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Research Article

Dexmedetomidine or Clonidine: Anesthetist's Choice in Laparoscopic Gynecological Surgeries

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2. Key words

Dexmedetomidine; Clonidine; Hemodynamics; Laparoscopic Gynecological Surgery.

1. Abstract

Laparoscopic surgeries have revolutionized surgical domains. It involves inflation of abdomen with carbon dioxide (CO_2) which alters hemodynamic and metabolic parameters. This randomized prospective study was conducted in the department of Anesthesiology, tertiary care government hospital on 48 patients undergoing diagnostic laparoscopy with expected duration of the procedure lasting between 15 to 30 minutes. The heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) , Mean blood pressure (MBP) and SPO2 were measured 15 minutes before induction (baseline), after peak drug effect, after induction and then during capno. The primarily focus was on hemodynamic monitoring for the two drugs: Dexmedetomidine and Clonidine in patients after capno for 15 minutes, post proseal at 5, 10 & 15 minutes respectively. The mean weight of study groups was (53.79±9.24) and (51.66±7.45) kilograms for Group D (Dexmedetomidine) and Group C (Clonidine) group respectively. The mean age was (28.20±6.39) and (26.25±4.81) years for two groups respectively .The mean HR of Dexmedetomidine group varied from 69.54 to 83.67 / min whereas in Clonidine group it varied from 79.92 to 90.46/min. The systolic blood pressure varied from 108.75 to 130 mm of Hg in Group D and 101.67 to 121.54 mm of Hg in Group C and diastolic blood pressure from 67.67 mm of Hg to 79.58 mm of Hg and for Group C from 58.21 to 78.75 mm of Hg. The mean BP also followed similar trend varying from 54 to 96.42 mm of Hg for Group D and 58.11 to 93.13 mm of Hg for Group C. Minimal variations were seen in SPO2 monitoring with both groups remaining near 99%.In Group D LMA was inserted with ease in 20 (83.3%) patients in comparison to 18 (75%) patients in Group C .23 (95.63%) patients of group D and 22 (91.67%) patients of group C had LMA insertion in single attempt .The patient's limb movements were seen in 5 (20.83%) patients of group D and 6 (25%) patients of group C .In Group D lower number of patients required additional dose of Propofol, 6 (25%) in comparison to 10 (41.67%) patients of Group C . The only statistically significant result was in terms of Heart rate.

Thus one has to make a balance between the choices of drugs but one has to keep in mind the high cost of Dexmedetomidine drug which plays an important role in making choices in a resource limited developing country.

3. Introduction

Laparoscopic surgery has been a major revolution ever since it was introduced in 1950 [1] and has been the modality of choice over open surgical procedures as it causes fewer traumas, fewer postoperative complications and reduced post operative recovery time [2, 3].

The laparoscopic procedures involve inflation of abdomen with carbon di oxide (CO_2) which alters hemodynamic and metabolic parameters. These changes occur due to three physiological triggers increased intra abdominal pressure caused due to inflation with CO_2, absorption of CO_2 inducing neural response and positioning of the patient.

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Some of the well recognized hemodynamic changes due to insufflations of $C0_2$ are decrease in cardiac output, elevated arterial pressure, elevated pulmonary and systemic vascular resistance, decreased venous return due to pooling of blood in lower extremities ultimately leading to decreased cardiac output that is partly compensated by increased heart rate [4, 5, 6]. There is decreased pulmonary compliance by 30-50% in healthy individuals due to increased intra arterial pressure and diaphragm elevation [7]. The head up position aggravates femoral venous stasis leading to increased risk of thrombotic event [8]. In the pre laparoscopic assessment extra care is given to cardiovascular and respiratory system because of pneumoperitoneum specially those with low cardio pulmonary reserve[9]. The premedication requires proton pump inhibitors or H_2 blockers to prevent aspiration [10]. Gynecological laparoscopy requires on dansterone as pre anesthetic medication and anti cholinergic are avoided [11].

