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Epidural anesthesia followed by epidural analgesia produces less inflammatory response than spinal anesthesia followed by intravenous morphine analgesia in patients with total knee arthroplasty

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Background: Anesthesia and inflammatory response have been studied in major abdominal and thoracic surgical procedures, but not in major orthopaedic reconstructive procedures such as total knee arthroplasty. Most studies have compared general anesthesia with epidural anesthesia, but none has compared epidural with spinal.

Material/Methods: In a prospective randomized study, 2 groups of patients scheduled for total knee arthroplasty for osteoarthritis were evaluated regarding the inflammatory response to 2 types of regional anesthesia. In 30 patients (Group A) with spinal anesthesia followed by intravenous morphine analgesia, and in 26 patients (Group B) with epidural anesthesia followed by epidural analgesia, the inflammatory response was assessed through the calculation of leucocyte concentration (WBC), C-reactive protein (CRP), monocyte chemotactic protein 1 (MCP-1), interleukins (IL-1, IL-6, IL-10, IL-18), TNF-a, and leucocyte activation molecules CD11b and CD62l, in 3 blood samples (immediately before induction to anesthesia, immediately after closure of the operative wound, and at 24 hours post-operatively).

Results: The MCP-1 values showed a statistically significant increase ($p<0.02$) in the group of patients with spinal anesthesia. Of the leucocyte activation molecules, a high statistically significant increase was noticed in the expression of CD11b on monocytes in the sample taken 24 hours post-operatively in the patients of group A. Similarly, CD62l expression on neutrophils showed a high statistically significant reduction in the sample taken 24 hours post-operatively in the group of patients with spinal anesthesia compared to the group of patients with epidural anesthesia.

Conclusions: Our results show that epidural anesthesia followed by epidural analgesia produced less inflammatory response compared with spinal anesthesia followed by intravenous morphine analgesia in patients operated on with total knee arthroplasty, and that the most sensitive markers of those investigated were the CD11b and CD62l leucocyte activation molecules.

key words: anesthesia, epidural, spinal, inflammatory response, total knee arthroplasty

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Background

All perioperative and postoperative periods are characterized by immunological alterations and metabolic and endocrine reactions, resulting from tissue damage, anesthesia, and pain. These reactions, depending on their severity, can have variable effects, ranging from the patient's susceptibility to infection, wound healing, systemic inflammatory response syndrome, and multiple organ failure.

The effect of the type of anesthesia and postoperative analgesia on the immunological response following major surgical procedures has been the subject of numerous and occasionally conflicting studies [1–3]. Moreover, most of these studies have focused on major upper or lower abdominal or thoracic surgery, while few studies have been focussed on major orthopaedic joint reconstruction surgery [4,5]. Most of these studies have compared general anesthesia with epidural anesthesia, while no study, to our knowledge, has referred to the comparison of 2 different regional anaesthetic methods.

In this prospective randomized study we attempted to investigate the postoperative immunological reaction in patients who were subjected to total knee arthroplasties for degenerative arthritis of the joint, with 2 different methods of anesthesia (spinal and epidural) since most of these surgical procedures are performed through regional anesthesia.

Material and Methods

Sixty patients ASA I to III, who had osteoarthritis of the knee joint and who were scheduled for total knee arthroplasty, were enrolled in this study. They were assigned to 2 groups by randomization with coded sealed envelopes, after permission from the Ethics Committee of our institution and having signed an informed consent. The first group of 30 patients (group A) had their operation with spinal anesthesia and the second group (group B) had their operation with epidural anesthesia.

All patients were given 2mg of midazolam IV before the start of the anesthesia. The spinal anesthesia was done by an atraumatic 25G needle, with ropivacaine 0.5%, 20 mg, and fentanyl 0.020 mg through a mid-line approach at the L3-L4 level. The epidural anesthesia was done with a Tuohy epidural needle (size 18G, Braun, Germany), through a loss-of-resistance technique with air, at the L3-L4 level and advancement of the epidural catheter up to 4cm cephalad. The anaesthetic agents used were ropivacaine 0.75%, 112.5–150 mg (15–20 ml) and fentanyl 0.03–0.05 mg, depending on the patient's BMI.

Patients who were taking non-steroidal anti-inflammatory medications and patients on anti-immune system medications including opioids were excluded from the study.

