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Continuous femoral nerve block enhances outcome of spinal anaesthesia in preventing perioperative cardiac complications in patients with cardiac risk

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ABSTRACT

Background: Elevated brain natriuretic peptide (BNP) is crucial to detect perioperative adverse cardiovascular events in patients with cardiac risk, even at low elevation of BNP level or when myocardial necrosis has not been already established. This study aims to compare between two anaesthesia methods in preventing perioperative myocardial infarction for patients having cardiac risk undergoing total knee arthroplasty (TKA).

Patients and methods: Fifty adult patients planned for TKA with risk factors as ischemic heart disease, diabetics, hypertensive, heavy smokers or body mass index ≥ 35 were categorized randomly into two groups. Group (S): received spinal anaesthesia followed by continuous ultrasound guided femoral nerve block once spinal motor blockade had been resolved. Group (G): received combined general and lumber epidural anaesthesia. BNP, cardiac troponins, pain severity, analgesic consumption, patients' satisfaction and adverse cardiac events were observed preoperatively and extended to 2 days postoperatively.

Results: Baseline readings of BNP and cardiac troponins were comparable in both members. At 24 and 48 hours postoperatively, it decreased significantly in group S compared to group G. Mean Visual analogue score was significantly lower in group S comparative to group G at all times except at 40 and 48 hours postoperatively. Morphine utilization was significantly lower in group S. Patients in group S were significantly more satisfied than those in group G.

Conclusions: The use of spinal anaesthesia with continuous femoral nerve block can reduce the prevalence of perioperative myocardial infarction in patients with cardiac risk undergoing TKA.

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BNP; cardiac troponin; myocardial infarction; TKA

1. Introduction

Despite great progress in surgical and anaesthesia approaches, perioperative myocardial ischemia (MI) is still among the severest burden facing anaestheologists during this period, especially in vulnerable group of patients with cardiac risks like CAD [1,2]. Besides the fact that perioperative ischemia is popular chief forecaster of various cardiac events like unstable angina and sudden death, it accounts for hospital mortality rates up to 25% [3]. This could be explained on the basis of difficulty in recognizing perioperative MI, as the classical clinical presentation and the ordinary ECG derangements are always obscured. Moreover, serum markers of MI like creatine kinase brain isoenzyme (CK-MB) and cardiac troponin don't vary significantly meanwhile [4,5].

Troponins are a group of peculiar cardiac enzymes that entails three subunits I, C and T. They are found in every striated muscle, set on the actin filaments and coordinates muscular contraction in a voltage charged manner. Particular gene encodes for troponin **I** and is considered a highly exclusive pointer for myocardial insult in adults [6,7].

Also, brain natriuretic peptide (BNP) is released largely from the myocardial myocytes in reaction to ventricular wall stress, volume overload or myocardial ischemia [8]. Its effects are mediated through escalation of intracellular cyclic guanosine 3′,5′-monophosphate, with a resultant diuresis, natriuresis, arterial and veno dilatation. Moreover, it impedes fibroblast generation, myocardial hypertrophy and decreases diastolic velocity. Several advances reported its predictive value in estimating cardiac insult even without cardiac necrosis [9,10].

Total knee arthroplasty (TKA): a popular surgical practice accompanied with significant level of postoperative pain. Untreated pain is accompanied by medical complications, increased cardiac burden in patients with low cardiopulmonary reserve, increased efforts and elevated expenses. Different anaesthesia methods do not have the same effects regarding their efficacy in suppressing this stress and reducing associated perioperative myocardial insult [11–13].

There are few publication demonstrating the prognostic benefit of regional anaesthesia in abolishing the imposed surgical stress in patients with cardiac risk [14,15].

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The purpose of the current study is to verify if extension of spinal anaesthesia with postoperative ultrasound guided femoral nerve block could decrease perioperative MI in patients with cardiac risk scheduled for TKA comparing with combined general anaesthesia and lumber epidural.