General anesthesia remains the technique of choice for laparoscopic technique [1, 12, 13]. with regional 9spinal/ combined epidural spinal) remaining controversial. Some of the uncommon complications are undesired insufflations of $C0_2$ [14], venous air embolism [15], subcutaneous emphysema and mediastinum and pneumonia pericardium [16].

Dexmedetomidine is alpha-2 agonist that acts by inhibiting catecholamine release providing analgesia and sedation with minimal respiratory depression [17, 18]. Patients in our study received 1mcg/Kg body weight bolus over 20 minutes. Clonidine on the other hand is also an alpha-2 agonist additionally suppress rennin angiotensin aldosterone rennin system (RAAS) [4]. We used Clonidine in dose of 1mcg/Kg body weight bolus over 15-20 minutes.

4. Material and Methods

This randomized prospective study was conducted in the department of Anesthesiology, tertiary care government hospital on 48 patients undergoing diagnostic laparoscopy with expected duration of the procedure lasting between 15 to 30 minutes. Informed consent was taken from every patient. Complete pre operative pre anesthetic evaluation by anesthesiologist of all patients was done. 48 patients were divided into two groups randomly as group D (Dexmedetomidine) and group C (Clonidine) , each comprising of 24 patients each. After securing the iv cannula the resident doctor was asked to prepare all study medications as per the group assigned. An investigator, a qualified Anesthesiologist who was blinded to the group allocation administered the drug and recorded hemodynamic parameters and patient response to insertion of proseal LMA. The intravenous access of all the patients was secured in the preoperative holding area and maintenance fluid started. Patient was preoxygenated with 100% O_2 for 3 minutes, anesthesia was induced with 1mcg/Kg body weight Fentanyl and 2 mg/Kg of Propofol. Approximately sized LMA proseal was inserted to secure airway. Anesthesia was maintained with isoflurane in air added O_2.

4.1. Inclusion criteria

- Age -18-50 years
- ASA class I and II
- Procedure Diagnostic laparoscopy
- Mouth opening> 3 fingers

4.2. Exclusion criteria

- ASA grade
- Bleeding disorders
- Patient on anticoagulants
- History of allergy to anesthetic drug
- Hepatic , renal disease
- Pregnant women
- Obese
- Full stomach

The study drug was prefilled and coded identical 20 ml syringes containing study drug as per randomized protocol in following dilutions:

- Dexmedetomidine 20 ml (2 mcg/ml)
- Clonidine 20 ml (10 mcg/ml)

The investigators were blinded as syringes were loaded by resident doctor who was not included in study. The monitoring continued for 15 minutes before intubation to 15 minutes after extubation. Standard monitoring including electrocardiography, non invasive arterial pressure, pulse oximetry, end tidal CO_2 and gas analysis was done during induction and maintenance of anesthesia. The heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean blood pressure (MBP) and SPO_2 were measured 15 minutes before induction (baseline), after peak drug effect, after induction and then during capno. Our study primarily focused on response of patient and hemodynamic monitoring for the two drugs: Dexmedetomidine and Clonidine in patients after

capno for 15 minutes, post proseal at 5, 10 & 15 minutes respectively. We however did not record post extubation parameters.

5. Results

The mean weight of study groups was (53.79±9.24) and (51.66±7.45) kilograms for Group D (Dexmedetomidine) and Group C (Clonidine) group respectively **(Table 1)**. The mean age was (28.20±6.39) and (26.25±4.81) years for two groups respectively **(Table 2)**. As shown in **(Table 3)** the mean HR of Dexmedetomidine group varied from 69.54 to 83.67 / min whereas in Clonidine group it varied from 79.92 to 90.46/min. The difference of HR between the two study groups was statistically significant p=0.001043 (p<0.05) **(Figure 1)**.