All patients in both groups were operated on by the same surgeon, with the same operative protocol. No tourniquet was used, 1 dose of second-generation cephalosporin was given preoperatively and 2 other doses were given postoperatively. The same surgical approach was used and the same type of prosthesis was implanted. No blood transfusion was given intra-operatively, but all patients were supplied with a post-operative auto-transfusion system (Stryker, New Jersey). All patients were given enoxaparin 40 mg daily for 30 days post-operatively, as antithrombotic prophylaxis.

Post-operative analgesia in the patients of Group A was obtained by patient-controlled intravenous analgesia (PCA) with morphine, and in the patients of Group B by the administration of a combination of ropivacaine and morphine through epidural PCA. In both groups analgesia was assessed by Numerical Rating Scale (NRS), from 0 (no pain) to 10 (maximum pain) at 1, 6, 12 and 24 hours post-operatively, at rest and in motion, and the dose was regulated in an attempt to keep pain at not greater than 3 in all patients.

In all patients the following were calculated: total leucocyte count, neutrophil and monocyte count, CRP, IL-1b, IL-6, IL-10, IL-18, TNF-a, MCP-1, leucocyte CD11b, and CD62L cell surface expression, in 3 consecutive blood samples. The first sample was taken immediately before induction of anesthesia, the second was taken immediately after the closure of the operative wound (immediately post operatively), and the third was taken 24 hours postoperatively.

IL-6 levels were measured using an enzyme-linked immunosorbent assay by a commercially available kit (Bender MedSystems GmbH, Vienna, Austria) with a lower limit of detection for IL-6 of 0.92 pg/ml. The overall intra- and inter-assay coefficient of variation has been calculated to be 3.4% and 5.2%, respectively. The same commercially available kit was utilized for determination of soluble IL-10 levels, IL-1b, IL-18 and TNF-a. IL-10 with minimum detectable value of 0.05pg/ml and the overall intra- and inter-assay coefficient of variation has been calculated to be 6.8% and 7.5%, respectively. IL-1b with minimum detectable value of 0.3 pg/ml and the overall intra- and inter-assay coefficient of variation has been calculated to be 5.1% and 8.6%, respectively. IL-18 with minimum detectable value of 9 pg/ml and the overall intra- and inter-assay coefficient of variation has been calculated to be 6.5% and 8.1%, respectively. TNF-a with minimum detectable value of 5 pg/ml and the overall intra- and inter-assay coefficient of variation has been calculated to be 7.7% and 8.1%, respectively.

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Table 1. Patients' characteristics.

	Type of anaesthesia		p-value
	Spinal	Epidural	
Female gender (no,%)	26 (83.3)	21 (79.2)	0.695
Age (years; mean ±SD)	68.53±5.67	69.63±6.21	0.503
BMI (Kg/m^2; mean ±SD)	33.51±4.83	34.53±6.35	0.504
Duration of surgery (min; mean ±SD)	72.53±12.41	74.62±19.47	0.650
ASA (no,%)			0.998
I	5 (16.7)	4 (16.7)	
II	14 (46.6)	11 (45.8)	
III	11 (36.7)	9 (37.5)	

Human MCP-1 levels were measured again using an enzyme-linked immunosorbent assay by a commercially available kit (Bender MedSystems GmbH, Vienna, Austria) with minimum detectable value of 2.3 pg/ml. The overall intra- and inter-assay coefficient of variation has been calculated to be 4.7% and 8.7%, respectively.

Regarding flow cytometric analysis of surface molecules, the activation status of neutrophils and monocytes was assessed by 2-colour flow cytometry. Briefly, peripheral blood leukocytes were stained with CD11a, CD11b, and CD62L monoclonal antibodies (all from Becton-Dickinson) after red blood cell lysis with ammonium chloride. Acquisition and analysis were performed on a FACS Calibur cytometer equipped with CellQuest software (both from Becton-Dickinson). Monocytes and neutrophils were identified via their forward and light-scatter characteristics and the results were expressed as the mean fluorescence intensity (MFI) of CD11a, CD11b and CD62L.