2. AIM of the study

The primary endpoint was evaluating the influence of two anaesthesia methods on perioperative levels of cardiac troponins and BNP in patients with cardiac risk undergoing TKA to clarify which of these methods could preclude perioperative MI. Secondary outcomes included postoperative pain assessment using visual analogue scale, total analgesic consumption, patient satisfaction and cardiovascular complications (myocardial infarction, arrhythmias, heart failure, hypotension, hypertension and the need for perioperative inotropic agents).

3. Patients and methods

This randomized, comparative study was performed at Alexandria University hospitals, after attaining local ethical committee approval and patients' written consent following full explanation of the whole procedure. Registration in Clinical Trials. gov (NCT05340946) was done before the start of the study.

Inclusion criteria include: patients having concurrent or with known risk of coronary artery disease (CAD), scheduled for unilateral total knee arthroplasty. Established of CAD was ascertained by history taking and verification of typical or atypical angina with aid of several diagnostic tools like a positive stress test and ECG finding. Risks for CAD included; age (> 65 years old), chronic hypertension, BMI > 35 kg/m^2, heavy smokers, serum cholesterol level exceeding 240 mg/dL, and uncontrolled diabetes mellitus. Exclusion criteria included the following conditions:

- Patient refusal.
- Diminished visual acuity.
- Pre-existing neurological, dementia, or neuropsychological disease.

- Marked reduction of left ventricular ejection fraction < 40%.
- Severe valvular heart disease ± decompensated heart failure.
- Renal failure requiring hemodialysis, or hepatic insufficiency.
- Contraindications to medication used in the current study.
- Hinders to regional blocks (local infection at injection site, and concurrent use of an antiplatelet drugs).
- Patients with abnormal coagulation or bleeding disorders.

No premedication was given preoperatively to either group, and all patients were allowed to fast according to standard guidelines for preoperative fasting during anaesthesia practice. Antihypertensive and anti-anginal drugs was continued till the day of operation. The operative risk was assessed using Lee index by a cardiologist [11]. Also, all patients were taught on how to use the ten cm linear visual Analogue scale (VAS), with o = pain free, while 10 = the worst intractable pain.

A total of 50 patients with American society of Anesthesiologists (ASA) physical status II, of both sexes who fulfilled the selection criteria were randomly recruited utilizing closed envelope method to one of two groups (25 patient) each:

- Group G (n = 25 patient): received combined general and lumber epidural anaesthesia.

- Group S (n = 25 patient): received spinal anaesthesia. Once the spinal anaesthesia-induced motor blockade had resolved, continuous ultrasound-guided femoral nerve blockade was activated for postoperative analgesia.

On arrival to the operating theatre, I.V line was inserted. A venous sample was taken just before induction of anaesthesia as a baseline value for serum troponin and BNP in both groups, then patients were preloaded with infusion of 10–12 ml /kg of ringer's lactate solution. All standard monitoring was applied prior to induction to both groups; included ECG, invasive blood pressure (IVBP), pulse oximetry (spo_2), in addition to end tidal CO_2 in group (G).

4. Anaesthesia technique

For group (G): before anaesthesia induction, an epidural catheter was sited at the L3 _ L4 intervertebral space using local anaesthesia, through median approach utilizing loss of resistance technique. 3 mL test dose Lidocaine 1.5% was used to rule out intrathecal or intravascular siting of the catheter. After 3 minutes interval, activation of epidural anaesthesia was done by a bolus mixture of 10–20 mL of 0.25% bupivacaine and 2 µg /kg fentanyl. Somatosensory blockade was evaluated using ice pages and pinprick test. Induction of general anaesthesia then followed- after pre-oxygenation period for 3 minutes with 100% oxygen- by fentanyl 1–1.5 µg/kg, lidocaine 1.5 mg/kg and 1–1.5 mg/kg propofol in increments of each 10 mg till loss of consciousness. Endotracheal intubation was established by aid of cisatracurium 0.15 mg/kg. Maintenance of anaesthesia was through isoflurane

1–1.5% with 50% oxygen in air, increments of i.v fentanyl 0.5 µg/kg for analgesia if heart rate or systolic blood pressure was increased by more than 20% of the pre-induction level, plus incremental dose of cisatracurium 0.03 mg/kg to maintain muscle relaxation according to nerve stimulation. Mechanical ventilation was set to maintain $ETCO_2$ between 32 – 35 mmHg and an oxygen saturation of 98%. At the end of surgery anaesthesia was discontinued and 100% oxygen was provided. Muscle relaxation were vanished using neostigmine 0.04–0.08 mg/kg and atropine 0.02 mg/kg. After regain of patients' airway reflexes and appropriate muscle strength, oral secretions were suctioned and extubation was done fully awake. Post-operative analgesia was started through activation of epidural blockade by a solution mixture of 10–20 mL 0.125% bupivacaine with 2 µg/kg fentanyl by a rate 6–10 mL /hr.

