ORIGINAL RESEARCH PAPER

Volume-7 | Issue-6 | June-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICAL EVALUATION OF HEMODYNAMICS AFTER ETOMIDATE INDUCTION FOR ADRENOCORTICAL INSUFFICIENCY COMPARED WITH PROPOFOL IN OFF PUMP CORONARY ARTERY BYPASS SURGERY

Anaesthesiology

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ABSTRACT

Etomidate is a short-acting intravenous anesthetic agent. It has rapid onset of action and safe cardiovascular risk profile. Etomidate induced adrenocortical insufficiency is dose dependent and reversible.The cortisol levels has been correlated with etomidate induced hypotension.We considered hypotension as a surrogate for reduced cortisol production.Aim of our study was to compare hemodynamics with 2 dosages of etomidate and propofol and increase in inotrope and vasopressor requirement within 24 hours.

KEYWORDS

Cardiac Anesthesia, Etomidate, Propofol, Adrenal Suppression, Acth, Cortisol, Off Pump Coronary Artery Bypass, Adrenocortical Insufficiency.

Previous Publications/Presentations of Dr Amarja Nagre – Publications -

- **Original Article** 'Single bolus dose of epidural magnesium prolongs the duration of analgesia in cardiac patients undergoing vascular surgeries'. Indian J Anaesth 2017;61:832-6.
- **Original Article** 'Comparison Of Immediate Extubation Versus Ultrafast Tracking Strategy In the Management Of Off Pump Coronary Artery Bypass Surgery' published in Annals of Cardiac Anaesthesia - Ann Card Anaesth 2018;21:129-33.
- **Citation by -** Hemmerling TM. Immediate extubation after cardiac surgery should be part of routine anesthesia practice for selected patients. Ann Card Anaesth 2018;21:114-5.
- **Original Article** 'Comparison of Ultrafast tracking Versus Conventional Strategy in Postoperative Management of Off Pump Coronary Artery Bypass Surgery' accepted by Journal of Cardiac Critical Care.
- **Original Article** 'Comparison of intranasal dexmedetomidine and oral midazolam as premedication for cardiac catheterization procedure in pediatric patients'.Anesth,Pain & Intensive Care;vol 20(3)July-Sept 2016.
- **Original Article '**Relationship Of Pump Flow And Expired Pump CO_2 On Cardiopulmonary Bypass: An Observational Study' published in International Journal of Scientific Research. Int J Sci Res 2018;7(5):814-815.
- **EDITORIAL-**The rise of cardiac anesthesia! Anesth,Pain & Intensive Care;vol 20(3)July-Sept 2016.
- **EDITORIAL-** "Preoperative Optimisation of IHD patient for non cardiac surgery: Well begun is half done ! published in Journal of Anaesthesia and Critical Care Case Reports 2016 Jan-April;2(1): 21-22.
- **Clinipics -** Off-pump coronary artery bypass surgery. Anesth,Pain & Intensive Care;vol 20(3)July-Sept 2016.
- **Case report -** Left ventricular false tendon in a patient undergoing mitral valve replacement.Annals of Cardiac Anaesthesia 2015:Issue 1,volume 18,108-110.
- **Case report -** Successful management of a patient with pacemaker for flap surgery of exposed pulse generator device.Journal of Anaesthesia and Critical Care Case Reports 2016 Jan-April;2(1):21-22.
- **Case report -** 'A Central Venous Catheter Complication : Fragmentation and Embolization causing Fatal Arrhythmias'. Journal of Anaesthesia and Critical Care Case Reports 2016 May-Aug;2(2):21-23.
- Dissertation on "Priming Principle and Induction dose of Propofol."during MD Anaesthesia.
- Article on 'Smoking- Surgery and Anaesthesia' published in Souvenir of Regional Conference of ENT MORCON 2016.

