The Egyptian Journal of Hospital Medicine Vol., 4 : 1 – 15 September 2001
I.S.S.N: 12084

Comparison of hemodynamic responses to dexmedetomidine versus esmolol in patients undergoing beating heart surgery

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Abstract

Background: Alpha 2-adrenergic agonists decrease sympathetic tone with ensuing attenuation of neuroendocrine and hemodynamic responses to anesthesia and surgery. Also, administration of beta -adrenergic antagonists contributes to prophylaxis against hypertension, tachycardia and myocardial ischemia and myocardial protection during cardiac surgery. The effects of dexmedetomidine (DEX), a highly specific alpha 2-adrenergic agonist, on these responses have not yet been fully reported in patients undergoing cardiac surgery. Esmolol (ESM) is a cardioselective, short-acting β -blocking agent. Previous studies have established the effectiveness of esmolol in the reduction of hemodynamic responses during anesthetic induction.

Aim: The study of hemodynamic responses of dexmedetomidine and esmolol and their effects on the anesthetic requirements during anesthesia in beating heart surgery.

Methods: Forty patients scheduled for elective beating heart surgery received a dexmedetomidine 1 ug/kg over 10 min before anesthesia was induced and 0.5 ug/kg/h thereafter until the end of surgery in the DEX group and a loading dose of 0.5mg/kg esmolol IV was given over 5 min followed by a continuous infusion of 50 ug/kg/h until end of surgery in the ESM group. Total intravenous anesthesia using fentanyl, cisatracurium and propofol and oxygen air mixture (40%-60%) was used until the end of surgery. Hemodynamics measured included heart rate, mean arterial pressure, filling pressures, cardiac index, systemic and pulmonary vascular resistances. The incidence of hypotension, hypertension, tachycardia, bradycardia, dysrhythmias, ST segment changes, total anesthetics requirements, muscle rigidity and postoperative shivering were recorded.

Results: DEX significantly decreased HR and CI to after to 70±6 bpm and 2.2±0.1 l/min/m^2 ($p<0.05$) 3 min then, increased HR and CI significantly to baseline recording to 77±9 bpm and 2.5±0.1 l/min/m^2 ($p<0.05$) after 10 min from the start of infusion. In the postinduction period HR insignificantly decreased to 71±8 bpm after sternotomy about 65 min from the start of infusion. The postinduction period showed insignificant gradual increase in HR to 79±6 bpm while, CI continued to be below or at the baseline reading till it reached the baseline recording at the end of surgery. ESM dropped HR insignificantly at 3 min of infusion to 73±8 bpm and significantly dropped CI to 2.1±0.3 l/min/m^2 ($p<0.01$). HR and CI continued to show insignificant changes till the end of surgery but HR exceeded the baseline readings and CI did not reach it. DEX significantly increased MAP and SVRI to 101±13 mmHg ($p<0.05$) and 3985±243 dyn.s.cm^5.m^{-2} ($p<0.01$) at 3 min of infusion then significantly decreased to baseline reading to 89±10 mmHg and2428±276 dyn.s.cm^{-5}.m^{-2} at 10 min time interval. MAP

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continued to decrease till it developed a significant drop to 74±9 mmHg poststernotomy around 65 min after the start of infusion and gradually increased insignificantly to 78±6 mmHg at the end of surgery while, SVRI did not show any significant changes. In ESM group, MAP was decreased significantly to 87±14 mmHg ($P < 0.05$) 3 min after the start of infusion and did not show any significant change till the end of surgery while, SVRI did not show significant changes during different studied time intervals. The CVP, PCWP, MPAP and PVRI did not show any statistically significant change at the study time intervals in both groups. DEX had less incidence of intraoperative bradycardia (2 vs. 4 patients), tachycardia (0 vs. 2 patients), hypertension (0 vs 2), hypotension (2 vs 4) and ST changes (1 vs5). DEX also decreased the requirements of fentanyl (26.3±4.3 vs 35.4±5.1 ug/kg)), propofol (810±43 vs 935±52 mg) and midazolam. The incidence of fentanyl-induced muscle rigidity (5 vs 12 patients) and postoperative shivering (4 vs 13 patients) were less in DEX group than ESM group.

Conclusion: Dexmedetomidine in patients undergoing beating heart surgery decreased intraoperative sympathetic tone, induced sedation, attenuated hyperdynamic responses to anesthesia and surgery and overall hemodynamic variability than esmolol. The need for anesthetics, muscle rigidity, perioperative myocardial ischemia and shivering were less also in DEX group.

