ISSN: 1607-8322, e-ISSN: 2220-5799 Anaesthesia, Pain & Intensive Care
Vol 28(4); August 2024 DOI: 10.35975/apic.v28i4.2503

ORIGINAL RESEARCH REGIONAL ANESTHESIA

A comparative study of adductor canal block with infiltration of the interspace between popliteal artery and the capsule of posterior knee or with periarticular infiltration after total knee arthroplasty

Hussein A. Hassan [1], Hany M. Elzahaby [2], Ashraf E. Elagamy [3], Mohamed M. Rashed [4], Mostafa M. Hussein [5]

Author affiliations:

1. Hussein Abdelnaser Hassan Tawfik, MSc, Assistant lecturer of Anesthesia, Intensive Care & Pain Management, Faculty of Medicine, Ain Shams University, Nasr City, Cairo, Egypt; Email: hussein_tawfik@med.asu.edu.eg; {ORCID: 0009-0000-0802-8372}
2. Hany Mohamed Mohamed El-zahaby, Professor of Anesthesia, Intensive Care & Pain Management, Faculty of Medicine, Ain Shams University, Nasr City, Cairo, Egypt; Email: hanyzahaby@hotmail.com; {ORCID: 0009-0003-8363-8711}
3. Ashraf Elsayed Abdelrahman Elagamy, Professor of Anesthesia, Intensive Care & Pain Management, Ain Shams University, Nasr City, Cairo, Egypt; Email: elagamy_ashraf@yahoo.com; {ORCID: 0000-0001-6896-7662}
4. Mohamed Mohsen Mohamed Rashed, MD, Lecturer of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Nasr City, Cairo, Egypt; Email: mohsen.Mohamed1983@gmail.com; {ORCID: 0000-0001-9649-5930}
5. Mostafa Mansour Hussein Khalil, Assistant Professor of Anesthesia, Intensive Care & Pain Management, Faculty of Medicine, Ain Shams University, Nasr City, Cairo, Egypt; Email: drahmed.mostafa.mohamed@med.asu.edu.eg; {ORCID: 0000-0003-1579-2605}

Correspondence: Hussein Abdelnaser Hassan Tawfik, Email: hussein_tawfik@med.asu.edu.eg; Tel: +201011206329

ABSTRACT

Background & objective: Appropriate perioperative pain management, with multimodal analgesia regimens combining regional anesthesia and systemic analgesics, is crucial for optimum results in individuals undergoing total knee arthroplasty (TKA). We evaluated the efficacy of combined Adductor Canal Block (ACB) and infiltration in the interspace between the popliteal artery and capsule of the knee (IPACK) supplementing against ACB and Periarticular Infiltration (PAI) on postoperative pain scores, use of opioids, and early physical therapy in patients subjected to TKA under spinal anesthesia (SA).

Methodology: In the current prospective, randomized, comparative clinical trial, 40 individuals undergoing TKA were arbitrarily distributed in two groups. Group A comprised of patients undergoing ultrasound-guided ACB plus IPACK block; Group B comprised of patients undergoing ACB plus PAI block at the beginning of the surgical procedure.

Results: The ACB + IPACK group exhibited notably lower VAS scores ($P < 0.05$) compared to the ACB plus PAI group. Group A consumed 67.5 ± 21.6 mg of pethidine over the first 48 h, while Group B consumed 87.5 ± 33.9 mg of pethidine. The range of movement of the knee and walking distance also revealed that the values were considerably higher in Group A compared to Group B.

Conclusion: The utilization of both adductor canal block and the interspace between the popliteal artery and the knee capsule provides improved analgesia than adductor canal block and periarticular injection, while preserving the knee joint motor power in the postoperative period.