Statistical analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 19.0 (SPSS, Inc., Chicago, IL, USA). The normality of quantitative variables was tested by the Kolmogorov-Smirnov test. Normally distributed variables were expressed as mean ± standard deviation (SD), while non-normally distributed variables were expressed as median and interquartile range. Between-groups differences of all markers of inflammation were assessed by Student's t test or Mann-Whitney U test, while within-groups differences were examined by one-way repeated measures ANOVA or Friedman test; post-hoc analysis was performed using Bonferonni's correction. Quantitative variables were expressed as frequencies and percentages (%) and they were analyzed using the chi-square test. All tests were 2-tailed and statistical significance was considered for p values less than 0.05.

Results

Group A consisted of 30 patients (26 women and 4 men, no exclusions). Their age ranged from 55–76 years (average 68.53 years) and their BMI ranged from 25.4–42.2 (average 33.51). In Group B, 4 patients were excluded, in 2 the epidural catheter was dislodged, and the other 2 required intraoperative blood transfusion, leaving a total of 26 (21 women and 5 men). Their age ranged from 57–80 years (average 69.6 years) and their BMI ranged from 27.1–49 (average 34.5). Similarly, patients of both groups were comparable regarding the ASA distribution and the duration of surgery (Table 1).

The detailed results of the assessed haematological parameters in relation to the type of anesthesia are shown in Table 2. Both the total white cell concentrations and the neutrophil concentrations increased significantly in the samples taken 24 hours post-operatively, compared to the samples taken pre-operatively and immediately after closure of the wound. However, this increase was significantly less in the group of patients with epidural anesthesia (group B). The monocyte concentrations and the CRP similarly increased in the 24-hour post-operative sample but did not show any difference between the 2 groups of anesthesia.

The values of IL-1b, IL-6, IL-10, IL-18, TNF-a, and MCP-1 showed a statistically significant increase in the samples taken 24 hours post-operatively compared with the pre-operative and immediate post-operative samples, but no statistically significant difference between Group A and Group B, excluding only the MCP-1 values, which were significantly higher ($p<0.02$) in the group of patients with spinal anesthesia (Group A) (Table 3). Regarding the leucocyte activation molecules, a high statistically significant increase was noticed in the expression of CD11b on monocytes in the sample taken 24 hours post-operatively compared with the pre-operative sample and the immediate post-operative

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Table 2. Leucocyte concentration and CRP in relation to the type of anaesthesia.

	Type of anaesthesia		p-value[1]
	Spinal	Epidural	
WBC			
Pre –	6.75±1.85 K/μl	6.45±1.68 K/μl	0.533
1st post –	6.12±1.51 K/μl	6.19±2.26 K/μl	0.884
2nd post –	10.72±2.14 K/μl	9.15±2.11 K/μl	0.010
p-value[2]	<0.001	<0.001	
NEU (neutrophils)			
Pre –	3.95±1.33 K/μl	3.90±1.49 K/μl	0.888
1st post –	4.01±1.35 K/μl	4.02±2.11 K/μl	0.974
2nd post –	8.29±2.03 K/μl	7.11±1.86 K/μl	0.032
p-value[2]	<0.001	<0.001	
MONO (monocytes)			
Pre –	394.67±117.70 K/μl	382.50±88.67 K/μl	0.676
1st post –	326.29±166.28 K/μl	322.50±124.18 K/μl	0.928
2nd post –	812.62±169.94 K/μl	785.83±282.61 K/μl	0.684
p-value[2]	<0.001	<0.001	
CRP			
Pre –	0.26 (0.12–0.97) mg/dL	0.23 (0.18–1.15) mg/dL	0.433
1st post –	0.55 (0.14–0.82) mg/dL	0.62 (0.16–1.14) mg/dL	0.443
2nd post –	9.35 (7.09–11.81) mg/dL	8.58 (6.10–13.85) mg/dL	0.931
p-value[2]	<0.001	<0.001	

Biochemical markers (WBC, NEU and MONO) are expressed as mean ± SD; CRP values are expressed as median and interquartile range; [1] statistical significance between the two groups; [2] statistical significance between the three measurements within each group.

sample in the patients with spinal anesthesia (Group A). Similarly, CD62L expression on neutrophils showed a high statistically significant reduction in the sample taken 24 hours post-operatively in the group of patients with spinal anesthesia as compared to the group of patients with epidural anesthesia. The expression of CD11a and CD62L on monocytes, and CD11a and CD11b on neutrophils did not show any significant alterations both between the samples and between the 2 groups (Table 4).