Table-1 Weight of patients in both study groups

GROUP	MEAN	S.D.
Dexa	53.79	9.24064
Clonidine	51.66	7.4581

Table-2 Age of patients in both groups

GROUP	MEAN	S.D.
Dexa	28.2	6.38598
Clonidine	26.25	4.81167

Further during the study period the SBP varied from 108.75 to 130 mm of Hg in Group D and 101.67 to 121.54 mm of Hg in Group C. The difference was not statistically significant. P=0.48 (p<0.05) **(Figure 2)**. The DBP for Group D varied from 67.67 mm of Hg to 79.58 mm of Hg and for Group C from 58.21 to 78.75 mm of Hg, the difference was not statistically significant, p=0.29 (p<0.05) **(Figure 3)**. The MBP also followed similar trend varying from 54 to 96.42 mm of Hg for Group D and 58.11 to 93.13 mm of Hg for Group C, with the difference been statistically insignificant,

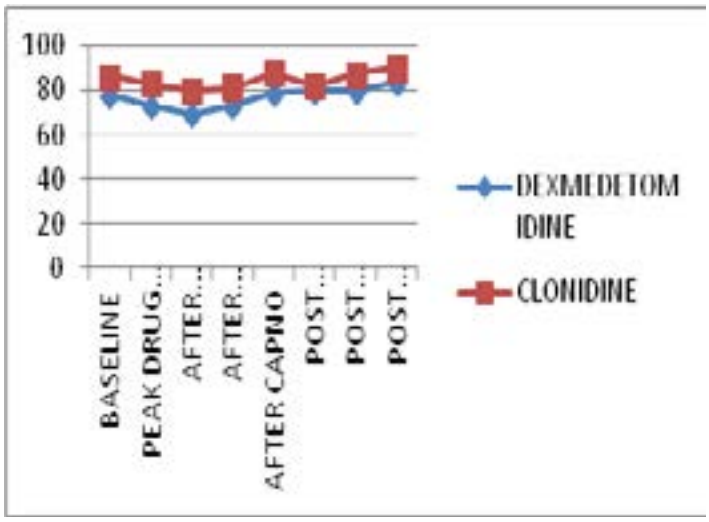

Figure 1: Effect of Dexmedetomidine & Clonidine on Heart rate (HR) per minute

Table -3 Hemodynamic profile of patients in study groups

Table	3 Hemodynamic profile of patients in study groups		Table		3 Hemodynamic profile of patients in study groups		Table		3 Hemodynamic profile of patients in study groups	
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Cloni	Dexa	Cloni	Dexa	Cloni
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	74.67	96.42	90.29	99.08	99.2
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	69	84.18	82.56	99.08	99.2
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	59.96	81.42	73.66	99.08	99.75
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	58.21	81.97	72.69	99.08	99
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	75.08	54	58.11	99	99
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	73.38	88.06	87.53	99	99
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	78.75	82.32	93.13	99.04	99
Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	Table	3 Hemodynamic profile of patients in study groups	73.25	83.49	88.89	99.04	99

p=0.45(p,0.05) **(Figure 4)** Minimal variations were seen in SPO2 monitoring with both groups remaining near 99%.

In Group D LMA was inserted with ease in 20 (83.3%) patients in comparison to 18 (75%) patients in Group C **(Figure 6)**. The difference with ease of insertion with both drugs was not statistically significant p=0.477 (p<0.05) **(Table 4)**.

23 (95.63%) patients of group D and 22 (91.67%) patients of group C had LMA insertion in single attempt **(Figure 7)**. The difference however was not statistically significant, p=0.5509, p<0.05 **(Table 5)**.

The patient's limb movements were seen in 5 (20.83%) patients of group D and 6 (25%) patients of group C but the results were not statistically significant, p=0.731, p< 0.05 **(Figure 8, Table 6)**.

Cases where LMA insertion could not be accomplished, additional Propofol was given. In Group D lower number of patients required additional dose of Propofol, 6 (25%) in comparison to 10 (41.67%) patients of Group C **(Figure 9)**. The difference was not statistically significant, p=0.2206, (p<0.05).

