

## CLONIDINE REDUCES POST OPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC GYNECOLOGICAL SURGERY

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### ABSTRACT

**Objective:** Post operative nausea and vomiting (PONV) is a distressing phenomenon after obstetrics laparoscopic surgery. In this study we assessed the efficacy of oral clonidine in controlling PONV in patients undergoing this type of surgery.

**Methodology:** In this prospective double blind study, 86 patients in ASA class one or two were selected. The study group (n=43) received clonidine 0.2mg tablet with 50ml water 60-90 minutes before surgery while control group (n=43) received placebo (the tablets were made at Ahwaz Pharmaceuticals Department). All patients were monitored for 24 hour post-operatively for presence of PONV. Hemodynamic changes after intubation between these groups were compared. Sedation and pain scores were also recorded during recovery using Ramsay score and by visual analogue scale respectively.

**Results:** Mean age in clonidine group was 28.5 years, and in control group was 30 years. Nine (21%) patients in study group and 19(44%) patients in control group nauseated. Seven (16.3%) patients in study group and 15 (34.9%) patients in control group vomited (P<0.05). Moderate pain was reported in 18 (41.9%) patient in study group as compared to 15 (34.9%) in control group. Severe pain was reported in seven (16.3%) patients in study group as compared to 21(48.8%) in control group (P<0.01). Four (9.3%) patient in clonidine group and 12 (27.9%) in control group received rescue anti-emetics (P<0.05). Mean blood pressure after intubation did not change in 35 (81.4%) of clonidine group compared to 26 (60.5%) in control group. Mean blood pressure on intubation decreased in five (11.5%) in clonidine group as compared to three (7%) in control group (p<0.02). Heart rate was reduced in five (11.5%) study group, while only two (4.7%) in control group (p=0.001). Ramsay sedation score was higher in most patients in clonidine group. Twelve (27.9%) patients in clonidine group had Ramsay score >3 compared to only 4 (9.3%) patients in control group (P<0.01).

**Conclusions:** Clonidine had statistically significant effect in reducing incidence of both nausea and vomiting. In addition it has favorable outcome on post operative pain score. Despite some limitations regarding higher sedation scores, no cases of significant hypoxemia or drop in blood pressure and heart rate was seen in both groups. It is an oral effective, inexpensive, readily available drug with low side effects and thus we suggest its routine use in laparoscopic surgery.

**KEY WORD:** Nausea, Vomiting, Laparoscopy, General anesthesia.

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### INTRODUCTION

Despite advances in anesthesia and surgery nausea and vomiting (PONV) is still a frequent problem. Reported incidence is 40-85% after different type of operations and 40-75% after

laparoscopic surgery.<sup>1,2</sup> Factors such as age, gender, pregnancy, menstrual cycle, previous history of nausea and vomiting or motion sickness, duration of anesthesia, obesity, use of nitrous oxide, opioids, smoking and certain types of surgery like laparoscopy are implicated as causative factors.<sup>1,2</sup> Laparoscopy is used more frequently for diagnosis and surgery.

Pneumoperitoneum induced by laparoscopy can stimulate vagal response and induce release of various emetogenic substances such as 5-hydroxytryptamine and acetylcholine and hence increase nausea and vomiting.<sup>3</sup> Females are 2-3 times more prone to PONV especially following gynecologic laparoscopic surgery with an incidence rate of 30-60%.<sup>1</sup>

PONV leads to delay in patient discharge, dehydration, more bleeding, suture dehiscence, risk of aspiration and patient discomfort along with increase hospital fees. Several drugs are tried to reduce its incidence including metochloprimide, droperidol and ondanestrone.<sup>1,2,4</sup> Clonidine is an  $\alpha_2$  sympathetic stimulant and has drawn attention as having anti-emetic properties which has been investigated in several situations such as breast, shoulder and strabismus surgeries.<sup>5-10</sup> It has been found to have hemodynamic, sedative and analgesic effects.<sup>2</sup> In this study we evaluated the efficacy of clonidine and compared its anti emetic properties to placebo in gynecologic laparoscopic surgery.