Discussion

A number of studies have reached conflicting conclusions regarding the influence of the type of anesthesia and postoperative analgesia on the immunological response to operatively induced stress. Conrick-Martin et al. [1], in a meta-analysis comparing the effect of spinal or epidural anesthesia with general anesthesia on postoperative natural killer T lymphocyte function, concluded that the anesthetic technique did not appear to significantly affect the function of these cells postoperatively. Similarly, combined general anesthesia and epidural anesthesia did not seem to protect patients from the immunosuppression caused by the surgical procedure [3]. On the other hand, Alhers [2] reported on 54 patients undergoing major abdominal surgery with a thoracic epidural anesthesia and concluded that this method reduced stress response and prevented stress-induced perioperative impairment of pro-inflammatory lymphocyte function. Similarly, Wolf [4] reported that the sympathetic block induced by epidural anesthesia resulted in a profound suppression of hemodynamic and stress responses to pediatric surgery, and Hong et al. [5] reached similar conclusions after radical retropubic prostatectomies.

There have been no prospective randomized studies regarding the effect of 2 methods of regional anesthesia on patients operated on for total knee arthroplasty. In our study we investigated 2 groups of patients with osteoarthritis of the knee joint, operated on by the same surgeon, who were comparable in their demographic data, ASA status, and intra-operative (surgical procedure, surgeon and implant) and post-operative protocol; they differed only in the method of regional anesthesia (spinal or epidural) and postoperative analgesia. All operations in our study were performed without tourniquet in order to avoid the presence of another factor that could possibly increase the surgical inflammatory response [6,7]. Furthermore, we avoided blood transfusion, unless required by the intra-operative condition of the patient, in order to exclude yet another factor that could possibly affect the immunological status of the patients.

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Table 3. Levels of cytokine values in relation to the type of anaesthesia.

	Type of anaesthesia		p-value[1]
	Spinal	Epidural	
IL-1b			
Pre –	0.51 (0.36–0.73) pg/ml	0.48 (0.37–0.95) pg/ml	0.714
1st post –	0.59 (0.41–0.89) pg/ml	0.55 (0.41–1.09) pg/ml	0.875
2nd post –	0.79 (0.65–0.94) pg/ml	0.85 (0.63–1.67) pg/ml	0.351
p-value[2]	0.010	0.004	
IL-6			
Pre –	0.68 (0.59–1.29) pg/ml	0.66 (0.44–1.76) pg/ml	0.651
1st post –	0.67 (0.49–0.92) pg/ml	0.73 (0.46–2.13) pg/ml	0.626
2nd post –	36.30 (19.80–59.55) pg/ml	40.00 (17.10–86.75) pg/ml	0.554
p-value[2]	<0.001	<0.001	
IL-10			
Pre –	1.49 (1.25–1.91) pg/ml	1.40 (1.24–2.11) pg/ml	0.972
1st post –	1.81 (1.35–2.04) pg/ml	1.61 (1.37–2.03) pg/ml	0.547
2nd post –	6.29 (4.05–9.16) pg/ml	6.06 (3.44–9.85) pg/ml	0.903
p-value[2]	<0.001	<0.001	
IL-18			
Pre –	206 (139–274) pg/ml	204 (76–361) pg/ml	0.702
1st post –	163 (104–211) pg/ml	132 (69–184) pg/ml	0.203
2nd post –	213 (167–302) pg/ml	168 (82–304)pg/ml	0.130
p-value[2]	<0.001	<0.001	
TNF-a			
Pre –	6.47 (3.78–7.63) pg/ml	6.11 (5.20–7.36) pg/ml	0.770
1st post –	7.40 (4.84–12.55) pg/ml	6.71 (4.79–7.52) pg/ml	0.167
2nd post –	8.55 (6.12–12.12) pg/ml	8.55 (7.67–8.84) pg/ml	0.340
p-value[2]	0.008	0.042	
MCP-1			
Pre –	96.70 (74.60–108.00) pg/ml	97.40 (82.60–112.00) pg/ml	0.780
1st post –	67.70 (56.20–111.32) pg/ml	76.00 (62.60–89.30) pg/ml	0.834
2nd post –	133.00 (90.60–154.25) pg/ml	94.65 (72.30–107.00)pg/ml	0.020
p-value[2]	<0.001	0.002	

Cytokine levels are expressed as median and interquartile range; [1] statistical significance between the two groups; [2] statistical significance between the three measurements within each group.

