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Original Research Article

A comparative assessment between dexmedetomidine and nitroglycerine for controlled hypotensive anaesthesia

Dr. Sashi Kant Joshi[1], Dr. Saurabh Singh[2], Dr. Arjun Prasad[3]

[1]Senior Resident, Department of Anaesthesiology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

[2]Senior Resident, Department of Anaesthesiology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

[3]Associate Professor & HOD, Department of Anaesthesiology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India

Corresponding Author: Dr. Saurabh Singh

Abstract

Aim: To compare the efficacy of and safety of dexmeditomidine versus nitroglycerine during hypotensive anaesthesia induced by either drug in adult patients posted for elective spine surgeries.

Material and methods: This was a prospective, randomized, and double blinded clinical comparative study conducted in the Department of Anaesthesiology Jawaharlal Nehru medical college and hospital Bhagalpur, Bihar, India from July 2018 to February 2019. 80 participants belonging to ASA class I or I between 20 and 55 years of age scheduled for elective spine surgeries were include in this study. The study drug dexmeditomidine was given to group DX in the dose of 1 micro gram/kg body weight in a 600 seconds infusion before induction diluted to 10 ml with normal saline followed by maintenance dose at infusion rate of 0.2- 0.7 micro gm/kg. The group NG received 10 ml plain normal saline over 600 seconds before induction followed by maintenance dose of nitroglycerine at an infusion rate of 0.5-10 micro gm/kg/min. different parameter were compared in both the groups.

Results: The basal heart rates are comparable between the two groups and the difference is not statistically significant. There is a statistically significant difference between the two groups after starting loading dose infusion and induction, where in statistically significant fall in HR is noted in group DX. But after laryngoscopy and intubation there is increase in heart rate in both groups which more in group NG compared to group DX ($p<0.001$). The intraoperative mean HR during surgery is significantly lower in group DX compared to group NG($p<0.001$). At 15 min minutes there is no significant difference in the 2 groups with respect to the average surgical field grading of each study population. At 30 min there is significant difference between 2 groups with group DX having average surgical field grade of 1.88 ±0.52, which is less compared to that of group NG, 2.54±0.49($p<0.001$). The average intraoperative surgical field grade was 2.18±o.51 in group DX, which was significantly better than 2.41±0.61 in group NG ($p=0.29$).

Conclusion: Dexmedetomidine and Nitroglycerine both can be used with great safety profile to achieve controlled hypotension during spine surgeries.

Keywords: Controlled Hypotension, Spine Surgeries, Dexmedetomidine, Nitroglycerine

Introduction

Induced or controlled hypotension is a method by which the arterial blood pressure is decreased in a predictable and deliberate manner.[1] The intent of deliberate hypotension is to reduce bleeding and thus facilitate surgery and to decrease the amount of blood transfused. Controlled hypotension is a technique used to limit intraoperative blood loss to provide the best possible field for surgery.[2,3] A dry field results in more precise dissection and less risk of damage to vital structures. Trauma and tissue infection are minimised because fewer sutures are required and less electrocoagulated, devitalised tissue remains in the wound. Initially, induced hypotension was thought to decrease the surgical time due to improved visibility; however, this thought has later been proven to be untrue. The threat of serious complications resulting from poor visibility and neurological damage associated with hypotensive anaesthesia makes it important for anaesthetists to produce optimal surgical conditions. So the aim should be to reduce blood pressure as little as possible while providing the best possible surgical field. this surgery can be done under local anaesthesia as well as general anaesthesia. General anaesthesia is often chosen over local anaesthesia blocks because there are chances of incomplete block and discomfort to the patient with local anaesthesia whereas in general anaesthesia patients are pain free and additionally various drugs used to produce general anaesthesia also helps in achieving controlled hypotension.[4] Controlled hypotension is the commonly used technique to limit blood loss and improve visualization in the surgical field during FESS surgery. Various techniques have been adopted to achieve controlled hypotension. One of them is use of pharmacological drugs in the form of volatile anaesthetics, direct-acting vasodilators, autonomic ganglion-blockers, α-adrenergic receptor blockers, beta-adrenergic blocking agents, prostaglandin E1, magnesium sulphate and calcium channel blockers.[5-11] Dexmedetomidine is a α2-adrenoceptor agonist. Literature is not enough to evaluate its effects on lowering the heart rate and mean arterial pressure but still it was considered to be a good agent for producing controlled hypotension.[6,12,13] the main advantages of dexmedetomidine infusion are the absence of reflex tachycardia and no chances of rebound hypertension as the sympathetic nervous system is suppressed.[14,15] Nitroglycerine is a directly acting vasodilator and it is frequently used to produce controlled hypotension because it is easily treatable and having very rapid onset as well as rapid offset of action. However the disadvantages of nitroglycerine are reflex tachycardia and venous congestion leading to increased blood loss.[16] Even though dexmedetomidine and nitroglycerine is popularly used as hypotensive agents not many studies have been done on evaluating the efficacy of controlled hypotension in spine surgeries while using the novel alpha 2 agonist dexmedetomidine in comparison with nitrogl ycerine as hypotensive agent. Hence a prospective randomisd double blinded clinical study was done to compare the efficacy of and safety of dexmeditomidine versus nitroglycerine during hypotensive anaesthesia induced by either drug in adult patients posted for elective spine surgeries