Introduction

Administration of beta-adrenergic antagonists contributes to myocardial protection during cardiac surgery. Esmolol is a cardioselective, short-acting β-blocking agent. Because it is rapidly metabolized by an aryl esterase in the blood, its elimination half-life is only 9 min.[1] Thus, the negative inotro -pic effect of β-adrenergic antagonism may not be an issue if esmolol is infused during anesthesia. Previous studies have established the effective -ness of bolus doses of esmolol in the reduction of hemodynamic responses during anesthetic induction.[2] However, prevention of the hemodynamic respo -nses to intubation has not been complete.[3,4] In addition, cardiac arrhy -thmias as prolonged QT interval syndrome or an acute myocardial infarc -tion have occurred during anesthesia.[5,6] Although β-adrenergic blockade is often a useful therapeutic approach, it may not always be practical in the setting of preexisting bronchospasm or reactive airway disease.[7] Because of the potential adverse effects of persistent tachycardia that failed to respond to esmolol or myocardial ischemia especi -ally during beating-heart surgery, it was suggested that dexmedetomidine repres -ents a potentially useful therap -eutic approach when treating such patients.[8] Dexmedetomidine is a more specific and selective α_2 agonist and has a shorter duration of action than clonidine. It produces dose-dependent sedation and analgesia.[9] These prope -rties make it theoretically a suitable agent for use as a part of an anesthetic regimen in patients undergoing beating heart surgery. In patients having non-cardiac surgery, perioperative adminis -tration of dexmedetomidine decreases the need for anesthetics and induces sympatholysis with ensuing hemody -namic and neuroendocrine stability.[10]

Aim of work

The aim of the present study was to compare the hemodynamic responses to esmolol infusion and that of dexmed -etomidine infusion during beating heart operations. As secondary variables, were also the effects of both drugs on the occurrence of perioperative

myocardial ischemia, fentanyl-induced muscle rigidity, requirements for anest -hetics, and on postoperative shivering.

Patients and Methods

After written informed consent was obtained during the preoperative interview, forty patients scheduled for beating heart surgery were randomized to two groups: the ESM group (n=20), and DEX group (n=20).

Exclusion criteria included ASA physical status V, a myocardial infarc - tion within one week before surgery, evidence of renal or hepatic failure, history of severe asthma, or history of allergy or idiosyncratic reaction to β-adrenergic blocking drugs. Ejection fraction and left ventricular end-diastolic pressure were obtained from the cardiac catheterization report. The patients received their regular antia - nginal medication till surgery. Electrocardiographic (ECG) informat - ion recorded included rhythm, presence of ST- or T-wave changes, PR interval, QRS duration, QT interval, and R-R interval. ST depressions greater than 0.6mm were considered significant.

All patients were premedicated with midazolam 0.1 mg/kg, morphine 0.1 mg/kg, and scopolamine 0.2–0.3 mg intramuscularly approximately 60–90 min prior to arrival in the operating room.

Prior to induction of anesthesia, ECG leads II and V5 were continuously recorded. After placement of peripheral intravenous (IV) lines and a radial arterial line, a Becton Dickinson (Criticath ^{TM} SP 5107HTD) pulmonary artery catheter was positioned for rea - dings of cardiac output (HP Component Monitoring system M1094A Hewlett Packard, Palo Alto, CA). All baseline measurements were taken after a 5-min stabilization period. These included heart rate (HR), mean arterial pressure [MAP], central venous pressure (CVP), mean pulmonary arterial pressure [MPAP], pulmonary artery wedge pressure (PAWP), and cardiac output (CO). The study drug infusion (dexmedetomidine or esmolol) was then commenced. The infusion rate of dexmedetomidine was set to deliver 1 ug/kg/min for 10 min before anesthesia was induced and 0.5 ug/kg/h thereafter until the end of surgery in the DEX group. A loading dose of 0.5mg/kg esm -olol IV was given over 5 min followed by a continuous infusion of 50 ug/kg/h until end of surgery in the ESM group. Prior anesthesia induction, hemodyn -amic measurements were recorded after the 3, 10 and 20 min (before induction) after the start of infusion of the study drug.

Anesthesia was induced with propofol 0.5-1 mg/kg then,10 ug/kg fentanyl was given in 5 min. During fentanyl infusion, ventilation was assis - ted manually with 100% oxygen. If clinically significant, fentanyl-induced chest wall muscle rigidity developed (recorded as yes or no) 0.15 mg/kg cisatracurium was given immediately. Otherwise cisatracurium was adminis - tered for muscle relaxation 1 min after completion of the fentanyl infusion. The patients were intubated when the hemo -dynamic measurements were made and muscle relaxation was complete. After intubation, anesthesia was maintained with a continuous infusion of fentanyl (3 ug/kg/h), cisatracurium (0.3 ug/kg/h), continuous propofol infusion 4-6 mg/kg/h and oxygen air mixture (40%—60%). Supplementary anesthe - tics and other drugs (an increase or a decrease of supplemental fentanyl, mid -azolam, administration of a fluid challenge, ephedrine, dopamine, or gly - ceryl trinitrate) were administered stepwise according to prespecified

hemodynamic criteria. Ringer's lactate solution was infused at an approximate rate of 10 ml/kg/h. Controlled mechan -ical ventilation was adjusted to maintain end-tidal carbon dioxide between 34 and 40 mmHg.

