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Comparison of preemptive ketamine on postoperative analgesic effect between major open and major laparoscopic gynecological surgery

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Abstract

Objective of the study was to compare the preoperative ketamine on postoperative pain relief action between major open and major laparoscopic surgical procedures in female Jordanian population. Our investigation included 119 female adult patients, aged 31-55 years, classed I-II by the American society of Anesthesiologists (ASA) and scheduled for different elective major open and major laparoscopic surgical interventions under balanced general endotracheal anesthesia after obtaining written informed consent from all participants at King Hussein hospital, King Hussein medical city, Amman, Jordan, during the period Jan 2012-Jan 2014. All the participants were divided according to type of surgical approach into two groups. Group I patients (n=59) were exposed to major open gynecological surgery and group II patients (60) were exposed to major laparoscopic gynecological surgery. In both groups, intramuscular ketamine 0.5 mg/kg was administered after general intravenous anesthesia was induced and 5 minutes before incision was made. Postoperative pain relief quality was evaluated using the numerical pain rating scale (0-10) where 0=no pain, 1-3=mild pain, 4-6=moderate pain, 7-9=severe pain and 10=worst severe pain; time to first pain killer demand and total analgesic consumption, during the first 24 postoperative hours. Results were statistically assessed using the student‘t’ test with a probability value less than 0.05 considered significant. The mean score was 7.2, 5.9 and 5.2 at 0.2 and 6h time intervals, respectively in group I. The mean score was 5.1, 4.2 and 3.4 at 0.2 and 6h time intervals, respectively in group II (P<0.05). Intramuscular ketamine 0.5mg/kg administration after induction of intravenous general anesthesia and 5 minutes pre-incision shows a preemptive action in decreasing pain after gynecological laparoscopic surgery.

Keywords: Gynecology, laparoscopy, open, ketamine, preemptive, pre-incision; pain: postoperative.

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Introduction

Postoperative pain not only complicates the consciousness and recovery but prolongs hospitalization. Post-tissue insult extended pain and hyperalgesia (caused by primary excitatory neurotransmitters transmitting pain and releasing themselves in the spinal cord and stimulating NMDA receptor locations) is attributed to central sensitization in the spinal cord. Glutamate and aspartate (primary excitatory neurotransmitters) stimulate N-methyl-D-aspartate (NMDA) receptors which are incriminated in the wind up occurrence of central sensitization caused by noxious stimuli of operative insult at the central nervous system. NMDA receptor has a crucial role in pain processing as wind up, spinal neural plasticity and hyperalgesia. Interception and nociceptive input with the blockage of NMDA stimulation is mandatory for prophylactic pain relief.

Preemptive analgesia (using local anesthetics and opiates) is intended to decrease the severity and period of postoperative pain. It avoids post surgical insult pain by the use of NMDA receptor antagonist. Woolf CJ, et al demonstrated a central part of post-insult pain hypersensitivity [1]. Pre-insult different anti-nociceptive methods are more potent in decreasing the post-insult central sensitization in comparison to post-insult injection

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[1]. Lebrun T, et al showed a lack of preemptive analgesic action on postoperative pain after oral surgery [2] and Adam F, et al found that preoperative analgesic has no preemptive pain relief action in patients scheduled for total mastectomy [3]. This technique may decrease anesthetic needs and can be used as part of general anesthesia. Agent combination used for anesthesia includes short acting anxiolytic, intravenous anesthetics and moderate or short acting opioids. These drugs may cause respiratory inhibition and hypotension if large doses are administered.

Ketamine hydrochloride is a general anesthetic with short acting strong analgesic property, acting on nicotinic and muscarinic receptors [4]. Ketamine is a direct blocker at the receptors engaged in central sensitization. For the analgesic and antinociceptive hypnotic actions, ketamine blocks non-competitively (antagonism) the NMDA receptors, non-NMDA glutamate receptors and opiate receptors in the central nervous system of the central nervous system. Subanesthetic dose of ketamine decreases peripheral afferent noxious activation preventing central sensitization of nociceptors Ketamine may exaggerate effects of hypnotics and opioids, decrease anesthetics needs, enhance rapid recovery and prevent adverse effects of anesthetics.

The aim of our study was to compare the preoperative ketamine on postoperative pain relief action between major open and major laparoscopic surgical procedures in female Jordanian population.