For group (S): patients received spinal anaesthesia using 25 gauge spinal needle-through L3-L4 interspace- and via median approach with a bolus 10–15 mg hyperbaric bupivacaine 0.5% and 25 µg fentanyl. In case of failed spinal anaesthesia, patient was omitted from the study. At the end of the surgical procedure and wound dressing, patients were shifted to post-anesthesia care unite (PACU). Once the spinal-provoked motor blockade was completely resolved, continuous ultrasound-guided femoral nerve blockade was established under strict aseptic condition. In the supine position, via the in-plane approach and through the longitudinal alignment of the transducer with the femoral nerve lying perpendicularly, the needle was introduced until the injection site was determined, where 15 ml bupivacaine boluses 0.25% was injected, then the catheter was proceeded along the needle and sited inferiorly relative to the femoral nerve. After withdrawing the needle, proper catheter position was ascertained by injection of 2–3 ml normal saline with real-time ultrasound vision, then infusion of 0.125% bupivacaine was started with a rate 6–10 ml/hr.

Precise fluid replacement was provided to all participants following the standard guidelines applied during anaesthesia. Perioperative hypothermia was aborted by warming of i.v fluids and forced air warming. Other Perioperative events like hypotension, hypertension, desaturation and arrhythmia which might aggravate MI were identified early and managed properly.

In the PACU, patients were observed for continuous ECG monitoring with automated ST segment display using lead II and V_5, central venous pressure, pulse oximetry (SPO_2) and continuous invasive blood pressure for 48 hrs. Peripheral venous blood samples for BNP and cardiac troponin, were obtained preoperatively just before induction of anaesthesia (as a baseline value), at the end of the surgical procedure, after 24 and 48 hrs postoperatively. We used commercially available kits (Triage Brain natriuretic peptide, Biosite; France), (Troponin I Immunassay, Biosite; Germany) respectively. verification of methods and degrees of sample concentrations was done before sample assessment, and according to the accompanied instructions; for plasma BNP using immunoassay ELISA, a reference sample exceeding 80 pg/ml was referred as significance of hormonal stimulation in patients with CAD [16], plasma Troponin T was assessed via the electrochemiluminescence immune assay (ECLIA) with Elecsys immunoassay analyser, considering a significant value of less than 0.03 $ngLmL^{-1}$ [17].

Postoperative Visual Analogue Score (VAS) was assessed every 6 hrs in the first 24 hrs postoperatively, then every 8 hrs in the second day postoperatively. Rescue analgesia was in the form of 2 mg i.v bolus of morphine if VAS remained > 4, up to maximum of 10 mg/8hrs. Also, patients' satisfaction, need for rescue analgesia, total dose of postoperative morphine consumption and occurrence of any adverse cardiac events were recorded for each group at the end of the second day postoperatively.

Any decline in systolic blood pressure within 20% below base-line value was defined as hypotension and managed with 5–10 mg boluses of i.v ephedrine and 5 ml/ kg saline infusion, which was repeated if needed. Desaturation was defined as an oxygen saturation below 94% and was treated by increasing FIO_2. Patient satisfaction were noted on a four-point scale of "completely dissatisfied" to "completely satisfied" as follows: completely dissatisfied, dissatisfied, satisfied, and completely satisfied.

5. Statistical Analysis

Calculation of sample size was done with reference to a previous study on cardiac patients with CAD risk factors undergoing lower limb surgeries, assessing the results of three different anaesthesia techniques on the level of brain natriuretic peptide [18]. Consequently, a 25 for each research group sample size was approximated achieving minimum 80% power ($\alpha = 0.05$) to identify at least a change of 30%.