Hemodynamic measurements were obtained after intubation (The hemodynamic response to tracheal intub -ation was determined as maximal incr -eases in MAP, and HR within 10 min after intubation versus baseline values), skin incision, sternotomy, and at the end of surgery. Calculated indices used to compare cardiovascular function betw -een the two groups are as follows: Cardiac index (CI, L/min/m^2) = CO/BSA, where CO is cardiac output (L/min) and BSA is body surface area (m^2);Stroke volume index (SVI, mL/m^2) = CI/HR, where HR is heart rate (bpm); Systemic vascular resistance index (SVRI, dyne.s.cm^{-5}.m^{-2}) = (MAP-CVP)/CI x 80; and Pulmonary vascular resistance index (PVRI, dyne.s.cm^{-5}.m^{-2}) = (MPAP-PAWP)/CI x 80.

At the end of surgery, the study drug infusion was discontinued and the patient was transferred to the surgical intensive care unit. The lungs were ventilated after operation until stable hemodynamics and clinically adequate recovery from anesthesia and restor -ation of spontaneous respiration were achieved. Meperidine was admin -istered in 12.5mg increments for pain control and shivering. Postoperative shivering was recorded as “yes” or “no”. Fluid loading and vasoactive medication were administered accor -ding to clinical hemodynamic criteria.

Statistical Analysis

The results were reported as mean values ± standard deviations (SD). Hemodynamic data were analyzed with repeated-measures analysis of variance (ANOVA) to compare changes within each group and paired Student's t-test to compare different group data. Significance was $P < 0.05$.

Results

The demographic characteristics were similar in both groups with respect to age, weight, height, sex distribution, number of patients with previous myoca -rdial infarction, ASA physical status, and the number of patients taking preoperative beta blockers or calcium antagonists medication. There were no differences in physical examination variables and cardiac function (ejection fraction). The duration of surgery, and anesthesia; the number and type of the grafts were also similar in both groups as seen in table (1).

Table (1): Demographic data of both groups (mean±SD)

Parameter	DEX group	ESM group
Age (yr)	55.3±8.3	57.3±6.7
Weight(kg)	79.2±11	77.5±7.6
Height(cm)	174±9	170±12
Male/female	14/6	15/5
ASA class III/IV	16/4	17/3
Previous MI	6	4
β-blockers	14	13
Ca-antagonists	9	11
Ejection fraction	53±4	52±5
Duration of anesthesia	255±28	261±31
Duration of surgery	175±24	181±19

Number of grafts	3.2±1	3.3±1

Changes in Hemodynamic Variables During the Study:

Changes in HR with time in the preinduction period during DEX infusion showed a significant decrease to 70±6 bpm ($p<0.05$) after 3 min from the start of infusion. Then, it was increased significantly to baseline reco - rding to 77±9 ($p<0.05$) after 10 min from the start of infusion (table: 2). During the postinduction period the changes in HR with time did not show any significant change apart from an insignificant decrease to 71±8 bpm after sternotomy about 65 min from the start of infusion and did not show any change till the end of surgery (table: 3). Two patients in this group developed junctional escape rhythm and infrequent premature beats was noticed in another patient (table:4). The HR dropped insignificantly in the ESM group at 3 min infusion to 73±8 bpm during the preinduction period and continued to decrease insignificantly to 70±8 bpm before intubation. The changes in HR with time during the postinduction period showed insignificant gradual increase in HR to 79±6 bpm at the end of surgery. Two patients in the ESM group developed persistent tachycardia not responding to an increase in ESM infusion and one patient developed atrial fibrillation as shown in table (2),(3) and (4). So, dexmedetomidine reduced the HR more than esmolol and maintained this change till the end of surgery.

Changes in MAP with time during DEX loading period showed a significant increase to 101±13 mmHg ($p<0.05$) at 3 min from the start of infusion then significantly decreased to baseline reading to 89±10 mmHg ($p<0.05$) at 10 min time interval. MAP continued to decrease with time insignificantly in the pre and postinduction period till it developed a significant drop to 74±9 mmHg poststernotomy around 65 min after the start of infusion and gradually increased insignificantly to 78±6 mmHg at the end of surgery. In ESM group, MAP was decreased significantly to 87±14 mmHg ($P < 0.05$) 3 min after the start of infusion and did not show any significant change till the end of surgery as shown in table (2) and (3).

The CVP, MPAP and PCWP did not show any statistically significant change at the study time intervals in both groups as presented in table (2) and (3).

Changes in CI with time during DEX infusion showed a significant reduction to 2.2±0.1 l/min/m^2 ($p<0.05$) after 3 min from the start of infusion and significantly increased to 2.5±0.1 l/min/m^2 after 10 min time interval and continued to be below or at the baseline reading during the postinduction period till it reached the baseline recording at the end of surgery. ESM produced a significant drop in CI after 3 min from the start of infusion to 2.1±0.3 l/min/m^2 ($p<0.01$). CI continued to show insigni - ficant changes till the end of surgery and did not reach the baseline readings.