We attempted, thus, to reduce the limitations of other similar studies, in which the alterations seen in the inflammatory markers could be attributed to a variety of factors such as tissue damage, the insertion of the implant, and the method of blood transfusion [8]. In order to exclude the possibility that any alterations in the inflammatory markers' levels could be attributed to the surgical trauma, we calculated the levels of these markers in 3 blood samples, taken pre-operatively, immediately post-operatively and after 24 hours, for each method of anesthesia.

According to our findings, the fact that the inflammatory mediators IL-6, IL-1b, and TNF-a increased during the first post-operative 24 hours, as seen in the comparison between the 3 blood samples, without any significant difference between the 2 methods of anesthesia, indicate that they were due to the inflammation caused mainly by the surgical procedure. The increase, however, seen to a lesser extent in the MCP-1 and more significantly in the levels of CD11b on monocyte and the decrease of CD62L expression on neutrophils 24 hours post-operatively in the group of patients with spinal anesthesia, suggests that epidural anesthesia may cause a significantly reduced inflammatory response in patients undergoing total knee replacement surgery.

We decided to investigate not only pro-inflammatory and anti-inflammatory cytokines, but also leucocyte markers since the latter appear to be more sensitive in the early detection of the

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Table 4. Surface molecules markers of inflammation in relation to the type of anaesthesia.

	Type of anaesthesia		p-value[1]	95% CI of the difference
	Spinal	Epidural		
11A – M				
Pre –	34.22±10.05	34.31±10.98	0.976	–5.84 to 5.66
1st post –	32.21±9.15	31.00±10.66	0.539	–2.84 to 5.37
2nd post –	31.33±8.29	30.65±9.10	0.730	–3.44 to 4.88
p-value2	0.157	0.164		
11B – M				
Pre –	602.40±257.93	614.50±181.19	0.847	–136.96 to 112.76
1st post –	603.17±265.87	642.20±263.97	0.550	–122.33 to 65.96
2nd post –	846.63±213.24	630.01±178.92	<0.001	122.36 to 320.27
p-value2	<0.001	0.771		
62L – M				
Pre –	93.89±35.92	95.11±25.69	0.890	–18.69 to 16.26
1st post –	98.93±39.26	103.72±24.20	0.310	–18.34 to 10.38
2nd post –	102.20±25.95	104.68±22.06	0.726	–15.70 to 11.00
p-value2	0.465	0.250		
11A – N				
Pre –	10.71±3.05	10.95±2.46	0.757	–1.78 to 1.30
1st post –	11.04±3.24	11.32±2.32	0.865	–0.96 to 0.81
2nd post –	10.91±1.86	10.69±2.34	0.597	–0.80 to 1.36
p-value2	0.797	0.415		
11B –N				
Pre –	740.56±301.25	784.05±262.63	0.580	–200.01 to 113.02
1st post –	694.16±263.22	747.59±282.18	0.628	–157.97 to 96.17
2nd post –	685.95±275.99	678.32±207.66	0.872	–126.45 to 148.67
p-value2	0.641	0.200		
62L – N				
Pre –	135.33±43.37	139.40±41.90	0.730	–27.55 to 19.41
1st post –	159.04±49.60	161.47±32.10	0.993	–18.66 to 18.81
2nd post –	79.29±27.67	114.91±29.44	<0.001	–46.34 to –21.54
p-value2	<0.001	<0.001		

Markers of inflammation are expressed as mean ± SD; CI, confidence interval; [1] statistical significance between the two groups; [2] statistical significance between the three measurements within each group. M – monocyte; N – neutrophil.

post-operative response to stress [9]. CD62L (or L-selectin) is a surface adhesion molecule responsible for the rolling and initial attachment of stimulated leukocytes to the vessel wall at sites of damaged or activated endothelium [10,11]. CD11b is a part of the CD11b/CD18 surface adhesion molecule, and is a member of the [beta]$_2$ integrin family. Upon activation, neutrophils and monocytes up-regulate CD11b, which mediates the firm adhesion of activated neutrophils and monocytes to endothelial cells, platelets, extracellular matrix, smooth muscle cells, fibrinogen, etc [12,13], whereas L-selectin is shed from their membranes, allowing the rapid detachment of leukocytes from the endothelial surface and transmigration into the injured tissues. Experimental studies have shown that L-selectin is essential for the initial neutrophil rolling interaction with the inflamed endothelium and for a CD11b/CD18-dependent transition from rolling to sticking and migrating.