6. Discussion

In the current study we emphasized on the hemodynamic effect of two commonly used alpha-2 agonists Dexmedetomidine and Clonidine in laproscopic gynecological surgery particularly post

	HR	SBP	DBP	MBP	SPO2
t value	-3.76594	0.05003	0.54837	0.10403	-1.00636
p value (<.05)	0.001043	0.480401	0.296039	0.459312	0.16566
	Significant	Not significant	Not significant	Not significant	Not significant

Table -4 Comparative ease of LMA insertion in study groups

Group	DIFFICULT	EASY	Grand Total
I	4	20	24
II	6	18	24
Grand Total	10	38	48
The chi-square statistic is 0.5053. The p-value is .477197. This result is not significant at p < .05.			

Table -5 Numbers of attempts of LMA insertion in study groups

	ATTEMPT		
Group	1	2	Grand Total
I	23	1	24
II	22	2	24
Grand Total	45	3	48
The chi-square statistic is 0.3556. The p-value is .550985. This result is not significant at p < .05.			

Table -6 Patient Limb movements in study groups

	MOVEMENT		
Group	NIL	PRESENT	Grand Total
I	19	5	24
II	18	6	24
Grand Total	37	11	48
The chi-square statistic is 0.1179. The p-value is .731284. This result is not significant at p < .05.			

Table -7 Supplemental Propofol requirement in study groups

	SUPPLEMENT PROPOFOL		
Group	NO	YES	
I	18	6	24
II	14	10	24
Grand Total	32	16	48
The chi-square statistic is 1.5. The p-value is .220671. This result is not significant at p < .05.			

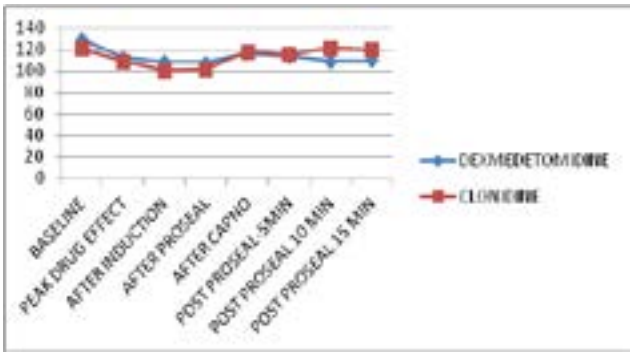

Figure 2: Effect of Dexmedetomidine & Clonidine on Systolic Blood pressure (SBP)in mm of Hg

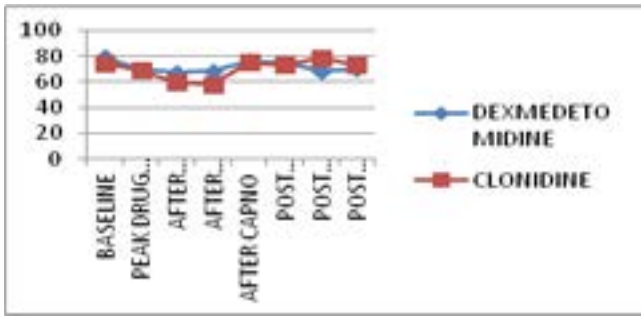

Figure 3: Effect of Dexmedetomidine & Clonidine on diastolic Blood pressure (DBP)in mm of Hg

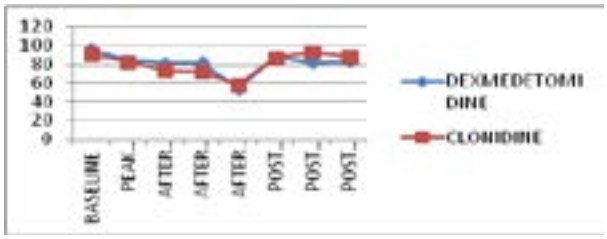

Figure 4: Effect of Dexmedetomidine & Clonidine on Mean Blood pressure (MBP) in mm of Hg