SVI in DEX group did not show any significant change at different time intervals before and after induction of anesthesia till the end of surgery. In ESM group, SVI decreased significantly to 29±4 ml/min/m^2 ($p<0.05$) at 3 min of the start of infusion then gradually incr - eased insignificantly to 31±4 ml/min/m^2 at the end of surgery.

SVRI in the DEX group showed a significant increase to about double the baseline reading after 3 min from the

start of infusion to 3985±243 dyn.s.cm^{-5}.m^{-2} ($p<0.01$). At 10 min time interval SVRI decreased significantly to 2428±276 dyn.s.cm^{-5}.m^{-2} and did not show a significant change till the end of surgery. In the ESM group SVRI did not show significant changes during different studied time intervals.

PVRI in both groups did not show statistically significant changes at different studied time intervals.

Table (2): Hemodynamic data of both groups before induction of anesthesia.

Parameter	Baseline	3 min after start of infusion	10 min after start of infusion	Before Induction
HR(bpm)				
DEX	78±7	70±6*	77±9*	78±8
ESM	74±6	73±8	72±7	72±5
MAP(mmHg)				
DEX	90±11	101±13*	89±10*	88±12
ESM	93±12	87±14*	86±9	84±15
CVP(mmHg)				
DEX	9±3	8±6	10±5	11±4
ESM	11±5	12±4	11±7	12±6
MPAP(mmHg)				
DEX	21±6	20±5	21±6	20±7
ESM	23±7	21±3	20±4	21±8
PCWP(mmHg)				
DEX	13±4	12±3	12±4	12±4
ESM	15±3	13±4	13±3	13±4
CI(l/min/m^2)				
DEX	2.6±0.2	2.2±0.1*	2.5±0.1*	2.6±0.1
ESM	2.7±0.1	2.1±0.3*	2.2±0.2	2.3±0.1
SVI (ml/beat/m^2)				
DEX	33±4	31±5	32±4	33±5
ESM	36±3	29±4*	30±5	32±5
SVRI(dyn.s.cm^{-5}.m^{-2})				
DEX	2292±251	3985±243*	2428±276*	2384±346
ESM	2398±246	2478±311	2494±324	2483±375
PVRI(dyn.s.cm^{-5}.m^{-2})				
DEX	257±36	229±33	251±34	242±29
ESM	284±47	273±41	241±39	268±35

*HR=heart rate, MAP=mean arterial pressure, CVP=central venous pressure, MPAP=mean pulmonary artery pressure, PCWP=pulmonary capillary wedge pressure, CI=cardiac index, SVI=stroke volume index, SVRI=systemic vascular resistance, PVRI=pulmonary vascular resistance, *p<0.05.*

Comparison of hemodynamic responses

Table (3): Hemodynamic data of both groups after induction of anesthesia

Parameters	Before Intubation	10 min after intubation	After skin incision	After sternotomy	End of surgery
HR(bpm)					
DEX	75±9	74±7	75±6	71±8	74±7
ESM	70±8	72±8	74±7	75±7	79±6
MAP(mmHg)					
DEX	84±8	82±9	81±8	74±9*	78±7
ESM	81±7	84±9	85±7	83±7	84±8
CVP(mmHg)					
DEX	12±5	11±3	10±2	10±3	9±4
*ES*M	11±4	10±2	10±3	11±4	11±3
PAP(mmHg)					
DEX	21±3	19±3	20±4	20±3	21±3
ESM	20±4	19±4	19±3	20±4	20±4
PCWP(mmHg)					
DEX	13±4	11±3	12±3	11±2	12±3
ESM	12±4	11±2	11±2	12±3	11±3
CI(l/min/m^2)					
DEX	2.5±0.2	2.6±0.1	2.5±0.2	2.5±0.1	2.6±0.1
ESM	2.3±0.3	2.3±0.1	2.2±0.1	2.3±0.2	2.4±0.1
SVI (ml/beat/m^2)					
DEX	34±9	36±6	34±8	36±5	37±6
ESM	32±7	32±8	30±7	31±6	31±4
SVRI(dyn.s.cm^{-5}.m^{-2})	2308±346	2248±253	2251±232	2280±261	2243±247
DEX	2483±375	2573±236	2627±244	2539±254	2446±251
ESM					
PVRI(dyn.s.cm^{-5}.m^{-2})	242±29	246±32	256±33	288±29	276±34
DEX	268±35	278±27	290±28	278±26	295±31
ESM					

*HR=heart rate, MAP=mean arterial pressure, CVP=central venous pressure, MPAP=mean pulmonary artery pressure, PCWP=pulmonary capillary wedge pressure, CI=cardiac index, SVI=stroke volume index, SVRI=systemic vascular resistance, PVRI=pulmonary vascular resistance, *p<0.05.*

Incidence of hypotension, hypertension, tachycardia, bradycardia, dysrhythmia and ST segment changes:

In DEX group hypotension was observed in 2 patients (10%) during the first hour of the start of infusion while in ESM group it happened in 4 patients (20%). Hypotension was treated with fluid loading, plasma expanders and vasopressors (ephedrine 5mg bolus). During DEX infusion no patients developed hypertensive episodes, whereas two patients in ESM group developed hypertensive episodes and

nitroglycerine infusion was used to control blood pressure (table: 4).