Faculty Speaker-

- Faculty Speaker on "Update on Anticoagulants" at IACTACON 2017- National Conference of Indian Association of Cardiovascular Thoracic Anaesthesiologists at Pune, Maharashtra from 16-19 February 2017.
- **Quizmaster** and Faculty Invitation at **Pre-workshop-hands-on-TEE training of 2nd International and 11th National Transoesophageal Echocardiography Workshop** under the banner of Indian Association of Cardiovascular and Thoracic Anaesthesiologists (IACTA) in collaboration with Indian Academy of Echocardiography (IAE), International Society of Cardiovascular Ultrasound (ISCU) and University of Minnesota, USA at Narayana Health city, Bangalore from 21to 24 August 2017.
- Faculty Invitation at **2nd International and 11th National Transoesophageal Echocardiography Conference** under the banner of Indian Association of Cardiovascular and Thoracic Anaesthesiologists (IACTA) in collaboration with Indian Academy of Echocardiography, International Society of Cardiovascular Ultrasound and University of Minnesota, USA at Narayana Health city, Bangalore from 25 to 27 August 2017.
- Faculty at **1st International and 10th National Transoesophageal Echocardiography Conference** under the banner of Indian Association of Cardiovascular and Thoracic Anaesthesiologists (IACTA) in collaboration with Indian Academy of Echocardiography, International Society of Cardiovascular Ultrasound and University of Minnesota, USA at Narayana Health city, Bangalore, from 26th to 28th August 2016
- Faculty at **Pre-workshop-hands-on-TEE training (PWTEET) of the 1st International and 10th National Transoesophageal Echocardiography Workshop in Operation theatre to train the delegates** under the banner of Indian Association of Cardiovascular and Thoracic Anaesthesiologists (IACTA) in collaboration with Indian Academy of Echocardiography, International Society of Cardiovascular Ultrasound and University of Minnesota, USA at NH-Narayana Health city, Bangalore,India from 22nd to 25th August 2016.
- Faculty Speaker on 'Congenital heart diseases for non-cardiac surgery' in **International conference TACON** at Ahmedabad, Gujarat on 26-28 August 2016.
- Faculty Speaker in Symposium on 'Cardiac Related Anaesthesia Problems'.Only Faculty for **4 lectures** on various topics at Nashik,Maharashtra on 17 July 2016.
- Faculty Speaker at National Conference of Indian Society of Anaesthesiologist ISACON to be held at Ludhiana, Punjab 26-29 November 2016.
- Faculty Speaker in CME for 'Cardiac patient for Non Cardiac surgery' at ISA Satara,Maharashtra on 30th September 2016.
- Faculty Speaker in CME on 'Management of IHD patient for Non Cardiac Surgery' at ISA Sangli,Maharashtra on 1st October 2016.
- Faculty Speaker in National Workshop on Snoring and Sleep Apnea on the topic "Anaesthesia in Obstructive Sleep Apnea" held at Aurangabad,Maharashtra on October 2015.
- **Quiz Master** in State Conference of Indian Society of Anaesthesiologist MISACON to be held at Aurangabad, Maharashtra 14-16 October 2016.
- Faculty Speaker in CME for 'Valvular Heart Disease patient for Non Cardiac surgery' at ISA Borivali,Maharashtra on 13th November 2016.
- Faculty Speaker at 'RECAP' – Postgraduate students assembly on 7 January 2017 at AFMC, Pune.

- Faculty Speaker on "Perioperative Stroke – Prediction, Prevention and Protection" at ISACON MAHA 2017, Maharashtra State Conference at Nanded, Maharashtra 6-8 October 2017.
- Faculty Speaker on 'Future after Post graduation' at ISACON MAHA 2017, Maharashtra State Conference at Nanded, Maharashtra 6-8 October 2017.
- Faculty Speaker for topic – 2D Echocardiography and FATE at CME – ISA Nashik and 2D Echocardiography workshop on 20 August 2017.
- Faculty at World Anaesthesia Day (WAD) Conference Mumbai. Topic – "On road to Anaesthesia Profession" on 14th-15th October 2017.
- Faculty Invitation for 2D Echocardiography lecture at CME by Indian Society of Anaesthesiologist, Aurangabad, Maharashtra on 18th October 2017.
- Faculty Speaker on 'Fatal Interactions between Brain and Heart' at **National Conference** of Indian Society of Anaesthesiologist ISACON 2017 at Kolkata 25th-29th November 2017.
- Faculty Instructor at "iHeartScan Echocardiography" at Bangalore by University of Melbourne (Australia) on 23-24 April 2018.