## METHODOLOGY

After approval of ethics committee of Jundishapur University of Medical Sciences and getting written informed consent, this double blind clinical prospective study was conducted during 2007 in Imam Khomeini hospital, Ahwaz. Eighty six women who were scheduled for gynecologic laparoscopic surgery with simple random sampling were selected. All patients had ASA class one or two, aged between 15-55, body mass index less than 30 with an operation time of less than one hour. Patients who had systolic blood pressure less than 90 or more than 160, previous anti emetic treatment or pregnancy were excluded from the study.

Forty three patients received either clonidine 0.2 mg orally with 50 cc water 60-90 minutes before anesthesia (clonidine group) or placebo (tablets were made at Ahwaz Pharmaceuticals Department). (Control group). Anesthesia was standardized and induced similarly in all patients. No other premeditation was given. Anesthesia was induced with midazolam 0.2mg/kg, fentanyl 2 $\mu$ g/kg followed by sodium thiopental 5mg/kg and tracheal intubation facilitated by 0.5 mg/kg atracurium and maintained under 50% N<sub>2</sub>O in O<sub>2</sub>. At the end of the procedure muscle relaxation was reversed with 0.05mg/kg neostigmin and 0.02 mg/kg atropine. All patients were monitored during recovery period with pulse oxymetry and non-invasive blood pressure measurement. Severe pain during recovery period was relieved with 50 mg intramuscular meperidine.

*Measurements:* Incidence of PONV was recorded in all patients for 24 hour post operatively. Patients who vomited at least twice in first 30 minutes, or had severe vomiting were treated with 10mg metocholpramide IV. Pain was measured by visual analogue scale. Sedation was assessed by Ramsay sedation scores. Ramsay scale<sup>11</sup> has 6 levels, namely: 1) an agitated patient, 2) a calm cooperative 3) respond to commands, 4) brisk response to glabellar tap, 5) sluggish response to glabellar tap and finally 6) no response to glabellar tap. Since sedation scores higher than three are considered significant for the anesthetist, we compared these scores in both groups using chi square test. We also compared the groups with respect to incidence hemodynamic changes following intubation. A change of more than 10% increase or decrease in mean blood pressure and heart rate in both groups was considered positive. Patient satisfaction was measured by using four point scale (1= very satisfied, 2=satisfied, 3=less satisfied 4=not satisfied). Data analyzes was made with Chi square and Fisher tests utilizing SPSS software version 13.

## RESULTS

Mean age in clonidine group was 28.5 years and in control group was 30 years. Nine patients (20.9%) of clonidine group developed nausea

Table-I: Incidence of nausea, vomiting, need for anti-emetics and pain among patients in clonidine and placebo-treated groups (n=43 each group) in women undergoing gynecologic laparoscopic surgery

Parameters	Clonidine group		Placebo group		P value
	Positive	Negative	Positive	Negative	
Nausea	9	34	19	24	0.021
Vomiting	7	36	15	28	0.048
Need of rescue anti-emetic in 24 hours	25	18	36	7	0.009
Post operative pain	4	39	12	31	0.027
Satisfaction	30	13	21	22	0.048

as compared to 19 (44.2%) of control group  $P < 0.05$ . (Table-I). Seven patients (16.3%) in clonidine group vomited as compared to 15 patients (34.9%) in control group. ( $P < 0.05$ ) (Table-I). Four (9.3%) patient in clonidine group and 12 (27.9%) in control group received metoclopramide ( $P < 0.05$ ) (Table-I).

Mean blood pressure on intubation and during surgery decreased in five (11.5%) as compared to three (7%) in control group ( $P < 0.05$ ). Heart rate was reduced in five (11.5%) while only two (4.7%) in control group during intubation and during operation it was reduced in eight (18.6%) clonidine-treated patients compared to two (4.6%) in control group (Table-II) ( $P < 0.05$ ). Moderate pain was reported in 18 (41.9%) patient study group as compared to 15 (34.9%) in control group and severe pain was reported in seven (16.3%) patients study group as compared to 21 (48.8%) in control ( $P < 0.01$ ) (Table-I). Ramsay sedation score more than three was higher in Clonidine group ( $p < 0.05$ ). (Table-III).