Analysis of data was achieved using SPSS soft ware package version 19 (Armonk; NY: IBM Cop.). Numerical quantitative l data were stated as mean ± standard deviation (SD). Categorical qualitative data were verified utilizing case number and percent (Fisher-exact X_2 test was utilized whenever feasible). Unpaired (t) test besides analysis of variance (ANOVA) was used for unpaired numerical variables was analyzed using. A (P) Value of ≤ 0.05 was judged as significant level. Moreover, ≤ 0.01 was counted highly significant.

6. Results

Fifty five patients were initially involved, five of them were soon dismissed as they did not fulfill the inclusion criteria. They were assembled randomly into two identical groups (Figure 1). Age, weight, sex, cardiac risk factors, length of surgery and anaesthesia were similar in all participants.

No statistically significant difference was noticed in the levels of brain naturitic peptide (pg/ml) and cardiac troponin I (pg/ml) measured preoperatively and at the end of surgery between both groups. However, their levels decreased significantly in group S after 24 hrs and 48 hrs postoperatively as shown in (Table 1).

Postoperative mean visual analog scale (VAS) was significantly lower in group S at the following time points: 6, 12, 18, 24 and 32 hours respectively (P = 0.034*, 0.021*, 0.043*, 0.045*, 0.04* respectively). However, no statistically significant difference was observed between both groups at 40 and 48 hours postoperatively (P = 0.424, 0.298 respectively) as shown in (Table 2).

Also, participant who requested extra doses of analgesia were significantly higher in group G than those in group S (p = 0.006*). Moreover, the mean doses of rescue morphine was significantly lower in group S comparable to group G (p = 0.043*) as shown in (table 3).

Members of group S were more significantly satisfied relative to those of group G (p = 0.05*) as shown in (Figure 2).

Finally adverse cardiac events- at the end of the second day postoperatively -varied significantly, being higher in group G comparable to group S (p = 0.04*) (Figure 3).

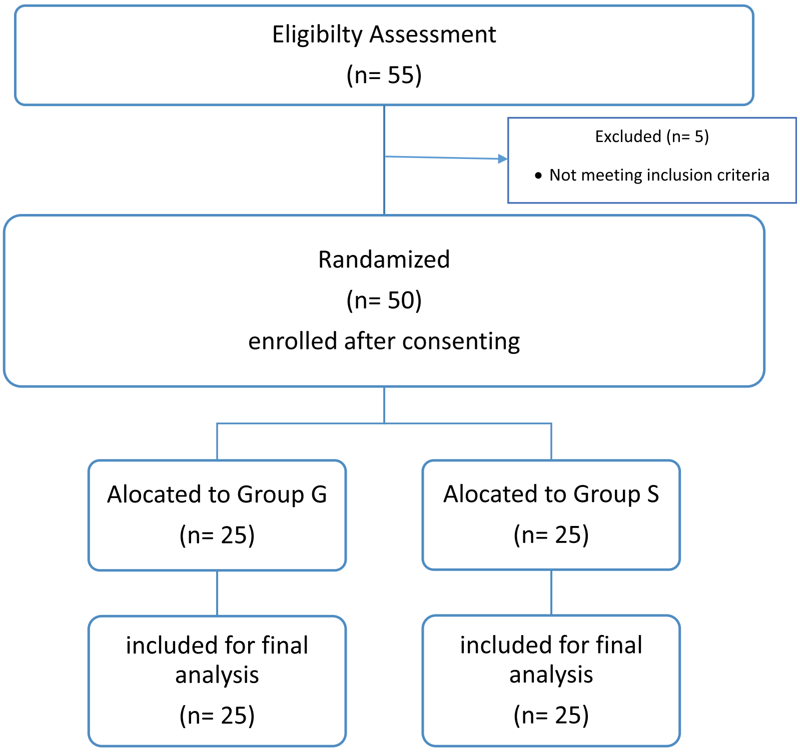

Figure 1. Study Flow Chart.

Table 1. Comparison between 2 studied groups according to levels of BNP and cardiac troponin.

