

CLINICAL STUDY

Prospective comparison of local, spinal, and general types of anaesthesia regarding oxidative stress following Lichtenstein hernia repair

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Abstract

As a tension-free repair technique, Lichtenstein operation has gained great popularity worldwide during the last decade. Expert centres do this technique using local anaesthesia in nearly 95 % of cases. However, general anaesthesia is used in many hospitals, while regional anaesthesia is preferred in some centres. To date, no study has compared different types of anaesthesia in respect of inflammatory response and oxidative stress specifically. The objective of this prospective study was to compare local, spinal and general types of anaesthesia regarding their effects on inflammatory response and oxidative stress in Lichtenstein hernia repair. Lichtenstein hernia repair causes only a mild oxidative stress. While total WBC and neutrophil count responses fade away after 24 hours in patients who are operated under local anaesthesia, these changes in spinal and general types of anaesthesia cases stay valid at 24th hour. Spinal anaesthesia is seen to be more advantageous than local and general types of anaesthesia when C-reactive protein as an acute phase marker is considered. Total antioxidant status shows minor alterations in three types of anaesthesia, however, general anaesthesia seems to be the least reliable among them. Overall, local and spinal anaesthesia methods can be accepted as better alternatives in comparison with general anaesthesia in regard to oxidative stress (*Tab. 2, Ref. 25*). Full Text (Free, PDF) www.bmj.sk.

Key words: inguinal, hernia, Lichtenstein, inflammatory response, total antioxidant status, anaesthesia, local, spinal.

As a tension-free repair technique, Lichtenstein operation has gained great popularity worldwide during the last decade. This technique, that does not need a long learning curve, offers surgeons and their patients a short operation time in an outpatient basis, minimal complication rates, early return to work, and virtually low recurrence rates even in non-expert hands (1).

Today, Lichtenstein repair has an advantage over newer tension-free techniques performed laparoscopically with its availability under local anaesthesia (2). Indeed, expert centres do this technique using local infiltration anaesthesia in nearly 95 % of cases (1–3). However, general anaesthesia is still used in the majority of cases in many hospitals (4–6). On the other hand, regional anaesthesia (spinal or epidural) is preferred in 5–15 % of open repairs in surgical departments (4, 5), and as a routine in some specialist centres performing tension-free repair technique with prosthetic material (7).

There are several studies in English literature comparing three different anaesthetic methods (local, regional and general) in hernia repair. Those studies have generally had outcome measures like, cardiopulmonary functions, clinical recovery profiles, postoperative pain, complications, and costs (8–12). To the best of our knowledge, no study to date has compared different types of anaesthesia in respect of inflammatory response and oxidative stress specifically. Therefore, we conducted a prospective study to compare local, spinal and general types of anaesthesia

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regarding their effects on inflammatory response and oxidative stress in Lichtenstein hernia repair.

Patients and methods

Thirty six patients who underwent elective inguinal hernia repair were included in this prospective study. Patients who had been taking antioxidants prior to the surgery were excluded. Lichtenstein operation was performed in all cases. An informed consent was obtained from each patient following counselling about the advantages and risk of the repair technique and three different methods of anaesthesia. Informed consent also contained the biochemical monitoring. No randomization was done. The subject number of each group was set at 12 at the beginning of the study. Twelve consecutive patients who preferred each anaesthesia method were included, and no more patients were enrolled when a group reached 12.

Operative procedures

American Society of Anaesthesiologist class was recorded in each case. The hernias were classified according to the Nyhus classification. All patients received single-dose antibiotic prophylaxis preoperatively (1 g of intravenous cephazoline). The Lichtenstein operation was performed routinely (16). A 6x11 cm polypropylene mesh was secured with 2-0 polypropylene suture as the standard. General anaesthesia was induced by thiopental (5–7 mg/kg) and vecuronium (0.1 mg/kg) and continued with 50 % nitrous oxide, oxygen and 1–2 % sevoflurane. Bupivacaine 0.5 % in an average dose of 15 mg was used for spinal anaesthesia. Local anaesthesia was performed by the surgeon by local infiltration technique described by Amid and colleagues (Amid et al, 1994), by using 20 ml of bupivacaine 0.25 % (Marcaine, 20 ml flacon) and lidocaine totally 20 ml on average. Midazolam in a dose of 0.1 mg/kg was used for sedation during repair with local anaesthesia.