### DISCUSSION

Since PONV is disturbing for the patients, its prophylactic treatment is very desirable. In a

study by Zhaoh, they compared the effects of clonidine and those of midazolam on postoperative shivering, nausea and vomiting in elderly patients with elective surgery for reduction of nausea. Oral clonidine  $4\mu\text{g}/\text{kg}$  was compared to  $0.05\text{ mg}/\text{kg}$  intramuscular midazolam.<sup>7</sup> He showed superior effect of Clonidine group.

Evaoddy et al compared  $2\mu\text{g}/\text{kg}$  intravenous clonidine to placebo in mastectomy operations. Clonidine group had significant less nausea and vomiting during 24 hour post operative period.<sup>8</sup> These studies compare followably with our results. In our study clonidine group had higher sedation scores and less pain ( $P < 0.01$ ).

Oral Clonidine was compared to oral midazolam by Grottke<sup>9</sup> in shoulder surgery and by Fuji<sup>10</sup> in pediatric strabismus operations, in both of which clonidine groups had less nausea and vomiting. In a study Kobayashin, et al<sup>11</sup> compared  $150\text{ mg}$  epidural to  $150\text{ mg}$  oral clonidine. Epidural group had significant less vomiting than oral group ( $p < 0.001$ ) and oral group better than placebo ( $p < 0.05$ ). In another study by Mikawa,  $4\mu\text{g}/\text{kg}$  oral Clonidine produced less nausea and vomiting compared to  $2\mu\text{g}/\text{kg}$  oral clonidine and  $0.04\text{mg}/\text{kg}$  oral midazolam.<sup>12</sup>

Table-II: Changes in the heart rate and blood pressure ( $\pm 10\%$ ) from baseline at intubation time among patients in clonidine & placebo-treated groups in women undergoing gynecologic laparoscopic surgery

Parameter		Clonidine group	Placebo group	P Value
Hear Rate change/ minute	Increase	3 (7%)	17(8.1%)	<0.05
	Decrease	5(11.6%)	2(4.7%)	
	Unchanged	35(81.4%)	24(55.8%)	
Mean Blood Pressure Change (mmHg)	Increase	3(7%)	14(32.6%)	<0.05
	Decrease	5(11.6%)	3(7%)	
	Unchanged	35(81.4%)	26(60.5%)	

Mean heart rate and blood pressure changes are lower in clonidine group ( $p < 0.05$ ). Better hemodynamic stability in clonidine group  $>10\%$  change in heart rate or mean blood pressure was considered significant

Table-III: Level of sedation on recovery (according to Ramsey score lower and higher than 3) among patients in clonidine- and placebo-treated groups (n=43 each group) in women undergoing gynecologic laparoscopic surgery

Ramsay sedation scale	Clonidine group	Placebo group	P Valued
<3	31	39	<0.05
>3	12	4	<0.05

Clonidine group had higher score (P<0.05)

Toshu Yotsui, found that clonidine premedication prevents sympathetic hyperactivity but does not suppress hypothalamo - pituitary - adrenocortical responses in patients undergoing laparoscopic cholecystectomy.<sup>3</sup> They showed reduction of hemodynamic effect in clonidine premedicated group to intubation and surgery that was in accordance with lower adrenaline plasma levels. We also found lower blood pressures and lower heart rates in clonidine group, although none to a serious degree. This reduction in blood pressures and heart rate can be favorable in plastic, orthopedic or ophthalmic surgeries.

Patients in Clonidine group needed fewer analgesics but they were more sedated. However hypoxia (PO<sub>2</sub> <93%) was not observed in both groups. Our study proves that clonidine is effective on reducing emesis in gynecologic surgery similar to non-gynecologic surgeries as reported previously. Clonidine is an inexpensive drug, easy to take orally, well accepted by patients and we suggest its routine use as premedication in laparoscopic surgery.

Despite its advantages clonidine causes higher sedation that will probably demand more recovery time, nursing work and vigilance.

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