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Research Article

Comparative Study of Post Operative Analgesic Effect of Intraperitoneal and Port Site Instillation of Dexmedetomidine with Bupivacaine and Bupivacaine Alone After Laparoscopic Cholecystectomy

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Abstract: Intraperitoneal instillation of local anaesthetics has been shown to minimize post-operative pain after laparoscopic surgeries. We compared the antinociceptive effects of intraperitoneal dexmedetomidine with bupivacaine to intraperitoneal bupivacaine alone in patients undergoing laparoscopic cholecystectomy. **Methods:** A total of 120 patients were included in this prospective, double-blind, randomised study. Patients were randomly divided into three equal sized (n = 40) study groups. Patients received intraperitoneal and port site instillation of bupivacaine 60 ml 0.25% in Group B, bupivacaine 60 ml 0.25% + dexmedetomidine 1 mcg/kg in Group BD and Normal saline 60 ml in control group(placebo)P before removal of trocar at the end of surgery. The quality of analgesia was assessed by visual analogue scale score (VAS). Time to the first request of analgesia, total dose of analgesic in the first 24 h and patient recovery time , patient satisfaction and adverse effects were noted. Statistical analysis was performed using SPSS version 21.0 Software . **Results:** VAS at different time interval when compared with control group(placebo),Bupivacaine and Bupivacaine +Dexmedetomidine group had less vas score throughout. There was significant difference in the VAS score between Bupivacaine, Bupivacaine+Dexmedetomidine(B+D) and control group with p value less than 0.05 during first 6 hours., time to first request of analgesia (min) was longest (345.40 ± 38.17, 258.8 ± 20.43,17.13 ± 2.37) and total analgesic consumption (mg) was lowest (68.25 ± 5.75, 80.80 ± 5.14, 183.48 ± 10.14) in Group BD than Group B and Group P.patient of group B+D had higher.satisfacion and earlier recovery than group p but similar to group B. **Conclusion:** Intraperitoneal Bupivacaine-dexmedetomidine combination is a better analgesic when compared to intraperitoneal instillation of bupivacaine, with well maintained haemodynamics postoperatively and superior satisfaction.

Keywords: Bupivacaine hydrochloride, dexmedetomidine hydrochloride, intraperitoneal injection,pain, post-operative.

INTRODUCTION

The field of surgery has been revolutionized by the advent of laparoscopic surgical procedures. The numerous reported benefits of the laparoscopic procedures like reduced blood loss, lower postoperative pain, better cosmesis, and shortened hospital stay have led to its increasing success over the last couple of decade (Shahi, K.S. *et al.*, 2015).One of the main demands for patients in post operative period is adequate analgesia. The surgical stress response reaches its peak during the first 24 hours postoperative period and has major effects on almost every body systems. Pain after laparoscopic surgery results from the stretching of the intra-abdominal cavity (Alexander, J. I. 1997), peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide (CO2) in the peritoneal cavity.A pain-free and stress free postoperative period definitely helps in early ambulation and recovery, thereby lowers down morbidity and mortality. Postoperative analgesia remains a major challenge after laparoscopic surgeries (Wu, J. M. *et al.*, 2007). Intra peritoneal local anaesthetic infilteration is a simple, cheap and safe method of providing post operative analgesia. Intraperitoneal instillation of local anaesthetic agents alone (El-labban, G. M. *et al.*, 2011) or in combination with opioids, (Ahmed, B. *et al.*, 2008; Golubović, S. *et al.*, 2009) α-2 agonists such as clonidine and dexmedetomidine (Ahmed, B. *et al.*, 2008) have

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shown reduction in post-operative pain following laparoscopic cholecystectomy. Dexmedetomidine has become one of the commonly used drugs in anaesthesia practice due to its hemodynamic, sedative, anxiolytic, analgesic, neuroprotective and anaesthetic sparing effect. High selectivity of dexmedetomidine to α_2-receptors has been exploited in regional anesthesia field. The aim of this study is to compare the analgesic effects of intraperitoneal and port site instillation of dexmedetomidine combined with bupivacaine to intraperitoneal and port site instillation of bupivacaine alone in patients undergoing laparoscopic cholecystectomy.