CD11a is expressed in combination with the CD18 beta chain. The complex is a member of the beta2 integrin family and is involved in leukocyte migration and diapedesis through the endothelial barrier into zones of inflammation. Interestingly, a recent study reported that CD11a/CD18 is shed from leukocytes in models of inflammation.

Hughes [9] studied 10 volunteers who underwent total hip or total knee arthroplasty for osteoarthritis, and showed that the increase

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seen in the leucocyte and endothelial markers could be used as an early diagnostic tool for potential infectious complications following this type of surgery. Our study thus is in agreement with the findings of these investigators. Furthermore, our findings are in agreement with other reports in the literature suggesting that epidural anesthesia could produce an attenuation of the inflammatory response [2], but such studies have concentrated on the investigation of inflammation, mainly following major abdominal surgical procedures, and not major joint reconstruction orthopaedic procedures. In our study, although the group of patients with epidural anesthesia and analgesia had a significantly attenuated inflammatory response, during the early and mid-term follow-up of our patients, no case of infection was noted in either of the 2 groups under investigation. Although the number of patients in our study is the largest regarding the inflammatory response to these 2 types of anesthesia, it is considered too small, from the orthopaedic point of view, to reach conclusions regarding postoperative infection of the implants used. Furthermore, the long-term functional result of our patients in both groups was similar, although there was a marginally smoother postoperative recovery of the group of patients with epidural anesthesia followed by epidural analgesia, expressed in faster mobilization and better range of early movement.

CD11b and CD62l alterations manifest themselves shortly after the initiation of the inflammatory response, thus our findings in the 24-hour samples could be attributed, in addition, to the different methods of postoperative analgesia and not solely to the methods of anesthesia.

Other methods of regional anesthesia and postoperative analgesia have become popular recently and seem to lead to reduced inflammation. Tang et al. compared the use of continuous femoral nerve block with patient-controlled intravenous analgesia in patients operated on for total knee arthroplasty and showed that the continuous femoral nerve block analgesia produced milder stress response, faster rehabilitation, and better patient satisfaction [14]. Similarly Martin et al. [15] studied 2 groups of patients who were operated on for total knee arthroplasty. One group of 20 patients had a continuous femoral block postoperative analgesia and the second group of 18 patients had an intravenous morphine PCA. They concluded that continuous femoral nerve block analgesia exerted a prolonged anti-inflammatory effect manifested mainly in improved functional recovery but with no alterations in tissue and plasma cytokine concentrations. In contrast, in our study the faster functional recovery observed in the patients of group B was accompanied by relevant alterations of the MCP-1 and, most strongly, of CD11b and CD62l inflammatory markers. Indeed these types of regional anesthesia and their effects on inflammation and postoperative recovery are subjects that need further investigation. It is our intention to proceed with a similar project in the near future.

The limitation of our study is that the inflammatory response measured by the selected markers could be due to other factors besides the type of anesthesia, such as surgical tissue damage and possibly implant insertion, as well as postoperative analgesia. We have attempted to strengthen this point, as stated previously, by calculating the chosen inflammatory markers in 3 different, in time, blood samples regarding both methods of anesthesia. However, the less inflammatory response seen in the group of patients with epidural anesthesia could be attributed, in addition, to the postoperative epidural analgesia, compared to spinal anesthesia followed by intravenous morphine analgesia.

The strong point of our study is that no prospective randomized comparison between 2 different methods of regional anesthesia for patients subjected to total knee arthroplasty has been reported so far, and that it is the largest number of patients studied to our knowledge in the literature.

Conclusions

We believe that epidural anesthesia combined with epidural analgesia can significantly reduce the amount of post-operative inflammatory response of patients subjected to total knee arthroplasty for osteoarthritis, and that the alterations of the levels of the circulating leucocyte surface molecules CD11b and CD62l are the most sensitive markers, of those tested, for the calculation of this response. Based on these findings we believe that epidural anesthesia followed by epidural analgesia could serve as a method of choice for these patients, leading to a better functional early result.

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