Tachycardia (HR >110 bpm) developed in 2 patients (10%) in the ESM group and indral o.1 mg bolus was used to control the HR while no tachycardia developed in DEX group. There were 4 patients (20%) developed bradycardia (HR<50 bpm) in DEX group and 2 patients (10%) in the ESM group that returned to normal with pharmacologic interventions in the form of atropine 0.01 mg/kg.

Myocardial ischemia in the form of ST segment depression was noticed in one patient in the DEX group (5%) and in 5 patients in the ESM group (25%) which was treated by nitrogly -cerine infusion as seen in table 4.

Table (4): Incidence of Hypotension, Hypertension, Bradycardia, Tachycardia, Dysrhythmia and ST depression in both groups.

Abnormality	Group	No. of patients	Management
Hypotension	DEX	2 (10%)	fluid challenge, vasopressors
(MAP<60 mmHg)	ESM	4 (20%)	(ephedrine)
Hypertension	DEX	0	
(MAP>120mmHg)	ESM	2 (10%)	vasodilators (nitoglycerine)
Bradycardia	DEX	2 (10%)	atropine
(HR <50 bpm)	ESM	4(20%)	
Tachycardia	DEX	0	
(HR >110 bpm)	ESM	2 (10%)	indral
Dysrhythmia:			
Junctional rhythm	DEX	2 (10%)	---
ESM 0			
Atrial fibrillation	DEX	0	
ESM 1 (5%)		defibrillation	
ST depression	DEX	1 (5%)	nitroglycerine
(persistent ST	ESM	5 (25%)	
depression >0.6mm)			

Supplementary Anesthetics

The mean total number of intraoperative interventions required to maintain the hemodynamic parameters within the predetermined limits was significantly less in the DEX group. The total fentanyl dose was significantly increased in the ESM group per patient (35.4±5.1 ug/kg) than in the DEX group (26.3±4.3 ug/kg). The total dose of propofol per patient was significantly higher in the ESM group (935±52 mg) than in DEX group (810±43 mg). Midazolam 0.1 mg bolus was used more frequently in ESM group to reach a total dose of 9.4±2.6 mg per patient while rarely used in DEX group.

Fentanyl-induced Muscle Rigidity, Postoperative Shivering, and Diuresis

Five patients (25%) in the DEX group and 12 patients (60%) in the ESM group had muscle rigidity during or immediately after the induction dose of fentanyl (P<0.01). Postoperative shiver -ing occurred more frequently in the ESM group than in the DEX group (13 versus 4 patients). The patients of the DEX group excreted more urine than

did the patients of the ESM group during operation (1345± 215 ml) versus (975± 589 ml).

Discussion

Alpha2-adrenoceptor agonists, have been widely studied in humans. The prototype clonidine exerts a biph - asic effect on arterial blood pressure starting with transient hypertension followed by a longer lasting reduction in blood pressure.[11]The increase in blood pressure is mediated by an alpha 2-adrenoceptor-induced vasoconstric - tive response in the peripheral vascula - ture. The blood-pressure-lowering effe - cts of clonidine are largely mediated by centrally located receptors in the lateral reticular nucleus and locus ceruleus, which ordinarily mediates a pressor response.[12] This hypotensive effect is consistent with a resetting of the baroreceptor system to maintain a lower blood pressure. The result is a marked reduction in sympathetic tone and an enhanced parasympathetic outflow. Clonidine's ability to reduce blood pressure is limited to these effects on the autonomic nervous system (e.g., clonidine is not a vasodilator).[13]

Although the bradycardic effect of alpha-2 adrenergic agonists has been known for a long time, the mechanism for this action is in doubt. Alpha-2 adrenergic agonists enhance the barore - flex sensitivity to increases in systolic arterial pressure. Clonidine reduces HR by reduced sympathetic tone and the increased vagal tone.[9,11]

Hypertension, tachycardia, arrhy - thmias and myocardial ischemia for β-adrenergic stimulation are common occurrences in coronary artery disease patients in the perioperative period.[14] Esmolol has been used extensively during CABG as prophylaxis against hypertension, tachycardia and myocar - dial ischemia. Bolus doses ranging from 0.5 to 1.0 mg/kg have been used follo - wed by 6-12 mg/min. These doses have been found to effectively treat increases in HR that occur during