Accepted Faculty Invitations -

- Faculty Invitation at GARC -Ganga Anesthesia Refresher's Course at Coimbatore for Pro and Con session on Attitude versus Skill for better outcome on 30th June 2018.
- Faculty Invitation at TACON 2018 for POCUS workshop and panel discussion.
- Faculty Invitation at International Transoesophageal Echocardiography Conference at Bangalore in August to conduct QUIZ.
- Faculty Invitation at State Conference of Indian Society of Anaesthesiologist to be held at Shirdi,Maharashtra in October 2018.

Introduction -

Etomidate suppresses corticosteroid synthesis in the adrenal cortex at early stages by reversibly inhibiting 11 beta hydroxylase, an enzyme important in adrenal steroid production.[1,2,3]This causes reduction in serum cortisol levels lasting for upto 24 hours.[4,5]Etomidate offers hemodynamic stability during induction[6,7] in hemodynamically compromised patients.[8] Propofol is a short-acting hypnotic agent which acts through GABA receptor potentiation and is a sodium channel blocker.Furthermore,the endocannabinoid system may contribute to its actions.It may result in vasodilatation and transient hypotension.[5] Our hypothesis was to test whether the adrenocortical suppression induced by etomidate administration leads to clinically evident hemodynamic perturbations requiring inotropes and/or vasopressors.

Materials and Methods-

The study enrolled 90 patients, randomly divided with 30 in each group. Primary outcome measure was hemodynamic instability manifested as hypotension requiring increase in inotrope or vasopressor agent.Secondary outcome measures were usage of blood products, fluid requirement, time to extubation and ICU length of stay.Two dosages of etomidate were used to prove that if clinical manifestation of adrenocortical insufficiency occurred with 0.3mg/kg and not with 0.15mg/kg, it would be prudent to use 0.15mg/kg dose.And as the action of propofol lasts for upto 10 minutes and has biological half life of 30- 60 minutes, so propofol group serves as a control. Inclusion criteria was patients undergoing off pump coronary artery bypass (OPCAB) surgery.Exclusion criterias were patients undergoing emergency surgery,associated valvular heart disease,with congestive heart failure,renal dysfunction,with preoperative inotropes,known adrenal or endocrine dysfunction.Randomization was done with sealed opaque envelope technique.All groups received Inj Midazolam 0.05 mg/kg intravenous(iv) as premedication.Group 1 was given Inj Etomidate 0.15 mg/kg iv with Inj Fentanyl 2-4 mcg/kg for induction of anaesthesia.Group 2 received Inj Etomidate 0.3 mg/kg iv with Inj Fentanyl 1-2 mcg/kg.Group 3 received Inj Propofol 1 mg/kg with Inj Fentanyl 2-4 mcg/kg.Rest all management was identical in all the 3 groups such as Inj Rocuronium 0.6 mg/kg was followed, maintenance was done with Inj Fentanyl, Inj Atracurium and Sevoflurane. Inotropes were started during or after grafting as per cardiovascular conditions.Most of the patient remained stable intraoperatively and none of the patient in any group underwent emergency conversion to on pump coronary artery bypass grafting (CABG) or had arrhythmias, oliguria or hypothermia.Hypotension was defined as systolic blood pressure (SBP) < 90 mmHg, diastolic blood pressure (DBP) <60 mmHg and mean blood pressure (MBP) <70 mmHg but no patient had hypotension to an extent to start inotropes or vasopressors postoperatively.

Results-

All the statistical analysis was done by using Minitab 15.Descriptive statistics were summarized as mean and SD when the results were normally distributed and as median and range when they were not. ANOVA test was used to determine the significance of normally distributed parametric values and Kruskal-Wallis Test for nonnormally distributed data.Categorical variables were presented using percentage. Statistical significance was accepted at P <0.05.Power of study was calculated to detect a 30% increase in the noradrenaline requirement between three group with two sided α of 5% and power 90% sample would be obtained with 25 patients in each group.