METHODS

This randomised, double-blind, prospective controlled trial was undertaken following approval from the Institutional Ethics Committee between November 2016 to April 2018 in a tertiary care hospital in the city of Haldwani. A total 120 participants were enrolled into the study. The patients were Aged between 18-65 years, with Physical status ASA 1 and ASA 2 of either sex undergoing Elective laparoscopic cholecystectomy under GA. Patients were excluded if the patients were aged < 18 yr old and >65year, refused consent, were allergic to local anaesthetic and study drug, with acute cholecystitis with severe cardiac, pulmonary. Neurological and psychiatric disease, those in whom procedure had to be converted to open cholecystectomy, in whom abdominal drain was put excluded from study and BMI>30kg/m^2.

In the operating room (OR), Electrocardiogram (ECG), saturation of oxygen (Sp02) and non invasive blood pressure monitoring were carried out and intravenous (IV) line was secured. Inj. Ringer Lactate infusion started with 8 mI/kg. patients were premedicated with Inj.Glycopyrrolate 0.2mg i.v, Inj Ranitidine 50 mg i.v., Inj. Ondansetron 4 mg i.v. All the patients received nalbuphine 10mg i.v. Anaesthesia induction was done with propofol - 2mg/kg and succinylcholine 1.5mg/kg i.v to facilitate intubation. All patients were intubated with apropriate sized oral cuffed endotracheal tube. Anaesthesia was maintained with nitrous oxide and oxygen mixture (50:50) with isoflurane. Ventilation is adjusted to maintain $EtCO_2$ between 36-42 mm of Hg. Vecuronium was used to maintain intraoperative neuromuscular blockade. Intravenous 75 mg diclofenac sodium was given intraoperatively in all patients. Neuromuscular blockade was reversed with neostigmine 5.0 mcg/kg and glycopyrrolate 1.0 mcg / kg after completion of surgery. All the surgeries were performed by surgeons with standard surgical technique using four ports. Intraperitoneal access was established through a umbilical incision. A carbon dioxide pneumoperitoneum was created using an insufflation pressure of 12 mmHg and a maximum flow of 2L/minute, controlled electronically during creation of the pneumoperitoneum and at later stages of the procedure. Pneumoperitoneum pressure was kept between 8-12 mm of Hg throughout the surgery. Intraoperative pulse, mean blood pressure (MBP), SpO_2 and $EtCO_2$ were monitored. Complete revisions of haemostasis was confirmed before the intraperitoneal instillation the drug.

The patients were allocated into three equal sized groups (N=40); Group (B): intraperitoneal bupivacaine 0.25%, made up to 60 ml (dilution by normal saline), Group (B+D): Intraperitoneal bupivacaine 0.25%, + 1µg/kg dexmedetomidine made up to 60 ml (dilution by normal saline) and Group (p=placebo) 60 ml normal saline.

The drugs were prepared and given to the investigators who was blind to the identity of drug. In the three study groups, out of 60 ml, 30 ml of the preparation of which 8ml was given at port site, 14 ml intraperitonel at creation of pneumoperitoneum, and 8ml at gall bladder base followed by rest 30 ml at same sites at the end of surgery. Intraperitoneal instillations guided by the camera on the surgical site. The intensity of the pain was assessed using visual analogue scale (VAS) at 0h, 2h, 6 h,12 h, and 24 h. Where zero score corresponds to ‘no pain’ and 10 corresponds to the ‘maximum’ or ‘worst pain. Rescue analgesia in the form of inj. diclofenac sodium 1.5 mg/kg i.m. was given for analgesia according to institutional protocol. If VAS>4 inj.tramadol 2 mg/kg i.v was given for analgesia. All patients stayed in PACU for 2 h after the end of surgery. The primary outcome variable was to compare pain (visual analogue scale [VAS]) score. The secondary outcome included time to the first request of analgesia in the post-operative period, total dose of analgesic used in 24 h period (post-operative) and any adverse/side effects, time to reach modified aldrete recovery score 9 and patient satisfaction. A total sample size of 120 patients (n = 40 each for three groups) was calculated using Power and Sample. size calculator (PS version 3.0.0.34), assuming 30% improvement in pain scores with alpha error of 0.05 and power of 80%Statistical analysis was performed using SPSS version 21.0 Software. Results were expressed as mean ± standard deviation, number and percentage (%).