CABG and to block the β-adrenergic effects of catecholamines associated with surgical stress.[15] It produced signi - ficant reductions in MAP, HR and CI in patients with coronary artery disease and the effects were reversed 30 minutes after discontinuation of the infusion.[16] Other study showed that esmolol was unsuccessful in controlling HR as it significantly lowered the MAP without decreasing the HR.[17] The lack of further attenuation of the HR may be related to the inability of esmolol to occupy sufficient additional β-adrene - rgic receptors to produce added β-blockade in patients on chronic β-blockers.[4] Hypotension is common side effect of intravenous esmolol. The incidence of hypotension was higher with esmolol (36%) than with propra - nolol (6%) at equal therapeutic endpo - ints.[5]The cardioselective drugs may cause more hypotension because β_1-induced myocardial depression and the failure to block β_2-prepheral vasodilat - ion. Phlebitis may occur at the site of intravenous administration after prolon -ged esmolol infusion.[6]

Hemodynamic Response

Dexmedetomidine's hemodynamic profile was found to be similar to that previously reported for clonidine.[11] An initial transient increase in blood press - ure, mediated by peripheral vasoconst - riction (pressor effect), was followed by a reduction in blood pressure (depressor effect) due to both a centrally and peri - pherally mediated sympatholytic action. Dexmedetomidine significantly blunted the responses of MAP and HR to intub - ation, skin incision, and sternotomy, decreased the overall variability of

MAP, and decreased the incidence of hypertension and tachycardia. Previo -usly, Flacke et al.[13] observed improved hemodynamic stability in patients having CABG who were given clonidine and anesthetized with high-dose sufentanil and supplemental isoflurane, whereas Abi-Jaoude et al.[18] did not find any such decrease. A decreased incidence of tachycardia has been a common finding in patients receiving DEX undergoing non-cardiac surgery.[10,19]

Bloor et al.[11] reported an initial brief increase in MAP associated with marked, but transient reduction in HR 2 min after a 75-mg iv dose of DEX in humans. As this decrease in HR was associated with an increase in systemic blood pressure it is probably mediated by the baroceptor reflex. A reduced infusion rate of DEX may decrease the hypertension and thereby reduce the associated bradycardia.[20]

In the present study, the intraop -erative incidence of tachycardia requi -ring treatment was more common in the ESM group than in the DEX group. Moreover, in another study, bradycardia was more common in patients with DEX premedication and undergoing abdominal hysterectomy than in patients receiving midazolam premedication.[21]

Alpha-2 adrenergic agonists, in high doses, will depress atrioventricular (AV) nodal conduction. There is a slight prolongation in the P-R interval in subjects receiving clonidine, which suggest that the drug be withheld in elderly patients and those with an existing prolongation of the P-R interval or bradycardia.[8]

In another study, there was no difference between ESM and DEX in the incidence of hypotension. However, the volume of fluid challenge needed to maintain adequate filling pressure and to prevent hypotension was slightly greater in the DEX group than in the ESM group.[20]

In the present study, ESM did not control the HR and MAP as DEX. There were fluctuation in the HR, MAP and hemodynamic responses to surgical stimulation were not blunted as in DEX group.

The CO data obtained after the DEX infusion from the present study indicated a marked reduction during the early transient increase in blood pressure. DEX activates peripheral presynaptic apha-2 receptors which serve to reduce the release of catecholamines. In addition there is a reduction in the central sympathetic outflow through action on the regula -tory centers in the brainstem. Both the central and peripheral effects contribute to the reduction in catecholamines.[19,20]

Maze et al[12] using a flow-directed pulmonary artery thermal dilution catheter, have shown comparable reductions in CO. Bloor et al.,[11] using a two-dimension dopplerechocardiogra -phic method, reported a 23% reduction in CO 60 min after a single 100-mg dose of DEX. These findings are also consistent with those reported by others after clonidine.[9,11]

There was an approximate doubling of the SVRI during the period of increased arterial blood pressure (initial transient pressor effect) and reduced CI. This marked increase in SVRI was short-lived (less than 2 min). The combined reduction in sympathetic activity and the apparent increased SVRI would be undesirable in patients with impaired cardiac function.

These findings differ from those studies of patients having CABG and who received clonidine, in which either no effect on cardiac index or SVR was seen, or cardiac index was decreased and SVR was increased during induct -

ion of anesthesia and intubation.[18] These differences may be due to the different alpha-1/alpha-2 selectivity or to different routes of administration of dexmedetomidine and clonidine. If these effects are substantiated, this is further reason to avoid the initial transient effect by using a slower infusion rate or different route of administration.[8]

As no direct myocardial depres - sant effects of clonidine or DEX have been found this reduction in CI would be consistent with reduced metabolic demands.[22]

In the present study, CI was decreased in the ESM group than the DEX group. CI was decreased from the start of infusion due to the myocardial depressing effect of ESM and did not reach the preoperative value at the end of surgery. In the ESM group the SVRI did not show a significant changes as in the DEX group.

Anesthetic Requirement

Some investigators have observed a decreased need for inhalational anesthetics or opioids by administering clonidine in some studies of patients having non-cardiac and cardiac surgical procedures,[23] but other researchers found no such effect.[8] The use of DEX has been shown to decrease isoflurane requirements to maintain hemodynamic parameters within predetermined limits, and to reduce the need for opiates in patients having non-cardiac surgery.[13] In the present study, the DEX infusion reduced the dose of fentanyl and decreased the total dose of propofol.