Keywords: Adductor canal block; IPACK; Local anesthetic; Multimodal analgesia; Pain, Postoperative; Arthroplasty

Citation: Hassan HA, Elzahaby HM, Elagamy AE, Rashed MM, Hussein MM. A comparative study of adductor canal block with infiltration of the interspace between popliteal artery and the capsule of posterior knee or with periarticular infiltration after total knee arthroplasty. Anaesth. pain intensive care 2024;28(4):620−625; **DOI:** 10.35975/apic.v28i4.2503

Received: February 10, 2024; **Reviewed:** March 13, 2024; **Accepted:** March 18, 2024

1. INTRODUCTION

The pain management strategy for total knee arthroplasty (TKA) is continuously growing in the aim of improving clinical outcomes, patient satisfaction, and reduce opioid use postoperatively.[1] Appropriate perioperative pain management, including the use of multimodal analgesia regimens combining regional anesthesia and systemic analgesics, is crucial for optimizing functional outcomes in total knee arthroplasty (TKA) patients. It promotes faster recovery and rehabilitation.[2]

Orthopedic procedures have witnessed the emergence of peripheral nerve blockade as a favored method for attaining optimal postoperative pain management. Several techniques, including ACB, sciatic nerve block, and femoral nerve block, have been studied in this regard.[3,4]

ACB, a widely used peripheral nerve block, is known for its effectiveness in reducing pain and opioid intake and has been found to affect quadriceps function.[3] Although ACB effectively targets the intra-articular and peri-patellar areas of the knee joint, it falls short in dismissing mild to severe posterior knee pain.[5]

Ultrasound-guided local anesthetic infiltration in the interspace between the popliteal artery and the posterior knee capsule (IPACK) offers effective analgesia to the posterior knee area while ensuring the common peroneal nerve remains unaffected.[6] Surgeon-performed peripheral nerve blockade (PAIs) has demonstrated practicality and viability as alternative options to conventional peripheral nerve blockade following TKA.[7]

We sought to judge the effectiveness of combining ultrasound ACB with either IPACK or PAI block on post-operative pain scale scores, opioid intake, and early rehabilitation performance in patients undergoing TKA.

2. METHODOLOGY

This prospective, double-blinded randomized study was conducted at Ain Shams University Hospitals from June 2023 to December 2023, after approval from the Ain Shams University, Faculty of Medicine, Research Ethics Committee (No. FMASU M D 154a/2022/2023) and registered with the Pan African Clinical Trial Registry under the ID number PACTR202306652234255. The study protocol was discussed with the participants and their written informed consent obtained.

2.1. Study participants

The study involved 40 patients who underwent total knee arthroplasty under spinal anesthesia. Patients under 75 years of age, both sexes, ASA I or II were selected for the study. Patient with history of hypersensitivity to local anesthetics, bleeding tendency, localized infection at the injection site, or previous neuropathy were excluded. The selected patients were randomly divided into two equal groups with a computer-generated randomization technique: Group A patients to undergo combined ACB and IPACK, and Group B to have combined ACB and PAI.

The primary outcome was the pain levels assessed using the VAS at two-hour intervals in the first postoperative 24 h, followed by four-hour intervals for the following 24 h. The secondary outcomes were the time to first rescue analgesia, total rescue analgesic use during the initial 48 h after the operation, ability to actively extend the knee, and walking distance after day-1 postoperatively.

2.2. Study Interventions

Throughout the surgical procedure, standard monitoring was used, encompassing electrocardiography, pulse oximetry (SpO_2), and non-invasive blood pressure. Prophylactic intravenous granisetron 1 mg was used to minimize postoperative nausea and vomiting (PONV). Intraoperatively, patients received sedation with midazolam 2 mg IV prior to spinal anesthesia. The participants received standard intrathecal anesthesia using 3.5 ml of hyperbaric bupivacaine 0.5%. In the event of hypotension, ephedrine 5–15 mg IV was used by slow titration.

2.2.1. Group A

Ultrasound-guided ACB was conducted at the mid-part of the thigh immediately after administering spinal anesthesia, while the patient stayed lying on their back. This procedure involved a high-frequency transducer (SonoSite™, Inc., Bothell, WA 98021, USA) to guide a 20 G SonoPlex needle and the administration of 20 ml of bupivacaine 0.25% in the adductor compartment. Next, 20 ml of bupivacaine 0.25% were used for the IPACK utilizing a SonoPlex 20 G needle, between the knee's posterior capsule and the popliteal artery while the knee was relatively flexed and externally rotated. The entire process was guided by a curved array transducer (SonoSite™, Inc., Bothell, WA 98021, USA).

2.2.2. Group B

After finishing spinal anesthesia while the patients were laid on their back, ultrasound-guided ACB was achieved. The surgical procedure concluded with the surgeon performing a PAI of the knee joint using 20 ml of bupivacaine 0.25%.