Methods

Our prospective and double blind investigation enrolled 110 adult female patients, aged 31-55 years, classed I-II physical status by the American society of anesthesiologists (ASA) and scheduled for different elective major open and major laparoscopic gynecological surgical procedures under balanced general endotracheal anesthesia after obtaining written informed consent from all participants and approval from our local royal medical services ethical and research committee at King Hussein hospital, King Hussein medical city, Amman, Jordan, during the period Jan 2012-Jan 2014. Patients with psychiatric disorders of any kind were ruled out from our study.

Patients were divided according to type of surgical approach into two groups. Group I patients (n=59) were exposed to major various elective open gynecological surgery and group II patients (n=60) were exposed to major different elective laparoscopic surgery. In both groups, intramuscular ketamine 0.5mg/kg was administered after general intravenous anesthesia was induced and 5 minutes before incision was made. Postoperative pain relief was accomplished using morphine intravenous 2mg if the numerical pain rating scale was more than 5. Pain severity was evaluated at time intervals 0, 2, 6 and 24 postoperative hours. Time interval 0 was defined as the time of fully consciousness.

Postoperative pain relief quality was evaluated using the numerical pain rating scale (0-10) where: 0=no pain; 1-3=mild pain; 4-6=moderate pain; 7-9=severe pain and 10=the worst severe pain. Time to first morphine demand and total morphine consumption during the first 24 postoperative hours were recorded.

Statistical analysis: Results were assessed using the Mann Whitney test with a probability value less than 0.05 considered significant.

Results

Table I: Demographic characteristics of patients (mean ± SD, range).

	Group I (n=59) Mean ± SD	**Group II (n = 60) Mean ± SD**	**P**
Age(years)	45.5 ± 9.5 (36-55)	41.0 ±10.0 (31-51)	>0.05
Duration of procedure (min)	113 ± 12.5	101 ± 8.5	>0.05
ASA I II	42 17	45 15	>0.05
Gynecology elective surgery	open	Laparoscopy	

There were no significant differences in demographic characteristics of patients between the two groups. Table I.

Numerical pain rating scale scores were shown in table II. During the 0, 2 and 6 hours postoperative time intervals, the numerical pain rating scale scores were significantly reduced in group II than that in group I. The mean score was 7.2, 5.9 and 5.2 at previous time intervals, respectively in group I. The mean score was 5.1, 4.2 and 3.4 at same previous time intervals in group II (P<0.05).

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The mean time for the first morphine demand was 112minutes in group II and 76 minutes in group I. It was significantly less in group I than in group II (P<0.05). In group I, 44.1% of patients did not require morphine postoperatively and 90% of patients in group II did not need morphine postoperatively (P<0.05). The total number of morphine administrations in the first postoperative 24hours was 33 in group I and 6 in group II (P<0.05). The mean morphine requirements per total patient number group was 1.1 mg in group I and 0.2mg in group II (P<0.05). Table II.

Table II: Quality of postoperative pain relief.

	Time intervals	Group I	Group II	P
NPRS* (mean ± SD)	0 h	7.2±1.3	5.1±1.2	<0.05
	2h	5.9±1.2	4.2±0.3	<0.05
	6h	5.2±1.1	3.4±1.3	<0.05
	24h	3.0±0.8	2.5±0.7	>0.05
Total number of morphine administrations	0h	26	6	<0.05
	2h	5	0	<0.05
	6h	2	0	<0.05
	24h	0	0	>0.05
Mean time for the first morphine demand(min)		76	112	<0.05
Mean morphine requirements per total patient number group(mg)		1.1	0.2	<0.05

*numerical pain rating scale

Discussion

Surgery induces tissue insult with pain. Improper postoperative analgesia may cause late mobilization and psychological negative impact. Our investigation found that preemptive pre-incision intramuscular ketamine reduced postoperative pain in patients undergoing gynecological laparoscopic surgery more than in patients undergoing gynecological open surgery. Opiates, non-steroidal anti-inflammatory agents and local anesthetic infiltration have probable preemptive actions.