Dysrhythmias

Alpha 2-adrenergic agonists are known to increase the gain of the baroceptor system resulting in vagally mediated dysrhythmias.[9] In DEX treated group these brady-arrhythmia occurred within minutes of the drug infusion. These events were associated with an increase in blood pressure and a reflex-mediated decrease in HR. It is probable that the dysrhythmias may be avoided by minimizing the pressor response by slowing the rate of DEX infusion.[8] In all likelihood, atropine pretreatment (or any other atropine-like drug) would have prevented these dysrhythmias. Less well conditioned individuals with higher heart rates and lower vagal tone should be less susceptible to bradycardia mediated by increased gain in the baroceptor system.[11]

Myocardial Ischemia and Infarction

Dorman et al.[23] and Quintin et al.[24] reported a decreased incidence and severity of ischemic S-T segment chan - ges in patients who were premedicated with clonidine and undergoing CABG, and a similar finding was reported in patients having non-cardiac surgery. In the present study, the DEX infusion was found to be associated with less ST-segment changes than ESM group.

Muscle Rigidity, Postoperative Shivering, and Diuresis

The proposed mechanisms for opioid-induced muscle rigidity are hypercapnia-induced pulmonary vasoc - onstriction and lack of normal cardiova -scular compensation of decrea -sed muscle blood flow.[25] In the present study DEX decreased the incidence of rigidity (although it did not abolish it entirely)

The incidence of postoperative shivering was decreased among patients given DEX. A similar effect has been observed after using clonidine in patients having non-cardiac and cardiac surgery.[26] Postoperative shivering is potentially harmful because it can increase the systemic oxygen consum - ption and, consequently, increase

cardiac workload. The increased workl -oad may lead to myocardial oxygen supply-demand imbalance.

Alpha 2-adrenergic agonists induce diuresis, possibly by attenuating the secretion of antidiuretic hormone or by blocking its effect on the renal tubules, by inhibiting the release of renin, or by releasing atrial natriuretic peptide.[27] In the present study, mean urine output was higher for patients in the DEX group, even though more patients in the ESM group received furosemide to promote diuresis. The volume of fluid challenge was slightly higher in the DEX group, but the total volume administered during operation was nearly the same in both groups.

Limitations in Interpreting the Results

The sample size of 20 patients in each treatment was too small to evaluate reliably differences between treatment groups. Another secondary end point, fentanyl-induced muscle rigidity, was quantified by a subjective assessment of the anesthesiologists as “yes” or “no”. This subjectivity limits the value of our finding that DEX attenuates rigidity.

In conclusion, in patients under -going beating heart surgery under total intravenous anesthesia, infusion of dexmedetomidine blunted blood press -ure response to intubation and surgery, decreased the intraoperative blood pressure variability and the incidence of tachycardia better than emolol. Dexmed -etomidine decreased the incidence of myocardial ischemia, the anesthetic requirements, the incidence of fentanyl-induced muscle rigidity, postoperative shivering and increased urine output.

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مقارنة تأثير الدكسمديتوميدين و الإسملول على نشاطية الدم في مرضى جراحة القلب النابض

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خلفية البحث: محفذات مستقبلات الفا تقلل من النشاط السيمبتاوى و ينشأ عن ذلك خفض فى النشاط العصبهرمونى و تقليل من نشاطية الدم عند إجراء التخدير و جراحة القلب. كذلك إستخدام مثبطات المستقبلات بيتا تساعد فى الحماية من زيادة نبض القلب وزيادة ضغط الدم وإفتقار عضلة القلب للدم و بذلك يتم حماية القلب خلال هذه الجراحة. الدكسمديتوميدين محفذ نوعى خاص لمستقبلات القا- 2 يؤثر فى نشاطية الدم فى مرضى جراحة القلب و لم تظهر الدراسات البحثية مدى هذه الآثار على الفلب و الدورة الدموية. اوضحت الآبحاث آثار الإسملول و هو مثبط لمستقبلات بيتا الخاصة بالقلب و دو مفعول قصير فاعليته فى التأثير على نشاطية الدم خلال الحث التخديرى فى جراحات القلب النابض.

الهدف: مقارنة آثار الدكسمديتومدين(الدكس) والإسملول على نشاطية الدم و كميات أدوية التخدير المطلوبة خلال جراحة القلب النابض.