Blood samples and assays

Blood samples were withdrawn from antecubital veins immediately before surgery (anaesthesia), and 12 and 24 hours after the operation. Cell counts were performed by using Cell-Dyn 4000 with argon-ion laser optical method.

Serum was separated from the cells by centrifugation at 3000 rpm for 10 min, and stored at -70 °C until CRP and TAS measurements.

CRP levels were determined by nephelometric analysis by using Dade Behring BN 100. Normal serum levels range from 0 to 6 mg/dl.

The total antioxidant status of the plasma was measured by using a Randox kit with a novel automated colorimetric measurement method for total antioxidant response (13). In this method, the hydroxyl radical, the most potent biological radical, is produced by the Fenton reaction, and reacts with the colorless substrate O-dianisidine to produce the dianisyl radical, which is bright yellowish-brown in color. Upon the addition of a plasma sample, the oxidative reactions initiated by the hydroxyl radicals present

in the reaction mix are suppressed by the antioxidant components of the plasma, preventing the colour change and thereby providing an effective measure of the total antioxidant capacity of the plasma. The assay results are expressed as mmol Trolox eq/L and the precision of this assay is excellent, being lower than 3 % (14).

Statistical analysis

Gender and hernia type characteristics of the groups were compared with chi-square test. Variance analysis was determined by ANOVA. Statistical significance was analyzed by Student's t test. Differences between the groups were calculated by the Mann–Whitney U test. The Wilcoxon signed rank test was used to evaluate paired data. Spearman's rank order correlation was performed between neutrophil count, CRP and TAS. $p < 0.05$ was considered significant.

Results

There were no differences between the groups regarding age, gender, ASA grading, and the side and type of hernia (Tab. 1). None of the patients included in the study developed infectious complications, seroma or hematoma. All the patients were discharged on the first postoperative day, after obtaining the 24-hour blood samples.

Leukocytes

No differences were found between local (LA), spinal (SA) and general (GA) anaesthesia groups regarding WBC and neutrophil counts at any specific time (Tab. 2). However, each group displayed some differences between their preoperative, 12-hour and 24-hour values. WBC count rose at 12th h and stayed high at 24th h in LA group, but the differences did not reach the level of significance. An obvious increase in WBC count was seen in SA group at 12th h comparing preoperative value ($p=0.001$). Its level at 24th h was significantly lower than that at 12th h ($p=0.05$), however, still significantly higher than the preoperative value ($p=0.001$). The significant rise in WBC count at 12th h ($p=0.001$) in GA group was followed by a small decrease at 24th hour. The difference between the preoperative value and that at 24th h was significant ($p=0.005$).

Tab. 1. Patient characteristics.

	Local	Spinal	General
Age (years)	50.0±18	50.1±14	40.5±15
Male/female	11/1	11/1	9/3
Right/left	10/2	6/6	8/4
Hernia type (Nyhus) II	5	5	2
IIIA	5	5	2
IIIB	8	2	2
ASA grading I	9	10	11
II	3	2	1

Data are expressed as mean±SD.
 $p > 0.05$ for all parameters in the table.

Tab. 2. Preoperative and postoperative leukocyte and neutrophil counts, and C-reactive protein and total antioxidant status values of the groups.

	Local	Spinal	General	
WBCs (/mm³)				
preoperative	7100±2052	7166±2208	7433±1960	no differences
12. hour	9916±2574	12000±4000*	11258±3098*	no differences
24. hour	9763±2318	10545±3445*#	10416±4063*	no differences
Neutrophils (/mm³)				
preoperative	4331±1508	4390±1990	4595±1213	no differences
12. hour	8913±4065*	7710±1544*	7115±3071*	no differences
24. hour	6538±2361#	7840±2511*	7516±3072*	no differences
CRP (mg/dl)				
preoperative	2.91±1.75	5.00±5.95	4.20±1.75	no differences
12. hour	5.33±3.55	10.67±15.11	18.75±13.88*	p=0.006; local vs general, p=0.03; spinal vs general
24. hour	31.54±26.55*#	14.00±16.18*	53.08±34.97*#	p=0.003; spinal vs general
TAS (mmol/l)				
preoperative	2.17±0.90	2.35±0.97	1.70±0.40	no differences
12. hour	1.93±0.74	2.12±0.89	1.42±0.20	p=0.06; local vs general, p=0.05; spinal vs general
24. hour	2.09±0.73	2.28±0.73	1.47±0.15	p=0.001; local vs general, p=0.002; spinal vs general

Data are means±SD.

