pektas S, Turan M, Karaman Y, Cakmak M, Gonullu M. Acute Back Pain Following Surgery under Spinal Anesthesia. Pain practice : the official journal of World Institute of Pain. 2015;15(8):706-11.
2. Lowery S, Oliver A. Incidence of postdural puncture headache and backache following diagnostic/therapeutic lumbar puncture using a 22G cutting spinal needle, and after introduction of a 25G pencil point spinal needle. Paediatric anaesthesia. 2008;18(3):230-4.
3. Dolin SJ, Cashman JN, Bland JM. Effectiveness of acute postoperative pain management: I. Evidence from published data. British journal of anaesthesia. 2002;89(3):409-23.
4. Kılıç E, Mızrak A, Göksu S, Cesur M. Fonksiyonel endoskopik sinüs cerrahisinde gabapentin ve nimesulidin preemptif analjezik etkinliği. AĞRI 2014;26(2):73-81.
5. Schwabe K, Hopf HB. Persistent back pain after spinal anaesthesia in the non-obstetric setting: incidence and predisposing factors. British journal of anaesthesia. 2001;86(4):535-9.
6. Brattebo G, Wisborg T, Rodt SA, Roste I. Is the pencil point spinal needle a better choice in younger patients? A comparison of 24G Sprotte with 27G Quincke needles in an unselected group of general surgical patients below 46 years of age. Acta anaesthesiologica Scandinavica. 1995;39(4):535-8.
7. Schultz AM, Ulbing S, Kaider A, Lehofer F. Postdural puncture headache and back pain after

spinal anesthesia with 27-gauge Quincke and 26-gauge Atraucan needles. Regional anesthesia. 1996;21(5):461-4.

8. Bajaj P, Ballary CC, Dongre NA, Baliga VP, Desai AA. Comparison of the effects of parecoxib and diclofenac in preemptive analgesia: A prospective, randomized, assessor-blind, single-dose, parallel-group study in patients undergoing elective general surgery. Current therapeutic research, clinical and experimental. 2004;65(5):383-97.

9. Tolska HK, Takala A, Blomgren K, Hamunen K, Kontinen V. Topical Ropivacaine in Prevention of Post-Tonsillectomy Pain in Adults. Anesthesia and analgesia. 2017;124(5):1459-66.

10. Whitlow PG, Saboda K, Roe DJ, Bazzell S, Wilson C. Topical analgesia treats pain and decreases propofol use during lumbar punctures in a randomized pediatric leukemia trial. Pediatric blood & cancer. 2015;62(1):85-90.

11. Nair B, Taylor-Gjevre R. A Review of Topical Diclofenac Use in Musculoskeletal Disease. Pharmaceuticals (Basel, Switzerland). 2010;3(6):1892-908.

12. Dureja GP, Iyer RN, Das G, Ahdal J, Narang P. Evidence and consensus recommendations for the pharmacological management of pain in India. Journal of pain research. 2017;10:709-36.

13. Quaynor H, Corbey M, Berg P. Spinal anaesthesia in day-care surgery with a 26-gauge needle. British journal of anaesthesia. 1990;65(6):766-9.

14. Nakamura S, Matsuura N, Ichinohe T. A new method of topical anesthesia by using anesthetic solution in a patch. Journal of endodontics. 2013;39(11):1369-73.

15. Keating SC, Thomas AA, Flecknell PA, Leach MC. Evaluation of EMLA cream for preventing pain during tattooing of rabbits: changes in physiological, behavioural and facial expression responses. PloS one. 2012;7(9):e44437.

16. Arnau B, Jovell E, Romero M, Gonzalez M, Esteba L, Garcia A. Lidocaine-prilocaine cream as analgesia for hysterosalpingography: a randomized, double blinded, controlled study. European journal of obstetrics, gynecology, and reproductive biology. 2014;182:216-9.

17. Hong JP, Nam SM, Im CY, Yoon S, Kim TI, Kim EK, et al. Comparison of analgesic effect of preoperative topical diclofenac and ketorolac on postoperative pain after photorefractive keratectomy. Journal of cataract and refractive surgery. 2014;40(10):1689-96.

18. Mohammadpour M, Jabbarvand M, Nikdel M, Adelpour M, Karimi N. Effect of preemptive topical diclofenac on postoperative pain relief after photorefractive keratectomy. Journal of cataract and refractive surgery. 2011;37(4):633-7.

19. Salgado Filho MF, Goncalves HB, Pimentel Filho LH, Rodrigues Dda S, da Silva IP, Avarese de Figueiredo A, et al. Assessment of pain and hemodynamic response in older children undergoing circumcision: comparison of eutectic lidocaine/prilocaine cream and dorsal penile nerve block. Journal of pediatric urology. 2013;9(5):638-42.

20. Pasqualucci A, de Angelis V, Contardo R, Colo F, Terrosu G, Donini A, et al. Preemptive analgesia: intraperitoneal local anesthetic in laparoscopic cholecystectomy. A randomized, double-blind, placebo-controlled study. Anesthesiology. 1996;85(1):11-20.

21. David JM, Duarte Vogel S, Longo K, Sanchez D, Lawson G. The use of eutectic mixture of lidocaine and prilocaine in mice (Mus musculus) for tail vein injections. Veterinary anaesthesia and analgesia. 2014;41(6):654-9.

22. Isiordia-Espinoza MA, Pozos-Guillen AJ, Martinez-Rider R, Herrera-Abarca JE, Perez-Urizar J. Preemptive analgesic effectiveness of oral ketorolac plus local tramadol after impacted mandibular third molar surgery. Medicina oral, patologia oral y cirugia bucal. 2011;16(6):e776-80.

23. Kati I, Tekin M, Silay E, Huseyinoglu UA, Yildiz H. Does benzydamine hydrochloride applied preemptively reduce sore throat due to laryngeal mask airway? Anesthesia and analgesia. 2004;99(3):710-2, table of contents.

24. Hancock MJ, Maher CG, Latimer J, McLachlan AJ, Cooper CW, Day RO, et al. Assessment of diclofenac or spinal manipulative therapy, or both, in addition to recommended first-line treatment for acute low back pain: a randomised controlled trial. Lancet (London, England). 2007;370(9599):1638-43.

25. Derry S, Moore RA, Gaskell H, McIntyre M, Wiffen PJ. Topical NSAIDs for acute musculoskeletal pain in adults. The Cochrane database of systematic reviews. 2015(6):Cd007402.