Results

There was no significant difference seen in demographic parameters (age, sex, BMI), duration of surgery etc. among three groups. The hemodynamic parameters in all the groups were comparable and found to be statistically insignificant.

When compared with control group (placebo), Bupivacaine, and Bupivacane + Dexmedetomidine group had less vas score throughout.There was a significant difference in the VAS score between Bupivacaine, B+D and control group with p value less than point 0.05 during the first 6 hours. During the first 4 hours there was no significant difference in vas score

between Bupivacaine +dexmedetomidine group and Bupivacaine group.After 6 hours ,there was no significant difference between the three groups**.**

(Table no- 1)

Pain score (VAS)	Bupivacaine		Bupivacaine + Dexmedetomidine		Normal saline		
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	p-value
0 hour	3.10	0.93	2.10	0.91	5.67	0.80	<0.001*
2 hour	3.60	0.98	2.60	0.91	4.85	0.80	<0.001*
6 hour	3.27	0.96	3.04	0.81	4.57	0.84	<0.001*
12 hours	4.53	0.90	4.20	0.91	4.83	0.76	0.133#
24 hours	3.13	0.77	2.87	0.74	3.03	0.76	0.563#

One-way ANOVA test *** Significant difference,# Non Significant difference**

In our study controlled group required rescue analgesia at 17.13 Min.±2.37 when compared with Bupivacaine +Dexmedetomidine 345.40 min ± 38.17 and for Bupivacaine it was 258.83 min ± 20.43 postoperatively which was found to be highly significant. This showed that Bupivacaine +Dexmedetomidine group provided adequate analgesia for the first 6 hours when compared to Bupivaicaine group which provided analgesia up to 4 hour 20 min.(table-2).

Table 02- Rescue Analgesia Timing

	Rescue Analgesia Timing				
	Number	Mean	Std. Deviation	F-value	p-value
Bupivacaine	40	258.83	20.43	56.890	<0.001*
Bupivacaine + Dexmedetomidine	40	345.40	38.17		
Normal saline	40	17.13	2.37		
Bupivacaine vs Bupivacaine + Dexmedetomidine					<0.001*
Bupivacaine vs Normal saline					<0.001*
Bupivacaine + Dexmedetomidine vs Normal saline					<0.001*

One-way ANOVA test *** Significant difference**

Total analgesic requirement was less in both the group compared to controlled group, controlled group required 183.14 mg ±10.14 of Diclofenac sodium compare to Bupivacaine +Dexmedetomidine which required 68.25 mg± 5.75 of Diclofenac sodium and Bupivacaine group which needed 80.80 mg ± 5.14 of Diclofenac sodium with p value <0.001 which was statistically significant.

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There was a difference in the amount of rescue analgesic requirement between Bupivacaine +Dexmedetomidine(68.25 mg± 5.75) and Bupivacaine(80.80 mg ± 5.14) and the p>0.05)the difference was found to be statistically insignificant .

Table 03- Total Analgesic Dose requirement

	Total Analgesic Dose requirement				
	Number	Mean	Std. Deviation	F-value	p-value
Bupivacaine	40	80.80	5.14	70.243	<0.001*
Bupivacaine + Dexmedetomidine	40	68.25	5.75		
Normal saline	40	183.48	10.14		
Bupivacaine vs Bupivacaine + Dexmedetomidine					0.001*
Bupivacaine vs Normal saline					<0.001*
Bupivacaine + Dexmedetomidine vs Normal saline					<0.001*

One-way ANOVA test *** Significant difference**

Though there was difference in timing to reach Aldreate recovery score of 9 between Bupivacaine+Dexmedetomidine (42.05±1.33) and Bupivacaine (48.28 ± 1.76) groups the difference was found to be statistically insignificant.(table-4).