2.3. Outcome assessments

Table 1: Comparative demographic data for the two groups

Parameter		Group A (n = 20)	Group B (n = 20)	P-value
Age (y)		53.2 ± 12.2	49.8 ± 10.8	0.357[t]
Weight (Kg)		91.45 ± 6.8	90.35 ± 7.1	0.619[t]
Sex	**Male**	14 (70)	11 (55)	0.333[x2]
	Female	6 (30)	9 (45)	
ASA	**I**	10 (50)	10 (50)	0.755[x2]
	II	11 (55)	9 (45)	
Surgery time (min)		114.9 ± 7.2	113.75 ± 6.7	0.605[t]
Tourniquet time (min)		79.1 ± 4.2	78 ± 3.4	0.372[t]

Data are presented as mean ± SD or numbers (percentage); T = student t test; X^2 = chi square.

Throughout the surgery, vital data, the time of performing the block, the duration of the surgical procedure, and the tourniquet time, were recorded intraoperatively. Following the surgery, the degree of postoperative pain was evaluated according to the Visual Analogue Scale (VAS) at 2-h intervals followed by four-hour intervals for the following 24 h until the need for rescue analgesia (VAS ≥ 3). Inj. pethidine 50 mg IV was given as a rescue analgesia on SOS basis.

The ability to extend the knee joint postoperatively was measured using an electrogoniometer program, and walking distance was measured in steps after 1 day postoperatively.

2.4. Statistical analysis

The sample size was determined with PASS 11.0, taking into consideration a previous study by Amer.[9] This sample size configuration was determined to provide 99% power to identify a difference of 11.0 between the mean of 32.4 assumed under the null hypothesis for both groups and the alternative hypothesis that the mean of Group 2 was 21.4, Employing a two-sided, two-sample t-test, we analyzed the data while considering the estimated group standard deviations of 3.2 and 2.8, as well as a significance level of 0.005. A 20% inflation was applied to the sample size to adjust for attrition issues expected in prospective studies.

For analyzing the data, the SPSS version 27.0 was used. Qualitative data relied on the use of frequency and percentage to convey information about the date, while quantitative data utilized mean ± standard deviation (SD) or median (interquartile range, IQR) to express numerical values. Independent-sample t-test was used to evaluate the significance of the difference between the two means. Chi-square (X2) test was used to evaluate proportions between two qualitative parameters. Mann-Whitney U test was employed to compare two groups within the framework of non-parametric data. A confidence interval of 95% was chosen, with an accepted margin of error of 5%. P < 0.05 signified statistical significance.

Table 2: Comparative VAS scores in both groups

Time (h)	Group A (n = 20)		Group B (n = 20)		P-value z
	Range	Median (IQR)	Range	Median (IQR)	
0	0-2	0 (0-1)	0-2	1 (1-1)	**0.002**
2	0-2	1.5 (1-2)	1-3	2 (2-3)	**0.0002**
4	0-2	0 (0-1)	1-4	3 (2.5-4)	**< 0.0001**
6	0-2	1.5 (1-2)	1-3	2 (2-3)	**0.0015**
8	0-2	0 (0-1)	1-4	2 (2-3)	**< 0.0001**
10	0-2	1.5 (1-2)	1-3	2 (2-3)	**0.0015**
12	1-3	2 (2-3)	2-4	3 (2-3)	**0.0205**
14	1-3	2 (2-3)	1-4	3 (3-4)	**0.0005**
16	1-3	2 (2-3)	1-4	3 (2.5-4)	**0.0015**
18	1-3	2 (2-3)	1-3	2 (2-3)	0.6572
20	1-3	2 (2-3)	1-3	2 (2-3)	0.4894
22	2-4	3 (3-3)	1-4	3 (3-4)	0.4657
24	2-4	3 (3-4)	2-5	4 (3-4)	0.0693
28	3-4	3 (3-4)	2-5	4 (3-4)	0.0751
32	2-4	3 (3-4)	2-5	4 (3-4)	0.2121
36	2-4	3 (3-4)	3-4	3.5 (3-4)	0.0714
40	2-4	3 (3-3.5)	2-4	3 (3-4)	0.2126
44	2-4	3 (3-4)	2-5	3.5 (3-4)	0.2309
48	2-4	3 (3-4)	2-4	4 (3-4)	0.0906

Data are presented as median (range) and IQR, z= Mann-Whitney test.