Parameter	Time	Group	Mean ± S.D.	P-value
BNP (pg/ml)	PREOPERATIVE	GP G	45.59 ± 15.09	0.467
		GP S	45.92 ± 12.35	
	END OF SURGERY	GP G	59.48 ± 15.87	0.339
		GP S	57.77 ± 11.74	
	POSTOP. DAY 1	GP G	85.164 ± 14.13	0.042*
		GP S	77.96 ± 14.21	
	POSTOP. DAY 2	GP G	83.60 ± 16.06	0.037*
		GP S	75.476 ± 14.86	
CARDIAC TROPONIN (pg/ml)	PREOPERATIVE	GP G	26.28 ± 8.55	0.095
		GP S	23 ± 8.62	
	END OF SURGERY	GP G	217.24 ± 36.8	0.467
		GP S	218.12 ± 37.98	
	POSTOP. DAY 1	GP G	289.76 ± 55.7	0.006*
		GP S	243.12 ± 68.18	
	POSTOP. DAY 2	GP G	255.24 ± 55.63	0.004*
		GP S	210.2 ± 59.22	

*p: significant if ≤ 0.05.
Data presentation: as mean ± standard deviation.

Table 2. Comparison between 2 groups according to postoperative (VAS).

Time	Group G	Group S	P- value
6 Hrs Postoperative	6.48 ± 1.3	5.72 ± 1.51	0.034*
12 Hrs Postoperative	5.08 ± 1.15	4.36 ± 1.26	0.021*
18 Hrs Postoperative	3.96 ± 1.15	3.4 ± 1.06	0.043*
24 Hrs Postoperative	3.4 ± 1.2	2.8 ± 1.2	0.045*
32 Hrs Postoperative	1.84 ± 0.88	1.36 ± 0.97	0.04*
40 Hrs Postoperative	0.76 ± 0.76	0.72 ± 0.66	0.424
48 Hrs Postoperative	0.4 ± 0.57	0.32 ± 0.47	0.298

*p is significant if $\leqslant 0.05$.
Data were presented as mean ± standard deviation.

Table 3. Comparison between 2 studied groups revealing number of patients who needed doses of rescue analgesics and mean dose of rescue morphine.

	Group G		Group S		
	No	%	No	%	*P*-value
No dose	2	(8)	10	(40)	0.006*
1 dose	3	(12)	6	(24)	
2 doses	5	(20)	4	(16)	
3 doses	7	(28)	3	(12)	
4 doses	8	(32)	1	(4)	
Mean dose of rescue morphine (mg)	33		13.5		0.043*