* p<0.05 compared with preoperative value.

p<0.05 compared with the value at 12th hour.

In LA group, neutrophil count first increased significantly at 12th h (p=0.007), then, showed a decrease at 24th hour. A similar increase was observed in SA group at 12th h (p=0.001), and stayed on a significantly higher level when compared with the preoperative value at 24th hour (p=0.001). This was also the case in GA group (p=0.02 at 12th h and p=0.004 at 24th h).

C-reactive protein

CRP began to rise in all three groups at 12th hour. This was more obvious in GA group (p=0.001) while the differences with preoperative values were just close to the level of significance (p=0.059 and p=0.063) in LA and SA groups. The 24-hour CRP values in LA and GA groups were significantly higher than 12-hour values (p=0.005 and p=0.001), whereas this rise in SA group was insignificant (p=0.09). However, the SA group had a significant increase when its preoperative and 2-hour values were compared (p=0.02).

The comparison of the three groups showed significant differences between LA and GA groups (p=0.006), and SA and GA groups (p=0.03) at 12th hour (Table 2). At 24th h, a sharp rise was observed in LA group and the significant difference between LA and GA groups disappeared at this time, while GA group still had a significantly higher CRP level than that of SA group (p=0.003).

Total antioxidant status

TAS values showed slight, but insignificant decreases in all three groups 12 hours after the operation. However, the difference between SA and GA groups was at just the level of signifi-

cance (p=0.05) at 12th h, while the preoperative values were statistically similar (Tab. 2). On the other hand the difference between LA and GA groups was close to, however did not achieve the level of significance (p=0.06). At 24th h, the TAS values of both SA and LA groups returned to a level very similar to their preoperative values, and these two groups had significantly higher TAS levels when compared to GA group (p=0.001 and p=0.002).

No correlations were found between leukocyte counts and TAS, as well as between CRP and TAS at any time.

Discussion

Inguinal hernia repair is one of the most frequently performed operations worldwide. It can be done as a day-case procedure with minimal morbidity. The choice of anaesthesia for hernia repair depends on patient and surgeon preferences and the feasibility of the techniques. Some centres prefer general or spinal types of anaesthesia, whereas local anaesthesia is popular in some others. In our own institutional surgical practice, we have employed all three methods, while there has been a recent trend towards local anaesthesia with sedation.

There are many comparative studies in literature trying to answer the question „What is the optimal anaesthesia type for inguinal hernia repair?“ Early studies which have used cardiopulmonary parameters, nausea-vomiting, difficult urination as outcome measures have revealed that local anaesthesia is more advantageous over general and regional types of anaesthesia (8–10). More recent reports have also focused on patient's satisfaction. Nordin and colleagues' multi-centre randomized trial has

shown that patients could feel pain intra-operatively when local anaesthesia was employed (15). However, the same report has revealed similarly very “yes” answer rates for three types of anaesthesia to the following question: “Would you consider receiving the same type anaesthesia again?” On the other hand, local anaesthesia is a more economic choice in comparison with regional technique, and also much cheaper than general anaesthesia (7).

To date, no study has specifically compared three types of anaesthesia for hernia repair or at other kinds of surgery in respect of oxidative stress and systemic inflammatory response. The only study that mentions this subject has shown that the extent of inflammatory response is slightly, but insignificantly, smaller when Shouldice hernia repair is carried out under local anaesthesia instead of general anaesthesia (16). In fact, the latter study primarily has compared the systemic inflammatory response after endoscopic hernia repair and Shouldice repair. The common parameter of this study and the present one is CRP level. This acute-phase protein appears as a result of effects of mediators that originate from the surgical trauma and regulates the inflammatory response (6, 16). Schwab and colleagues reported that CRP levels increased on the first and third postoperative days with no difference between endoscopic and conventional repair groups. They obtained the lowest CRP increase in local anaesthesia subgroup (16).

In the present study, a four-fold rise of CRP level was observed at 12th h in GA group. SA group had the mildest increases at 12-hour and 24-hour measurements. It had been previously shown that serum CRP level began to rise at 12th postoperative hour and reached its peak level at 48 to 72 hours (17). However, it did not seem to us reasonable and ethical to keep the patients in the hospital for a longer duration or to call them back for the 48 or 72-hour blood sampling. Nevertheless, the 24-hour values in the present study revealed meaningful and satisfactory results. Moreover, Uzunkoy et al, in a prospective randomized trial on laparoscopic and open hernia repair under general anaesthesia, found that CRP reached significantly higher levels at 24th h in comparison with preoperative values, and this picture did not change at 48th hour (18).

