Dexmedetomidine as adjuvant to anesthesia: a prospective, randomized trial

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Introduction. A number of investigators have identified antiemetic, antinociceptive and anesthetic sparing effects of dexmedetomidine [1,2]. We aimed to evaluate the impact of the intraoperative dexmedetomidine infusion on the opioids requirement, efficacy, safety and postoperative outcomes in patients undergoing gynecologic cancer surgery.

Materials and Methods. 120 adult women (20-79 years) undergoing extended abdominal hysterectomy were randomized into 2 groups: 1) control group (CON) n=60, 2) dexmedetomidine group (DEX) n=60.

Eligible patients were ≥18 yr old, ASA physical status of I–III. Patients were excluded if they were receiving an α2-agonist or antagonist within 14 days before the scheduled surgery or if they had any of the following: acute unstable angina, acute myocardial infarction in the past 6 weeks, heart rate (HR) <50 bpm, systolic blood pressure (SBP) <100 mm Hg, or heart block. Intraoperatively patients were excluded from the study if they had systolic blood pressure < 80 mmHg for > 5 minutes, heart rate < 40 bpm for > 5 minutes.

General anesthesia in all groups included sevofluran, fentanyl, ketamin, rocuronium bromide (BIS 40-60, TOF 0 counts), but in DEX group patients received additionally dexmedetomidine infusion. It has started 15 minutes before induction of anesthesia with the rate of 0,4 µg/kg/h. Postoperatively patients recieved NSAIDs. To assess the speed and quality of recovery the following were assessed: 1)extubation time; 2)frequency of postoperative nausea or vomiting (PONV); 3) numerical rating scale (NRS, 0-10); 4) total dose of rescue analgesics at the fist postoperative day. When a patient wanted pain relief or the NRS was ≥ 7, rescue analgesic (trimeperidine 20 mg IM) was administered. Incident of PONV defined as: postoperative nausea of ≥ 7 on the Nausea NRS (0-10); nausea resulting in a subject request for an antiemetic; an episode of emesis or retching. The postoperative outcomes were assessed for 24 hour postoperatively.

Results. Patients in both groups were comparable on demographic variables. Total dose of fentanyl did not differ between CON and DEX groups (0,0036±0,0008 mg/kg/h and 0,0033±0,0008 mg/kg/h, respectively, p=0,06).

No patients were excluded from the study due to intraoperative bradycardia or hypotension in CON group, but in DEX group 6 from 60 patients were excluded (p=0,01). (Table 1) Three of them were receiving beta1-blockers preoperatively. After registration of complications infusion of dexmedetomidine was stopped. All excluded patients were successfully treated and operated.

Table 1.Haemodynamics parameters in excluded patients

Patient (year)	MAP (mmHg) preoperative	HR(bpm) preoperative	Time of infusion min	MAP (mmHg) exclusion	HR(bpm) exclusion
B (59)	120	100	45	42,7	61
A (59)	103	58	75	66,0	38
L (57)	106	98	60	29,3	38
Z (41)	93	72	40	41,7	62
K (65)	104	60	50	39,8	38
M (63)	108	64	45	63,6	38

MAP: mean arterial pressure, HR: heart rate

MAP during anesthesia was lower in DEX group versus CON group after endotracheal intubation (p<0,01), after laparotomy (p=0,02) and at the end of surgery (p<0,01). (Table 2)

Table 2. Mean Arterial Blood Pressure (mmHg)

Time	CON (n=60)	DEX (n=54)
Preoperative	96,97±10,91	94,19±16,1247
Before induction	100,17±12,22	98,41±14,81
After intubation	104,33±18,61	88,07±17,75*
After laparotomy	104,57±15,82	98,01±16,61*
End of surgery	62,45±9,78	51,67±11,07*

CON: control group, DEX: dexmedetomidine group, * - p<0,05

Perioperative HR was also decreased in DEX group during endotracheal intubation (p<0,01) , after laparotomy (p<0,01) and at the end of operation (p<0,01). (Table 3)

Table 3. Heart Rate (beats/min)

Time	CON (n=60)	DEX (n=54)
Preoperative	79,29±10,34	78,18±13,01
Before induction	93,65±20,55	86,63±16,17
After intubation	93,61±18,55	80,40±15,30*
After laparotomy	77,67±12,41	66,27±9,85*
End of surgery	71,12±13,06	60,36±9,46*

CON: control group, DEX: dexmedetomidine group, * - p<0,05

Extubation time did not differ between groups (p=0,07). The frequency of PONV was lower in DEX group versus CON group (9,3% and 25%, respectively p=0,027). There were no differences in the postoperative pain intensity (p=0,3) and opioid consumption (p=0,053). (Table 4)

Table4 . Recovery variables

Variables	CON (n=60)	DEX(n=54)
Incidence of PONV (y/n)	15/45	5/54*
Extubation time (min)	48,9±43,7	38,6±52,1
NRS for degree of pain	2,4±2,6	2,8±2,6
Total dose of postoperative opioids (trimeperidine mg/kg/day)	0,65±0,16	0,60±0,18

CON: control group, DEX: dexmedetomidine group, * - p<0,05

Discussion. In our study intraoperative use of dexmedetomidine did not impact on extubation time, opioids requirement and postoperative pain intensity but significantly reduced the frequency of PONV. Dexmedetomidine decreased hemodynamic parameters during surgery up to significant intraoperative hypotension and bradycardia.

Klinger R.Y. et al. stated in 15,656 noncardiac surgical cases, that dexmedetomidine administration was not associated with more hypotension or bradycardia [3]. But a significantly higher percentage of patients met the composite endpoint criteria (hypotension, bradycardia, vasoactive agent administration). B. M. Biccard et al. showed that dexmedetomidine increased the incidence of perioperative hypotension, bradycardia, but it did not impact on the frequency major perioperative events [4]. Tufanogullari B et al. demonstrated that dexmedetomidine produced antiemetic, anesthetic- and opioid-sparing effects [1]. In our study dexmedetomidine reduced the incidence of PONV. The mechanisms by which α2 agonists reduces PONV are unclear [2]. The observed antiemetic effect of α2 agonists may be explained through a decrease in sympathetic tone; it has been suggested that PONV may be triggered by high catecholamine concentrations [5].

Dexmedetomidine is a potent α2 agonist with 8 times higher affinity for α receptors than that of clonidine. The POISE-2 trial showed that low-dose clonidine, compared with placebo, increased the risk of clinically important hypotension, clinically important bradycardia, and nonfatal cardiac arrest [6]. We should pay attention if we work with α2 agonist during surgery.

References.

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