Table 3: Comparing time for the first rescue analgesia and total dose of rescue analgesia in the first 24 h

Variable	Group A (n = 20)	Group B (n = 20)	P-value t
Time for the first rescue analgesia in first 24h (h)	15.8 ± 2.5	11.75 ± 1.5	**< 0.001**
Total dose of rescue analgesia (mg)	67.5 ± 21.6	87.5 ± 33.9	**0.032**

Data presented as mean ± SD, t = student t test

3. RESULTS

Of the 67 patients planned for total knee arthroplasty, 40 individuals participated in the study and were divided equally into two groups. The two groups revealed comparable demographic data (Table 1).

The main findings of this study showed that patients receiving ACB combined with IPACK revealed superior pain control, as the VAS score in the first 16 h postoperatively ranged 0–3 in Group A and 0–4 in Group B ($P < 0.05$) (Table 2).

Regarding the time to first rescue analgesia in the first 24 h, Group A had a longer duration than Group B (Table 3).

Also, the cumulative dosage of recue analgesia was less in Group A (67.5 ± 21.6 mg) compared to Group B (87.5 ± 33.9 mg) (Table 3).

The ability of the patient to extend the knee actively after 24 h postoperatively was better in Group A (29.15 ± 4.3 degree) compared to Group B (18.45 ± 3.9 degree) (Table 4).

The walking distance achieved after 24 h between both groups was compared, and a statistical distinction existed between them; it was better in Group A ($P < 0.001$) (Table 4).

4. DISCUSSION

The chief outcome of the current study is that ACB and IPACK blocks exhibit a superior analgesic efficacy compared to ACB and PAI blocks. The increasing number of total knee arthroplasty procedures performed worldwide in recent years has shed light on the need to develop efficient approaches for managing pain in patients experiencing these surgical procedures. A range of pain management treatments have developed, with peripheral nerve- blocking approaches gaining prominence in recent years.

ACB, commonly employed in knee surgeries, is a highly effective peripheral nerve block that facilitates both proper pain relief and early postoperative mobility by preserving the quadriceps muscle.[10] However, the ACB's analgesic effects are limited to the front portion of the knee, as it does not affect the deep genicular neurons responsible for relaying sensory information from the backside of the knee joint.

IPACK is a procedure that entails injecting a local anesthetic in the region situated between the posterior capsule and the popliteal artery and this effectively blocks the deep genicular nerves responsible for providing sensation to the back part of the knee joint. The method consists of carefully blocking only the sensory nerves located in the knee's posterior region,

specifically avoiding any impact on the motor function associated with the peroneal and tibial nerves' branches. This approach effectively reduces pain while preserving muscle strength.[11]

The present study estimated the pain score utilizing the visual analogue scale, cumulative pethidine usage during the initial 48 h after TKA, and time for first rescue analgesia, and the findings consistently revealed superior pain control in the ACB + IPACK block group in comparison with the ACB + PAI group.

Several studies resembling ours have been conducted.

Table 4: Comparative analysis of the activity after the treatment

Activity	Group A (n = 20)	Group B (n = 20)	P-value
Patient's capacity for active knee extension in first 24 h (degrees)	29.15 ± 4.3	18.45 ± 3.9	**< 0.0001 t**
Distance walked (steps)	8.1 ± 1	6.25 ± 1	**< 0.001**

Data presented as mean ± SD, T = student t-test

For instance, Jung et al. compared the opioid intake and pain scores between consecutive patients undergoing ACB + IPACK to previous consecutive patients who received ACB + PAI.[12] During the first and second days following TKA, they noticed that ACB+IPACK patients exhibited reduced VAS relative to the ACB+PAI group. However, no change in total opioid consumption was noted among groups.

A study by Tayfun et al. found that individuals receiving both ACB and IPACK exhibited shorter hospital stays, faster mobilization, reduced pain, and fewer opioid demands.[13] The study additionally showed that the group receiving both ACB and IPACK exhibited significantly improved knee extension ability and better walking distance within the initial 24 h compared to the ACB + PAI group.