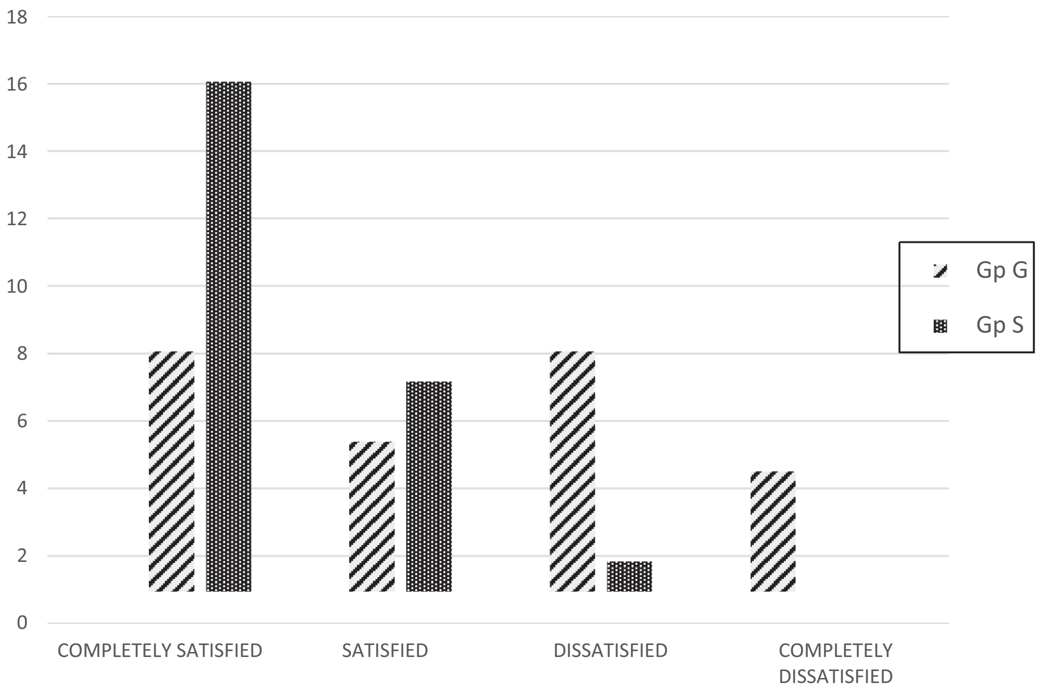

Figure 2. Graph showing patient satisfaction scale between the two studied groups.

7. DISCUSSION

The present study revealed no statistically significant difference between the comparable groups in the levels of brain naturitic peptide and cardiac troponin I measured preoperatively and at the end of surgery. However, they were significantly less in patients received spinal anaesthesia and ultrasound -guided femoral nerve blockade at postoperative day 1 and 2. These findings support that the technique using spinal anaesthesia augmented by continuous ultrasound-guided femoral nerve blockade was most efficient in preventing perioperative cardiac insult. The underlying mechanism may be attributed to blocking nociceptive signals by regional anaesthesia in patients with cardiac risk modulated the neurohormonal response more efficiently in a way that led to superior pain control

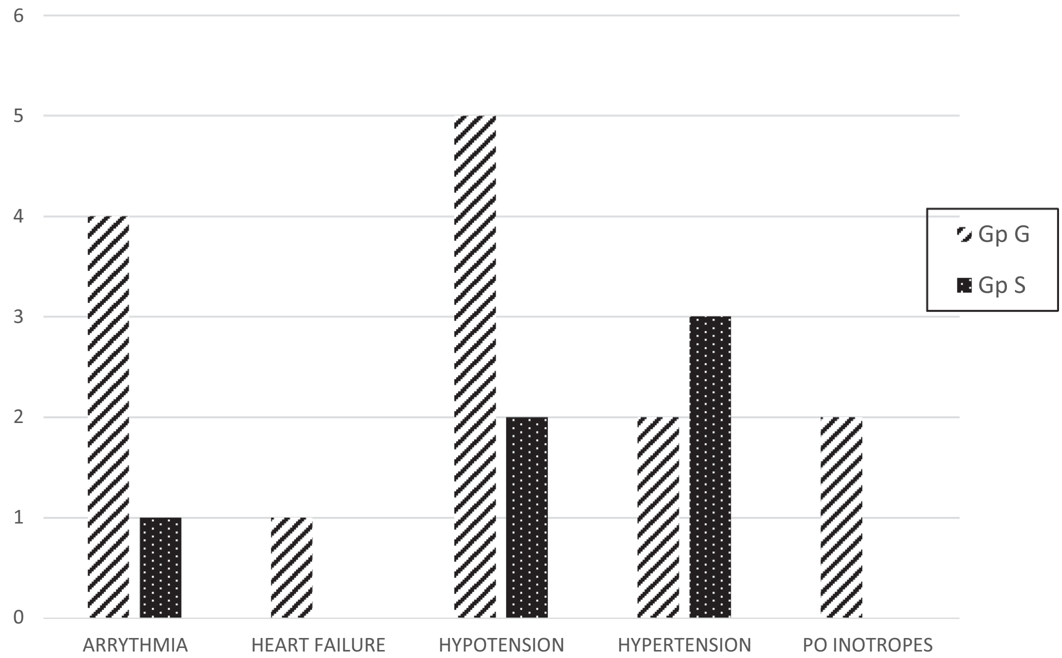

Figure 3. Graph showing comparison between the 2 studied groups according to adverse cardiac events at the end of the second day postoperatively.

and decreased release of BNP more promptly, thereby preventing episodes of transient myocardial ischemia and ventricular wall stress [19–22].