الطرق: تم تقسيم 40 مريض من مرضى قصور الدورة التاجية و الملحقون لإجراء جراحة القلب النابض إلى مجموعتين: مجموعة الدكس و أعطوا جرعة 1 ميكروجرام \ كجم على فترة 10 دقائق و استمر اعطاؤه بعد ذلك خلال العملية بجرعة 0.5 ميكروجرام \ كجم \ ساعة حتى نهايتها. و فى مجموعة الإسملول أخذ المرضى جرعة تحميلية 0.5 ملليجرام \ كجم على فترة 5 دقائق ثم استمر الدواء بجرعة 50 ميكروجرام \ كجم \ ساعة حتى نهاية العملية. استخدم الفنتانيل و السيساتراكيوريم و البروبوفول كوسيلة للحث التخديرى الوريدى العام مع خليط الاكسجين و الهواء بنسبة(40% - 60%) حتى نهاية العملية. إشتملت قياسات نشاطية الدم على نبض القلب و متوسط الضغط الشريانى و الدليل القلبى و المقاومة الوعائية الرئوية و العامة. كذلك إشتمل البحث على قياس معدل حدوث إرتفاع و إنخفاض فى ضغط الدم و زيادة او إنخفاض نبض القلب و حدوث إضطراب فى نبض القلب و تغيرات فى رسم القلب و حساب كمية ادوية التخدير و حدوث صلابة عضلات عند إستخدام الفنتانيل و حدوث رعشة بعد العملية.

النتائج: قلل الدكس بدرجة ملحوظة نبض القلب و الدليل الفلبى بعد 3 دقائق إلى 70±6 نبضة \ دقيقة 2.2±0.1 لتر\دقيقة\م^2 (دلالة إحصائية أقل من 0.05) ثم زاد النبض و الدليل القلبى زيادة ملحوظة إلى 77± 9 نبضة\دقيقة و 2.5± 0.1 لتر\دقيقة\م^2 (دلالة إحصائية أقل من 0.05) بعد 10 دقائق من إستخدامه. أما فى فترة ما بعد الحث التخديرى قل نبض القلب إلى 71± 8 نبضة\دقيقة بعد شق عظمة القص عند الدقيقة 65 من بداية إعطاء الدواء اما الدليل

القلبى فستمر فى النقصان بشكل غير ملحوظ إحصائيا حتى عاد إلى مستوى بداية الدراسة عند نهاية الجراحة. قلل الإسملول من نبض القلب و الدليل القلبى إلى 73±8 نبضة\دقيقة و 2.1 ±0.3 لتر\دقيقة\م^2 بعد 3 دقائق من بداية استخدام الدواء.و لم يحدث اى تغير ذو دلالة إحصائية فى كل من هما حتى نهاية الدراسة بل زاد نبض القلب عن اول قراءة و لم يصل الدليل القلبى اليها. زاد الدكس من متوسط ضغط الدم الشريانى و دليل المقاومة الوعائية العامة إلى 101± 13 ملليمتر زئبقي(دلالة إحصائية أقل من 0.05) و3986± 276داين.ثانية.سم$^{-5}$.م^2 (دلالة إحصائية أقل من 0.01) بعد 3 دقائق من استخدام الدواء و قللهما عند 10 دقائق تقليل دو دلالة إحصائية إلى 89± 10 ملليمتر زئبقى و 2428± 276 داين.ثانية.سم$^{-5}$.م^2 واستمر متوسط الضغط الشريانى فى الإنخفاض بدون قيمة إحصائية إلى74± 9 ملليمتر زئبقى(دلالة إحصائية أقل من 0.05) عند الدقيقة 65 من بداية البحث و شق عظمة القص و زاد إلى 78± 6 ملليمتر زئبقى عند نهاية الجراحة. اما دليل المقاومة الوعائية العامة فلم يظهر به اى تغير ملحوظ يذكر فى فترة ما بعد الحث التخديرى. قل متوسط ضغط الدم الشريانى مع الإسملول إلى 78± 14 ملليمتر زئبقى (دلالة إحصائية أقل من 0.05)بعد 3 دقائق من بداية الدواء و لم يحدث اى تغير ذو مدلول إحصائى حتى نهاية الجراحة. اما المقاومة النوعية فلم يحدث به اى تغير ذو مدلول إحصائى طوال الدراسة. لم يحدث اى تغير ذو مدلول إحصائى خلال الدرراسة فى الضغط الوريدى المركزى و متوسط الضغط الرئوى و الضغط الإنسدادى بالشريان الرئوى و دليل المقاومة الوعائية الرئوية .كذلك أظهر البحث أن الدكس مقارنة بالإسملول يقلل من زيادة او نقص النبض و إرتفاع او إنخفاض ضغط الدم و يقلل من حدوث تغيرات برسم القلب و يقلل من كميات ادوية التخدير المطلوبة أثناء الجراحة ويقلل من الصلابة العضلية الناتجة عن الفنتانيل و يقلل من حدوث رعشة بعد العملية.

الإستنتاج و التوصية: إستعمال الدكس فى مرضى جراحة القلب النابض يقلل منةالنشاط السيمبتاوى المصاحب لها و يحدث سكون و يقلل من نشلطية الدم خلال التخدير و الجراحة و يقلل من اضطرابات النبض و ضغط الدم خلالها عن إستخدام الإسملول. كذلك يقلل من كمية التخدير المطلوبة و حدوث رعشة بعد العملية و حدوث صلابة عضلية.