Also, Sankineani et al. found that patients getting ACB plus IPACK had a substantially increased walking distance and range of motion, along with lower VAS scores immediately after TKA than those undergoing ACB alone.[14]

Kertkiatkachorn et al. accomplished a randomized controlled experiment to examine the effectiveness of continuous ACB in combination with PAI +ACB + IPACK. The findings of their study indicated that patients receiving ACB and IPACK exhibited pain levels comparable to those in the control group.[15] However, they experienced decreased quadriceps strength on the first day following the surgery and necessitated increased morphine intake 48 h following TKA.

In contrast to the current findings, Patterson et al. indicated that the utilization of IPACK alongside ACB resulted in decreased pain scores immediately after surgery but did not provide any advantages in terms of pain relief during subsequent pain assessments. Additionally, they observed no substantial variance in opioid demands.[16]

In a comparative study by Elliot et al., the effectiveness of ACB and IPACK was evaluated in patients undergoing TKA, comparing them to IPACK and FNB.[17] The findings showed that while the ACB and IPACK groups had a shorter hospitalization period, there were no notable disparities in visual analogue scale scores or opioid utilization between both groups.

Considering the documented outcomes, the ACB and IPACK benefits remain uncertain, particularly when considering the feasibility and practicality of this intricate and time- intensive methodology. Furthermore, differences in PAI procedures, such as injection location, infiltration volume, variant combinations of injection cocktails, and injection timing, can result in various effects.[18] However, the outcome of PNB may be dependent on the clinical circumstances and operator expertise, despite the ultrasound guidance utilization, which is expected to enhance success rates and minimize the risk of nerve damage.[19]

5. LIMITATIONS

This study has several limitations. Firstly, it was a prospective study with a limited sample size. To mitigate the effect of confounding factors, a senior surgeon performed the procedures and a senior anesthesiologist adhered to conventional protocols for the nerve blocks.

6. CONCLUSIONS

To conclude, the ACB and IPACK combined technique provides a superior analgesic consequence than ACB and PAI during the postoperative period while preserving the knee joint's motor power. Furthermore, this combined technique offers an enhanced range of motion and an extended walking distance in comparison with ACB and PAI.

7. Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

8. Competing interests

The authors declare that there were no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

9. Ethics considerations

The study received approval from the Ain Shams University, Cairo, Egypt faculty of medicine's research ethics committee (FMASU M D 154a/2022/2023) and registered with the Pan African Clinical Trial Registry under the ID number PACTR202306652234255. The study protocol was thoroughly clarified to the participants before they provided their written informed consent.

10. Future scope

The integration of ACB+IPACK blocks into routine clinical practice can enhance the quality of care provided to patients undergoing total knee arthroplasty.

12. Authors' contribution

All authors have contributed intellectually to the manuscript and the manuscript has been read and approved by all the authors. All authors read and approved the final manuscript.