Several studies had checked the deep association between the increased plasma BNP and cardiac Troponins levels with the extent and seriousness of perioperative ischemic cardiac insult even in absence of obvious myocyte necrosis [23].

Atalay et al. [18] in their research on cardiac patients having CAD risk factors who underwent lower limb surgical procedures, reported lower levels of plasma BNP for patients in group T; received combined general anaesthesia and thoracic epidural anaesthesia-analgesia together with i.v patient- controlled analgesia (PCA), in comparison with patients in group G; received general anaesthesia with postoperative PCA and with patients in group L; received lumbar epidural anaesthesia. They concluded that local anesthetics and opioids could augment the clear influences of the thoracic epidural anaesthesia- analgesia.

Sahar et al. [22] investigated the effects of anaesthesia techniques on systemic inflammatory response and release of cardiac troponins after major abdominal surgeries. They concluded that combined general and lumbar epidural anaesthesia is accompanied by less perioperative acute inflammatory response in comparison with patients received general anaesthesia only.

Rodseth et al. [24] reported that increased levels of BNP in non-surgical patients were considered reliable prognostic marker to detect asymptomatic myocardial injury without obvious ECG changes.

In our study, postoperative (VAS) was significantly lower in group S at 6, 12, 18, 24 and 32 hrs . However, no statistically significant differences was reported between both groups at 40 and 48 hrs. Consequently, participants who required rescue doses of analgesics in group G was significantly higher than group S.

In hands with the present study, Paul et al. [25] conducted a systematic review assessing the analgesic outcomes of femoral nerve blockade ± sciatic nerve blockade with epidural neuraxial anaesthesia and PCA. They reported that femoral nerve blockade was excellent for postoperative-analgesia.

In line with our results, Amiri et al. [26] confirmed that the femoral nerve blockade following spinal anaesthesia has a beneficial effect and can lengthen the duration of postoperative analgesia, in comparison with patients received lumbar plexus block scheduled for intertrochanteric surgeries.

In against to our findings, Sundarathiti et al. [27] evaluated the consequences of continuous epidural anaesthesia versus continuous femoral nerve blockade in 61 patients planned for total knee arthroplasty surgeries under spinal anesthesia. They concluded that epidural anaesthesia- analgesia is more beneficial than continuous femoral blockade in enhancing postoperative analgesia.

In our study, patients were more significantly satisfied in group S than group G.

In support of our results, Pagnotto and Pagnano [28] reported that pain control strategies including nerve block techniques could provide better patients satisfaction after TKA surgeries.

In contrast to our results, de Matos et al. [29] conducted unblended, randomized study on 60 patients underwent TKA using continuous epidural analgesia versus continuous ultrasound guided femoral nerve blockade. They concluded that patients received continuous ultrasound guided femoral nerve blockade had the same level of satisfaction as those belonging to the epidural group after total knee arthroplasty.

Davis et al [30]. in their study evaluating combined sciatic and femoral nerve block versus epidural anaesthesia effects on postoperative pain control after TKA surgeries noted that patients' satisfaction didn't vary significantly between both groups.

Concerning adverse cardiac events in our study at end of second day postoperatively, no patient developed myocardial infarction in both groups, however, other minor but limited complications as hypotension, arrhythmias, and hypertension are significantly higher in group G. This is not surprising and can be related to the close relation between the higher level of BNP in group G and the greater incidence of perioperative cardiac events.

An imaginable drawback of this study is the limited sample size and the stable cardiac condition of the participants, which was associated with low incidence of adverse cardiac events and subsequently low power of analysis. Additionally, opioids and local anaesthetic used may also contributed to the positive impact of the technique using spinal anaesthesia and continuous femoral nerve block.

8. Conclusion

The technique using spinal anaesthesia combined with continuous femoral nerve blockade in patients with cardiac risk undergoing TKA provided lower levels of neurohormonal stress markers including BNP and cardiac troponins and was associated with better postoperative pain control compared to the technique using general anaesthesia and lumber epidural. Further studies with greater sample size population are advised in more complicated cardiac cases to assess and confirm the safety of the aforementioned anaesthetic technique.

Disclosure statement

No potential conflict of interest is declared

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