Table 04- Time to reach Aldrete score 9

	Time to reach Aldrete score 9 (in minutes)				
	Number	Mean	Std. Deviation	F-value	p-value
Bupivacaine	40	48.28	1.76	670.337	<0.001*
Bupivacaine+ Dexmedetomidine	40	42.05	1.33		
Normal saline	40	64.58	2.51		
Bupivacaine vs Bupivacaine + Dexmedetomidine					0.071#
Bupivacaine vs Normal saline					<0.001*
Bupivacaine + Dexmedetomidine vs Normal saline					<0.001*

There was no significant difference in the incidence of adverse effects between Bupivacaine, Bupivacaine and Dexmedetomidine combination and Normal saline groups. (Table-5)

Table 05- adverse effect

Post-operative Nausea and Vomiting	Bupivacaine	Bupivacaine + Dexmedetomidine	Normal saline	p-value
Present	4 (10.0%)	6 (15.0%)	2(5%)	0.077#
Bradycardia	Bupivacaine	Bupivacaine + Dexmedetomidine	Normal saline	p-value
Present	2 (5.0%)	3 (7.5%)	1 (2.5%)	0.232#
Hypotension	Bupivacaine	Bupivacaine + Dexmedetomidine	Normal saline	p-value
Present	2 (5%)	4(10.0%)	2 (5%)	0.359#

Highly satisfaction was significantly more among Bupivacaine and Dexmedetomidine combination in comparison to Bupivacaine and Normal saline groups. satisfaction was significantly more among Bupivacaine. No satisfaction was significantly more among Normal saline group.

Discussion

Laparoscopic techniques have gained popularity worldwide, mainly because of the fact that it involves small incision, short hospital stay, early recovery and early ambulation. Though it has got various advantages on its own, the peritoneal stretching due to the insufflation of gases results in excessive pain during post operative period.

Various modes of analgesia have been tried to overcome post operative pain. The techniques that can be employed for providing pain relief in Laparoscopic surgeries include surgery under sub-arachnoid block, parentral opioids and NSAIDs, Instillation of local anaesthetics intraperitoneally, etc In this modern age of surgery, intraperitoneal instillation of local anaesthetic agents has become an important measure to control post-operative pain, nausea, vomiting and reduced hospital stay (Chari, N. B. 2002).

The antinociceptive property of dexmedetomidine occurs at dorsal root neuron level, where it blocks the release of substance P in the nociceptive pathway and through action on inhibitory G protein, which increases the conductance through potassium channels (Kamibayashi, T., & Maze, M. 2000).

In our study we added dexmedetomidine to compare the antinociceptive efficacy if mixed with bupivacaine. Usha Shukla *et al.,* (2015), Vrinda p oza *et al.,* (2016), S. Chiruvella *et al.,* (Chiruvella, S., & Nallam, S. R. 2016) compared effects of local anesthetics and dexmedetomidine intraperitoneal instillation and our study is in concordance with their studies with respect to dexmedetomidine in terms of duration of analgesia, pain scores,total analgesia consumption.In our study mean duration of pain relief in Bupivacaine+dexmedetomidine group and bupivacaine group was 345.4 ±38.17 min and 258.83 ± 20.43 min respectively.In Saline (placebo) group it was about 17.13+/-2.373 minutes. S.Chiruvella *et al.,*.,compared Intraperitoneal dexmedetomidine combined with ropivacaine with that of intraperitoneal ropivacaine alone in the patients undergoing laparoscopic hysterectomy and found that time to first request of analgesia (min) was longest (126 ± 24 vs 59 ± 13) in RD group than in R group.

Usha Shukla, *et al.,* (2015) compared intra peritoneal dexmedetomidine or tramadol combined with bupivacaine to intra peritoneal bupivacaine alone in patients undergoing laparoscopic cholecystectomy), time to first request of analgesia (min) was longest (128 ± 20, 118 ± 22, 55 ± 18) in Group BD compared to group BT and group B. Vrinda P Oza *et al.,* (2016). compared the analgesic effect of intra peritoneal instillation of dexmedetomidine with bupivacaine with that of bupivacaine alone in patients undergoing laparoscopic surgeries.Duration of analgesia was longer in group B+D (14.5 hr) compared to group B (13.06 hr) which was significant.