9. REFERENCES

1. Lamplot JD, Wagner ER, Manning DW. Multimodal pain management in total knee arthroplasty. J Arthroplasty.

2014;29(2):329–334. [PubMed] DOI: 10.1016/j.arth.2013.06.005

2. Korean Knee Society. Guidelines for the management of postoperative pain after total knee arthroplasty. Knee Surg Relat Res. 2012;24(4):201–207. [PubMed] DOI: 10.5792/ksrr.2012.24.4.201
3. Li D, Ma GG. Analgesic efficacy and quadriceps strength of adductor canal block versus femoral nerve block following total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2016;24(8):2614–2619. [PubMed] DOI: 10.1007/s00167-015-3874-3
4. Soltesz S, Meiger D, Milles-Thieme S, Saxler G, Ziegeler S. Intermittent versus continuous sciatic block combined with femoral block for patients undergoing knee arthroplasty. A randomised controlled trial. Int Orthop. 2016;40(9):1861–1867. [PubMed] DOI: 10.1007/s00264-016-3117-3
5. Laoruengthana A, Rattanaprichavej P, Rasamimongkol S, Galassi M. Anterior vs posterior periarticular multimodal drug injections: a randomised, controlled trial in simultaneous bilateral total knee arthroplasty. J Arthroplasty. 2017;32(7):2100–2104. [PubMed] DOI: 10.1016/j.arth.2017.02.033
6. Sinha SK, Abrams JH, Arumugam S, D'Alessio J, Freitas DG, Barnett JT, et al. Femoral nerve block with selective tibial nerve block provides effective analgesia without foot drop after total knee arthroplasty: a prospective, randomised, observer-blinded study. Anesth Analg. 2012;115(1):202–206. [PubMed] DOI: 10.1213/ANE.0b013e3182536193
7. Kehlet H, Andersen LØ. Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practise. Acta Anaesthesiol Scand. 2011;778–784. [PubMed] DOI: 10.1111/j.1399-6576.2011.02429.x
8. Bringuier S, Dadure C, Raux O, Dubois A, Picot MC, Capdevila X. The perioperative validity of the visual analogue anxiety scale in children: a discriminant and useful instrument in routine clinical practise to optimise postoperative pain management. Anesth Analg. 2009;109:737. [PubMed] DOI: 10.1213/ane.0b013e3181af00e4
9. Amer N. Combined adductor canal and i-PAK blocks are better than combined adductor canal and periarticular injection blocks for painless ACL reconstruction surgery. J Anesth Clin Res. 2018;10(4):154–157. DOI: 10.15406/jaccoa.2018.10.00381
10. Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomised, controlled trial. Anesthesiology. 2014;120(3):540–50. [PubMed] DOI: 10.1097/ALN.0000000000000119
11. Cullom C, Weed JT. Anesthetic and analgesic management for outpatient knee arthroplasty. Curr Pain Headache Rep. 2017;21(5):23. [PubMed] DOI: 10.1007/s11916-017-0623-y
12. Jung DW, Shon WY, Seo SS, Kim OG, Lee IS. Comparison of the postoperative analgesic effect for infiltration between the popliteal artery and the capsule of the posterior knee and that of periarticular multimodal drug injection in total knee arthroplasty: retrospective study in the immediate postoperative period. Knee Surg Relat Res. 2020;32(1):1-9. [PubMed] DOI: 10.1186/s43019-019-0025-z
13. Et T, Korkusuz M, Basaran B, Yarımoğlu R, Toprak H, Bilge A, et al. Comparison of IPACK and periarticular block with adductor block alone after total knee arthroplasty: a randomised clinical trial. J Anesth. 2022;36:276–286. [PubMed] DOI: 10.1007/s00540-022-03047-6
14. Sankineani SR, Reddy ARC, Eachempati KK, Jangale A, Gurava Reddy AV. Comparison of adductor canal block and IPACK block (interspace between the popliteal artery and the capsule of the posterior knee) with adductor canal block alone after total knee arthroplasty: a prospective control trial on pain and knee function in immediate postoperative period. Eur J Orthop Surg Traumatol. 2018;28(7):1391–1395. [PubMed] DOI: 10.1007/s00590-018-2218-7
15. Kertkiatkachorn W, Kampitak W, Tanavalee A, Ngarmukos S. Adductor canal block combined with IPACK (interspace between the popliteal artery and the capsule of the posterior knee) block vs periarticular injection for analgesia after total knee arthroplasty: a randomised noninferiority trial. J Arthroplasty. 2021;36(1):122–129. [PubMed] DOI: 10.1016/j.arth.2020.06.086
16. Patterson ME, Vitter J, Bland K, Nossaman BD, Thomas LC, Chimento GF. The effect of the IPACK block on pain after primary TKA: a double-blinded, prospective, randomized trial. J Arthroplasty. 2020;35(6S):S173-S177.. [PubMed] DOI: 10.1016/j.arth.2020.01.014
17. Elliott CE, Myers TJ, Soberon JR. The adductor canal block combined with IPACK improves physical therapy performance and reduces hospital length of stay (Abstract 197). 40th Annual Regional Anaesthesiology and Acute Pain Medicine Meeting (ASRA), in Las Vegas, Nevada. 2015;14–16.
18. Andersen LO, Husted H, Otte KS, Kristensen BB, Kehlet H. High-volume infiltration analgesia in total knee arthroplasty: a randomised, double-blind, placebo-controlled trial. Acta Anaesthesiol Scand. 2008;52(10):1331–1335. [PubMed] DOI: 10.1111/j.1399-6576.2008.01777.x
19. Verlinde M, Hollmann MW, Stevens MF, Hermanns H, Werdehausen R, Lirk P. Local anaesthetic-induced neurotoxicity. Int J Mol Sci. 2016;17(3):339. [PubMed] DOI: 10.3390/ijms17030339