Ketamine is a general anesthetic with short acting analgesic characteristics [5]. Ketamine high intravenous dose administration has anesthetic property while low intravenous dose administration has analgesic property [6]. Ketamine binds to N-methyl-D-aspartate receptors which act in pain transmission, causing a non-selective antagonism decreasing hyperalgesia [7]. The NMDA receptors processing the nociceptive input is overcome by low dose of ketamine, resulting in a non-competitive block [8]. Ketamine can be cornered in the receptor channel until the channel reopens after agonist stimulation. Ketamine may prevent or reverse central sensitization decreasing pain. Preemptive ketamine is currently used to manage postoperative pain using intravenous and epidural routes of administration. In our study we used the intramuscular route. Ketamine is a nonspecific NMDA receptor antagonist which interacts with opiates receptors. Low dose ketamine inhibits the spatial and temporal mechanisms of secondary hyperalgesia, decreasing temporal summation of pain [9]. Ketamine has an opioid sparing action. The wind up explanation is blocked with increasing depth of anesthesia. The plasma ketamine concentration with clinical analgesia must be around 100-150 ng/ml [10]. The elimination half life of ketamine is around 130-155 minutes. The intrinsic analgesic characteristics of ketamine can decrease the postoperative pain. Direct pain relief action of ketamine may reduce the postoperative morphine demand. An insufficient afferent blockade can lead to reduced preemptive action of ketamine or a severe noxious stimulus can begin NMDA receptor stimulation and hyperalgesia. Low dose of ketamine is defined as a bolus dose of less than 1mg/kg injected intravenously. This may induce increased suppression of NMDA receptor stimulation. Enhanced pain relief with preemptive analgesia technique is promising in ambulatory, minimally invasive arthroscopic and laparoscopic surgery [11] where tissue insult is limited [12].

Various optimum peri-operative periods of administration have been used as at the induction of anesthesia or at the recovery .Preemptive pre-incision ketamine induced adequate analgesia with less postoperative morphine consumption in the first 24hours postoperatively in patients undergoing gynecological laparoscopic surgery. Postoperative pain is a result of peripheral and central sensitization. After free nerve endings activation by mechanical insult, chemical mediators of pain attain the pain more with primary hyperalgesia. Secondary hyperalgesia is produced when a alpha and beta nerve fibers are stimulated with peripheral sensitization.

Conclusion

Intramuscular ketamine 0.5mg/kg administration after induction of intravenous general anesthesia and 5 minutes pre-incision shows a

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preemptive action in decreasing pain after gynecological laparoscopic surgery.

References

1. Woolf CJ, Chong MS. Preemptive analgesia-treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg 1993; 77:362-79.
2. Lebrun T, Van Elstraete AC, Sandelo I, et al. Lack of a preemptive effect of low dose ketamine on postoperative pain following oral surgery. Can J Anesth 2006; 53:146-52.
3. Adam F, Libier M, Oszustowicz T, et al. Preoperative small dose ketamine has no preemptive analgesic effect in patients undergoing total mastectomy. Anesth Analg 1999; 89:444-7.
4. Taylor A, Stanbury L. A review of postoperative pain management and the challenges. Curr Anesth crit care 2009; 20:188-94.
5. Jung I, Kim YK, Kang MS, et al. Ketamine infusion therapy in a patient of posttraumatic syringomyelia. Korean j pain 2008; 21:248-51.
6. Sun JH, Koo MS, Nahm FS, et al. Pain management via a subcutaneous infusion of ketamine in a patient with complex regional pain syndrome: A case report. Korean J pain 2007; 20:190-4.
7. Traynelis SF, Wollmuth LP, McBain CJ, et al. Glutamate receptor ion channels: structure, regulation and function. Pharmacol rev 2010; 62:405-96.
8. Iikjaer S, Petersen KL, Brennum J, et al. Effect of systemic N-methyl-D-aspartate receptor antagonist (ketamine) on primary and secondary hyperalgesia in humans. BJA 1996; 76:829-34.
9. Arendt-Nielsen L, Petersen-Felix S, Fischer M, et al. The effect of NMDA antagonist (ketamine) on single and repeated nociceptive stimuli: A placebo controlled experimental human study. Anesth Analg 1995; 81:63-8.
10. Clements JA, Nimmo WS. Pharmacokinetics and analgesic effect of ketamine in man. BJA 1981; 53:27-30.
11. Kwok RF, Lim J, Chan MT, et al. Preoperative ketamine improves post operative analgesia after gynecologic laparoscopic surgery. Anesth Analg 2004; 98:1044-9.
12. Antonina S, Anita R, Indulis V. Low dose ketamine for supplement analgesia during minor day case gynecological surgery. Acta medica Lituanica 2012; 19(3):228-31.

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