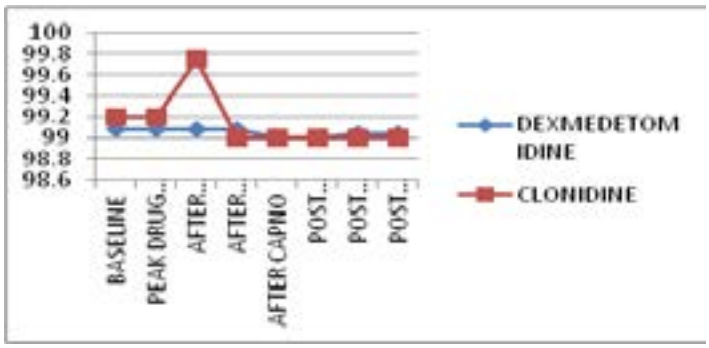

Figure 5: Effect of Dexmedetomidine & Clonidine on SPO_2 (%)

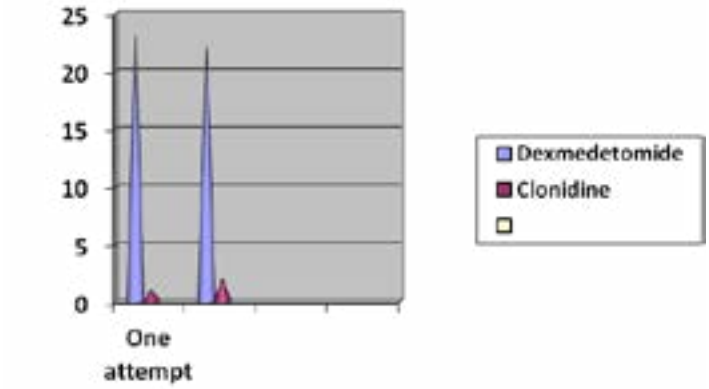

Figure 6: LMA insertion attempts

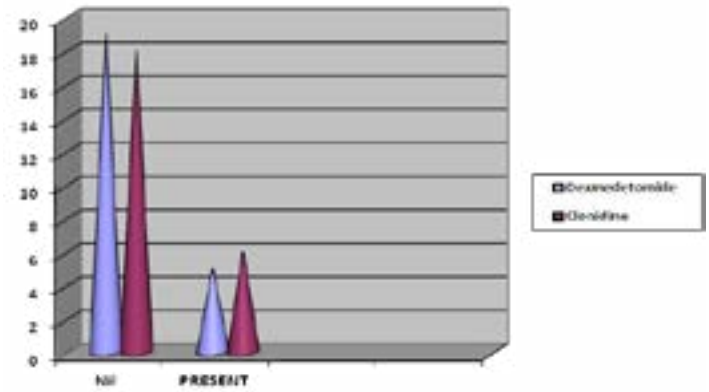

Figure 7: Patient limb movements

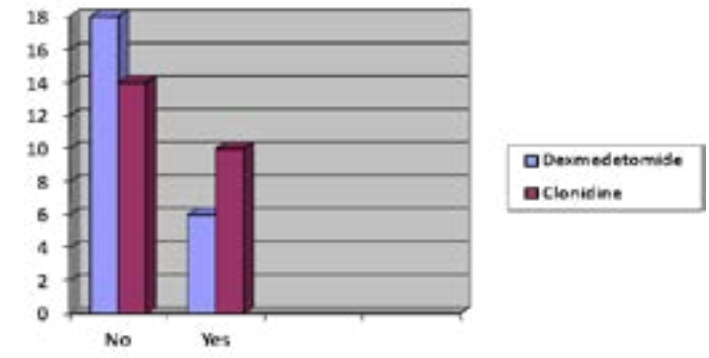

Figure 8: Propofol supplementation

15 minutes of capnoperitoneum. It was observed in our study that both the systolic and diastolic blood pressure were lower in Dexmedetomidine group in contrast to patients receiving Clonidine after capnoperitoneum at 5, 10 and 15 minutes although statistical significance was not observed. The most statistically significant finding in our study was in terms of heart rate. The heart rate was lower in both groups on comparison to baseline. Dexmedetomidine group had lower HR in comparison to Clonidine group and the result was statistically significant. In a study by Bhattacharyajee et al [19] on the effect of hemodynamic stability in 60 patients undergoing laparoscopic cholecystectomy, the heart rate in Dexmedetomidine group was significantly less after intubation and throughout period of pneumoperitoneum. The results of present study are similar to those by Bhattacharyajee et al. The lowering of the HR resulted in bradycardia in one of the patients that was reversed by using IV Atropine. Our findings are similar to those by Dhujoti et al [20] and S Kumar et al [21]. None of the patients in any group required airway or ventilator support and were managed with ease in post operative period. In an Indian study by P Indira et al [22] 50 ASA grade I and II patients scheduled for elective laproscopic cholecystectomy were randomly divided into two group- Dexmedetomidine and placebo. It was observed that Dexmedetomidine preoperatively attenuates sympatho adrenal stress response to laproscopy as heart rate, systolic BP, diastolic BP and mean arterial pressure were significantly less than placebo group.

Similar observations of reducing HR and BP were also noted in study by Kalpana vora et al [23] in their study on 70 patients with the use of Dexmedetomidine verses placebo. Gupta et al [24] also observed significant lowering of HR and systolic- diastolic blood pressure after Dexmedetomidine infusion in 60 patients undergoing laparoscopy. The effect on heart rate of Dexmedetomidine infusion calls for greater intraoperative vigilance and pharmacological intervention as supported by Talkie et al [25] study on 24 patients undergoing vascular surgery receiving continuous infusion of placebo or one of the three doses of Dexmedetomidine targeting plasma concentration of 0.15ng/ml (low dose), 0.30 ng/ml (medium dose) and 0.45ng/ml (high dose) from 1 hour before induction of anesthesia until 48 hours post operatively.