The demographic data was comparable in all groups.The statistical analysis showed both the groups of etomidate to have comparable hemodynamics.(Table 1,2,3,4) No clinical evidence of hemodynamic instability due to decrease in cortisol levels occurred in our study.Inj Noradrenaline was not required in any patient in all 3 groups. Comparison of ICU length of stay was similar in all groups with p value 0.849 not significant. Comparison of time to extubation in hours between 3 groups with p value of 0.749 was not significant.Usage of blood products, fluid requirement were not increased in any group.

Table 1-Comparison of heart rate

Heart Rate beats/min at hour (hr)	Group-1	Group-2	Group-3	F-Value	p-Value
	Mean±SD	Mean±SD	Mean±SD		
1 hr	95.37±9.37	88.2±14.3	87.53±12.98	3.684	0.029S
2 hrs	87.1±5.58	80.87±10.89	86.17±11.39	3.636	0.030 S
3 hrs	84.0±4.55	80.97±8.06	87.93±12.79	4.404	0.015S
4 hrs	85.17±4.14	78.73±7.56	84.33±11.05	5.602	0.005 S
6 hrs	81.63±4.46	78.37±6.38	81.73±11.43	1.724	0.184 NS
8 hrs	75.63±6.41	79.4±5.30	81.83±13.05	3.662	0.030 S
10 hrs	68.2±8.43	79.5±4.27	79.63±10.75	18.996	0.000 S
14 hrs	66.26±7.86	80.36±4.35	76.93±9.84	27.374	0.000 S
18 hrs	65.43±7.24	80.43±3.65	74.13±9.61	32.257	0.000 S
24 hrs	64.56±6.09	80.96±4.74	74.33±9.03	43.418	0.0

Table 2-Comparison of systolic blood pressure (SBP)

SBP mmHg at hour (hr)	Group-1	Group-2	Group-3	F-Value	p-Value
	Mean±SD	Mean±SD	Mean±SD		
1 hr	123.8±19.19	120.8±15.41	120.77±14.52	0.334	0.774 NS
2 hrs	122.77±14.22	121.73±8.18	123.23±9.24	0.150	0.861 NS
3 hrs	121.96±9.82	122.20±6.61	124.97±8.04	1.223	0.299 NS
4 hrs	124.73±10.63	127.90±6.22	128.4±6.33	1.856	0.162 NS
6 hrs	124.53±9.12	125.56±8.98	127.63±9.75	0.866	0.424NS
8 hrs	126.73±7.71	126.26±10.60	129.0±8.22	0.804	0.451NS
10 hrs	131.76±7.37	125.93±11.66	127.9±9.81	2.766	0.068 NS
14 hrs	131.83±5.62	126.7±8.90	125.10±8.45	6.109	0.003 S
18 hrs	130.37±7.54	125.86±7.36	128.4±8.70	2.452	0.092 NS
24 hrs	130.30±9.97	127.13±7.70	127.83±7.97	1.334	0.269 NS

Table 3- Comparison of diastolic blood pressure (DBP)

DBPmmHg at hour(hr)	Group-1	Group-2	Group-3	F-Value	p-Value
	Mean±SD	Mean±SD	Mean±SD		
1 hr	71.40±17.2	75.33±12.2	70.97±12.6	0.86	0.427 NS
2 hrs	77.63±12.4	75.10±	73.23±8.80	1.60	0.209 NS
3 hrs	75.57±9.79	75.57±5.99	74.00±7.94	0.38	0.686 NS
4 hrs	76.10±11.7	78.73±5.64	76.03±7.00	0.98	0.379 NS
6 hrs	76.13±10.0	76.83±7.67	75.50±8.51	0.17	0.842 NS
8 hrs	76.40±8.93	77.37±8.56	77.33±7.80	0.13	0.881 NS
10 hrs	78.93±8.30	77.60±9.35	76.60±8.49	0.54	0.585 NS
14 hrs	78.93±7.91	78.30±6.97	74.57±7.89	2.89	0.061 NS