S. K. Maharjan *et al.,* (2012), also favors our study performed in which they evaluate the analgesic efficacy of intra peritoneal bupivacaine and bupivacaine plus magnesium sulphate for postoperative pain relief after laparoscopic cholecystectomy. K.S. Shahi *et al.,* (2015). Compared Bupivacaine vs Bupivacaine with fentanyl with two different concentration of fentanyl (50mc and 100 mcs) intraperitonealy. The intergroup comparison of VAS scores at different intervals showed that group receiving 50ml of 0.2% bupivacaine with 100µg fentanyl had lower VAS score Intergroup comparison of VAS score at all time intervals however this was statistically significant only at 4 hrs and 6hrs which was similar to our study.

In our study there was no significant hemodynamic changes noted. PR, BP, SPO2 were maintained within 20% of the normal limit throughout the study. D.P. Bhattacharjee *et al.,* (2010), Usha Shukla, *et al.,* (2015) and co worker showed there was no significant change in the hemodynamics during the study which was similar to our study.

In our study it was found that the total dose of analgesic required in the post operative period was significantly less in both Bupivacaine plus dexdmedetomidine and bupivacaine group, when compared to the control group. Out of these two groups Bupivacaine + dexmedetomidine combination group needed less Diclofenac 68 ± 5.75mg, when compared with Bupivacaine group which needed 80.80. ± 34.81mg, though the difference was found to be statistically insignificant (p>0.05). But the saline group needed double the dose 183.48±10.14, which was statistically significant (p<0.05).

This difference in the Diclofenac requirement closely correlates with the study done by Sethy, A.K. (2018) where the total dose of pcm consumed in Bupivacaine+dexmedetomidine group was 1.2 ± 0.8 gm over 24 hour when compared to3.6 ± 0.4gm in bupivacaine group. This was statistically significant with a p value of<0.001.

Vrinda p oza *et al.,* (2016) also support our study in which they compared bupivacaine +dexmedetomidine combination vs bupivacaine intraperitonelyand found less analgesic (diclofenac) requirements in group Bupivacaine+Dexmedetomidine (1.76+0.20) compared to group Bupivacaine (2.56+0.16) which were statistically significant (P<0.05).

Usha Shukla, *et al.,* (2015) also support our study in whichthey compared bupivacaine+dexmedetomidine (BD) vs bupivacaine+tramadol (bt) vs bupivacaine (b) demonstrated total analgesic consumption (mg) was lowest (45 ± 15, 85 ± 35, 175 ± 75) in Group BD compared to BT and group B.

S. Chiruvella *et al.,* (2016) also supports our study Iin which they compared ropivacaine+dexmedetomidine (RD) and ropivacaine (R) intraperitonealy and found that total analgesic consumption (mg) was lowest (95 ± 15 vs 175 ±75) in RD group than in R group.

Ahmed *et al.,* (2008) observed that intraperitoneal instillationof meperidine or dexmedetomidine in combination with bupivacaine significantly decreases total rescue analgesia requirement in postoperative period.

In our study the median VAS score for Bupivacaine and dexmedetomidine combination group was 2.82 over 24 hours and in Bupivacain group median VAS score was 3.15, which was found to be statistically significant (p<0.05)

Vrinda p oza *et al.,* (2016) also support our study in which they compared bupivacaine +dexmedetomidine (BD) combination vs bupivacaine (B) intraperitonelyand found group BD (2.52±0.54hr) has less vas score than group B (2.42±0.57) (p value 0.37 NS) till 8hr post operatively but not significant which is similar to our study. Usha Shukla, et. al also support our study in which they compared bupivacaine+dexmedetomidine (BD) vs bupivacaine +tramadol (bt) vs bupivacaine (b) and found that the overall VAS in 24 h was also significantly lower in Group BD (1.80 ± 0.36) than and Group B (4.5 ± 0.92) which was similar to our study.In our study it there was no significant difference in alderete recovery score, patients satisfaction and occurrence of adverse effects.

CONCLUSION

We conclude that intraperitoneal instillation of local anaesthetic drug is useful for post operative pain relief for patients undergoing laparoscopic cholecystectomy and Bupivacaine-dexmedetomidine [60 mL bupivacaine 0.25% + 1 µg/kg dexmedetomidine] produces prolonged duration and less requirement of rescue analgesics in postoperative period compared to that with bupivacaine alone [intraperitoneal 60 mL bupivacaine 0.25%] with well

maintained hemodynamic postoperatively and superior satisfaction.