Neutrophil count is also an indicator of the inflammatory response. Yamauchi et al have shown that the degree of lymphocytopenia and neutrophilia correlated well with the extent of surgical trauma (19). Suter et al reported that in their study there was a sharp decline in the lymphocyte count 4 and 24 hours after the bilateral prosthetic hernia repair, whereas there was no difference in total white blood cell count and polymorphonuclear cell count (20). Contrarily, Uzunkoy and colleagues found significantly higher neutrophil counts in patients who underwent hernia repair under general anaesthesia, at 2nd, 24th, and 48th hours, while decreases in the number of lymphocytes were not significant at any time (18). On the other hand, Papaziogas et al found that neutrophil count displayed its peak at 12th hour postoperatively, then, decreased at 24th and 48th hours, in open hernia repair (21). Di Vita and colleagues observed a significant leukocytosis and neutrophilia 6 and 24 hours after Lichtenstein

hernia repair, while the cell counts at 48th hour were not different with preoperative values (22). In the present study, neutrophil count rose significantly in all anaesthesia type groups at 12th hour. It then decreased significantly in LA group at 24th h, but stayed at significantly higher levels than the preoperative values in both SA and GA groups at 24th hour. However, this picture in favour of local anaesthesia could not be reproduced when the groups had been compared to each other at specific times.

Interestingly, Lichtenstein hernioplasty has been blamed to be associated with a higher inflammatory response compared with suture repairs, possibly due to polypropylene mesh use (22). However, a more recent study has revealed that suture repair elicits more intense oxidative stress when compared to Lichtenstein repair (21). By using malondialdehyde (MDA) as the measure of oxidative stress, this study has revealed that oxidative stress following Lichtenstein repair peaks at 12th h, then shows a rapid fall at 24th h, and almost returns to the baseline value after 48 hours. Similarly, Polat et al have reported that Lichtenstein repair can cause an increase in MDA level 6 hours after the operation, but its 24-hour value is even lower than the preoperative level (23). Papaziogas has also reported that a positive correlation has been found between neutrophil count and MDA at 12th h, but not at 48th hour (21). In the present study, we could not determine any correlation between TAS and leukocyte counts or CRP.

Oxidative stress can be defined as an imbalance between oxidants and antioxidants in organism. Like lipid peroxidation, plasma total antioxidant status is a well-established marker of oxidative stress (24). Some studies have started to focus on TAS while searching oxidative stress following surgery. However, the sample size in that kind of studies-like the present one – has a rather limited number of subjects because of the high cost of TAS testing. The only study which has searched the relation between hernia repair and TAS measurement has revealed a significant increase in TAS values at just 5 minutes and then 48 hours postoperatively (25). However, this study has put 5 laparoscopic hernia repairs along with 10 laparoscopic colon resections into the same group of lower abdominal operations; therefore, the result coming from the study could not tell us a specific decision about oxidative stress following tension-free hernia repair with prosthetic material.

In our study, GA group had a lower TAS value at 12th h than those in LA and SA groups. The difference between GA and SA groups was just at the level of significance, while the difference between LA and GA groups did not reach the latter level. At 24th h, the value of both LA and SA groups returned to a level similar to the preoperative value, and the differences between these two groups and GA groups became highly significant. However, the baseline and 24-hour values within GA group were not statistically different. Therefore, a strong decision could not be obtained regarding TAS from the present study.

It could be thought that local anaesthesia might direct the surgeons to a gentler technique, as the patient is conscious, and could feel more pain when the surgeon is not cautious enough

and disrespectful to tissues (personal communication). We could say: "The gentler the surgical technique, the lesser the surgical trauma; the lesser the trauma, the milder the inflammatory response and oxidative stress". This might also be the case of spinal anaesthesia as the patient is awake as well. Therefore, we think that beside anaesthesia-patient relation, the interaction of the surgeon with the type of anaesthesia could be a contributing factor to the results of this kind of studies.

The data in our study were collected prospectively with a strict study protocol, but not randomised. Instead of putting the patients into groups in a random style, we preferred informing the patients about the procedure and the type of anaesthesia, their advantages and disadvantages, and let them choose their anaesthetic method. Besides, we must accept that some patients absolutely expect their surgery to be performed under a general anaesthesia. In our opinion, this is more ethical, and does not compromise the results and conclusions of the study.

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