18 hrs	77.97±7.64	76.97±6.75	78.10±7.62	0.21	0.808 NS
24 hrs	78.40±7.56	78.17±7.56	77.83±6.78	0.05	0.956 NS

Table 4 -Comparison of mean blood pressure (MBP)

MBP at hour (hr)	Group-1	Group-2	Group-3	F-Value	p-Value
	Mean±SD	Mean±SD	Mean±SD		
1 hr	88.93±17.3	90.23±13.1	87.30±12.82	0.30	0.738 NS
2 hrs	92.47±12.6	90.37±6.4	89.63±8.31	0.72	0.489 NS
3 hrs	90.77±8.79	90.73±5.63	90.63±7.62	0.00	0.997 NS
4 hrs	92.03±10.5	94.733±5.382	93.50±6.47	0.90	0.409 NS
6 hrs	92.07±9.01	92.80±7.72	92.53±8.65	0.06	0.944 NS
8 hrs	93.40±8.16	93.30±9.09	94.33±7.58	0.14	0.868 NS
10 hrs	96.40±7.50	93.17±9.74	93.40±8.58	1.30	0.277 NS
14 hrs	96.27±6.81	94.20±7.38	90.13±11.41	3.80	0.026 NS
18 hrs	95.17±6.90	92.90±6.82	94.43±7.34	0.81	0.447 NS
24 hrs	95.50±7.11	94.13±7.42	94.13±6.77	0.37	0.692 NS

Table 5 -Comparison of Dopamine requirement

Groups	N	Mean	Std. Deviation	F-Value	p-Value
Group-1	30	1.003	1.531	0.23	0.794NS
Group-2	30	0.843	1.484		
Group-3	30	1.113	1.622		

Table 6 -Comparison of Adrenaline requirement

Groups	N	Mean	Std. Deviation	F-Value	p-Value
Group-1	30	0.01700	0.01985	0.05	0.948NS
Group-2	30	0.01733	0.02363		
Group-3	30	0.01567	0.01888		

Table 7 -Comparison of Nitroglycerine requirement

Groups	N	Mean	Std. Deviation	F-Value	p-Value
Group-1	30	0.1700	0.1841	0.40	0.668 NS
Group-2	30	0.1800	0.2709		
Group-3	30	0.2333	0.3880		

Discussion-

Etomidate protects from myocardial ischemia, has less respiratory suppression and causes no histamine release.[9] It is a good induction agent with stable cardiovascular profile thus recommended in patients with poor left ventricular function.[5]Perhaps, the only concern is adrenocortical suppression after single dose or long term use.[10,11]

We compared two dosages of etomidate and propofol induction in terms of hemodynamic stability to rule out clinically evident adrenocortical suppression.Inotrope dose was not increased in any of the patient as a result of severe hypotension.(Table 5,6)None patient required treatment with Inj Hydrocortisone or laboratory investigation like serum cortisol levels.Inj Nitroglycerine requirement was also similar in all groups.(Table 7)Time to extubation was variable in groups but was not attributed to hemodynamic instability.Our study revealed that, the known adrenocortical suppression which occurs after etomidate administration does not occur to such an extent as to cause clinically evident hemodynamic perturbations.Basciani RM et al conclude that the laboratory indicators of adrenocortical insufficiency have not translated into increased vasopressor requirement or inferior early outcomes.[12] According to our study, etomidate in 2 doses did not exhibit severe and sustained hypotension due to adrenal suppression which needed inotropes or vasopressors, a finding similar to Morel et al.[13]Sarkar M et al also emphasize the lack of clinically significant hemodynamic changes after etomidate administration in children.[14]Furthermore, Singh R et al in their article have stated that the transient decrease in serum cortisol levels after a single induction dose of etomidate is not clinically significant.[15]

Limitation of our study is that the serum cortisol levels were not checked which should ideally be correlated with hemodynamics.

Conclusion – The known etomidate induced adrenocortical insufficiency did not translate into hemodynamic instability and increased vasopressor requirement in OPCAB patients.

Source of funding – Nil

Conflicts of interest - Nil

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