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Conflicts of Interest

There are no conflicts of interest.

REFERANCES-

1. Shahi, K.S., Bhandari, G., & Parmar, N.K. (2015). Evaluation of Intraperitoneal and Port Site Infiltration of Bupivacaine in Combination with Fentany lfor Management of Postoperative Pain following Laparoscopic Cholecystectomy: A Double Blind Randomized Study. *Prensa Med Argent 101-5.*
2. Alexander, J. I. (1997). Pain after laparoscopy. *British journal of anaesthesia*, *79*(3), 369-378.
3. Wu, J. M., Wechter, M. E., Geller, E. J., Nguyen, T. V., & Visco, A. G. (2007). Hysterectomy rates in the United States, 2003. *Obstetrics & Gynecology*, *110*(5), 1091-1095.
4. El-labban, G. M., Hokkam, E. N., El-labban, M. A., Morsy, K., Saadl, S., & Heissam, K. S. (2011). Intraincisional vs intraperitoneal infiltration of local anaesthetic for controlling early post-laparoscopic cholecystectomy pain. *Journal of minimal access surgery*, *7*(3), 173.
5. Ahmed, B., Elmawgoud, A. A., & Dosa, R. (2008). Antinociceptive effect of (α2 adrenoceptor agonist) dexmedetomidine vs. meperidine, topically, after laproscopic gynecologic surgery. *J Med Sci*, *8*, 400-4.
6. Golubović, S., Golubović, V., Cindrić-Stančin, M., & Sotošek Tokmadžić, V. (2009). Intraperitoneal analgesia for laparoscopic cholecystectomy: bupivacaine versus bupivacaine with tramadol. *Collegium antropologicum*, *33*(1), 299-302.
7. Chari, N. B. (2002). Intraperitoneal bupivacaine instillation for postoperative pain relief after laparoscopic cholecystectomy. *Indian J Anaes*, *46*(1), 49-52.
8. Kamibayashi, T., & Maze, M. (2000). Clinical uses of α2-adrenergic agonists. *Anesthesiology: The Journal of the American Society of Anesthesiologists*, *93*(5), 1345-1349.
9. Shukla, U., Prabhakar, T., Malhotra, K., Srivastava, D., & Malhotra, K. (2015). Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy: A comparative evaluation. *Indian journal of anaesthesia*, *59*(4), 234.
10. Oza, V. P., Parmar, V., Badheka, J., Nanavati, D. S., Taur, P., & Rajyaguru, A. M. (2016). Comparative study of postoperative analgesic effect of intraperitoneal instillation of dexmedetomidine with bupivacaine and bupivacaine alone after laparoscopic surgery. *Journal of minimal access surgery*, *12*(3), 260.
11. Chiruvella, S., & Nallam, S. R. (2016). Intraperitoneal instillation of ropivacaine plus dexmedetomidine for pain relief after laparoscopic hysterectomy: A comparison with ropivacaine alone. *Journal of Dr. NTR University of Health Sciences*, *5*(2), 93.
12. Maharjan, S. K., & Shrestha, S. (2012). Intraperitoneal magnesium sulphate plus bupivacaine for pain relief after laparoscopic cholecystectomy. *Journal of Kathmandu Medical College*, *1*(1), 21-25.
13. Bhattacharjee, D.P., Nayek, S.K., Dawn, S., Bandopadhyay, G., & Krishna. (2010). Effects of Dexmedetomidine on Haemodynamics in Patients Undergoing Laparoscopi Cholecystectomy- A Comparative Study *J Anaesth Clin Pharmacol, 26(1),45-4832.*
14. Sethy, A.K. (2018). Intraperitoneal Analgesia for Postoperative Pain Relief after Laparoscopic *Surgeries. Ann. Int. Med. Den. Res,4(1),SG09-SG12.*
15. Ahmed, B., Elmawgoud, A. A., & Dosa, R. (2008). Antinociceptive effect of (α2 adrenoceptor agonist) dexmedetomidine vs. meperidine, topically, after laproscopic gynecologic surgery. *J Med Sci*, *8*, 400-4.