Majority of cases in Dexmedetomidine group has LMA insertion done with great ease in single attempt and with minimal patient's limb movements **(Figure 6, 7, 8)** in comparison to Clonidine group but the results were not statistically significant.

The requirement of supplement dose of Propofol was more in

Clonidine group **(Figure 9)**. There were no cases with hypotension or rebound hypertension in any of the groups suggesting that both the drugs have equal safety. Dexmedetomidine produced bradycardia in one patient. Clonidine required additional supplementation with Propofol for optimum conditions for LMA insertion, 10 (41.67%) patients in contrast to Dexmedetomidine having 6 (25%) patients requiring Propofol. In a study by Panchgari et al [26] it was found that Dexmedetomidine reduces total analgesia requirement in laparoscopic surgeries under general anesthesia and causes minimal side effects comparing to placebo and therefore can be utilized as ideal anesthetic adjuvant during laparoscopic surgeries. They also observed bradycardia in two patients receiving Dexmedetomidine similar to our study.

Mullhalaya and Vallabha [27] compared hemodynamic effects of both Dexmedetomidine and Clonidine in 90 patients undergoing endotracheal intubation and showed that in bolus dose of Dexmedetomidine I mcg/Kg body weight administered over 10minutes before laryngoscopy and intubation attenuates sympathetic response to laryngoscope and intubation with any side effects than Clonidine.

Both the drugs decreased sympathetic out flow and favorable intraoperative cardiovascular and endocrine response and therefore may be of benefit in patients at risk of developing inadequate cardiac output or myocardial ischemia. T Tauttonem et al [28, 29, 30] in their study also did not found significant changes in hemodynamic of Patients receiving either of the two drugs.

Clonidine has been associated with lowering of post operative shivering [31] but we did not encounter post operative shivering in any of the patients in both groups. It might be due to anesthesia conditions: Propofol [32], Fentanyl [33] that has shown to reduce shivering. Anxiolytic potential of both drugs [34] is well known but we didn't observe it in our study.

Thus one has to make a balance between the choices of drugs but one has to keep in mind the high cost of Dexmedetomidine drug which plays an important role in making choices in a resource limited developing country.

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