Material and methods

This was a prospective, randomized, and double blinded clinical comparative study conducted in the Department of Anaesthesiology, Jawaharlal Nehru medical college and hospital Bhagalpur, Bihar, India from July 2018 to February 2019, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

80 participants belonging to ASA class I or I between 20 and 55 years of age scheduled for elective spine surgeries were include in this study. Participant with cerebrovascular diseases, hypertension, asthma, chronic obstructive lung disease, diabetes mellitus, and coagulation defects, hepatic or renal failure, psychiatric disease, BMI > 30, known drug allergy or substance abuse were excluded from the study. A routine pre anaesthaetic examination was conducted on the evening before the surgery assessing the general condition of the participant, including airway assessment and systemic examinations Routine investigations included CBC, RBS, RFT, coagulation profile, ECG, chest x ray. One PRBC was arranged

prior to the surgery after blood grouping and cross matching. The participant was randomly divided into 2 subgroups of 40 participant each using simple sealed envelope method.
Group A DX : dexmeditomidine group
Group B NG: nitroglycerine group.
The study drug dexmeditomidine was given to group DX in the dose of 1 micro gram/kg body weight in a 600 seconds infusion before induction diluted to 10 ml with normal saline followed by maintenance dose at infusion rate of 0.2- 0.7 micro gm/kg. The group NG received 10 ml plain normal saline over 600 seconds before induction followed by maintenance dose of nitroglycerine at an infusion rate of 0.5 - 10 micro gm/kg/min.
After arrival in the pre anaesthesia room 20 G and 18 Gintravenous cannula were inserted at different anatomical sites for the infusion of the study drug and for the administration of fluids and other drug/ blood respectively. Standard intraoperative monitoring including Spo2, ECG, NIBP, Et Co2 was performed. All the patients were given 0.02 mg/kg inj midazolam, inj ondensetron 0.05-0.1 mg/ kg and inj fentanyl 1 micro gm/kg as premedication. Lignocaine 1.5 mg/kg was given 45 sec before induction in both groups to supress haemodynamic response to laryngoscopy and tracheal intubation. Patients were preoxygenated for 180 seconds and induced with thiopentone 5 mg/ kg iv. inj succinyl choline 1.5 mg/kg iv. after airway was secured by conventional laryngoscopy with appropriate sized tube cuffed flexomettalic endotracheal tube, the patient was put in prone position with chest and pelvic rolls and abdomen hanging. The pressure points were padded. All patients were operated by the same surgical team. Anaesthesia maintained wit O^2 + N_2O + inj. vecurionium bromide + isoflurane 1%.
The parameters that were compared in both groups included the HR, SBP, DBP, MAP, Spo2, Etco2, visual blood loss estimation as reported by the surgeon in terms of Fromme - Boezaart surgica l field grading every 900 seconds, sedation in the post extubation period in terms of Ramsay sedation score (RSS)- post extubation. Adverse events - bradycardia (HR<50 bpm), hypotension (MAP< 65 mmhg), tachycardia (HR > 110 bpm).
HR, MAP, SBP, DBP, Spo2, Etco2 recorded at the following periods.

- T1- baseline (300 seconds after arriving in the pae room)
- T 2 – 120 seconds from the start of the bolus infusion
- T3- 300 seconds from the start of the bolus infusion
- T 4-480 seconds from the start of the bolus infusion
- T5- 30 seconds post intubation.
- T6- 300 seconds from intubation. T7- Start of surgery
- T8- 900 seconds after start of surgery.
- T 9- 1800 seconds from the start of the bolus infusion T 10- 2700 seconds from the start of the bolus infusion T11 - 3600 seconds from the start of the bolus infusion
- T 12 – 4500 seconds from the start of the bolus infusion T13- 5400 seconds from the start of the bolus infusion T14 - end of surgery
- T 15- 30 seconds post extubation.
- T 16- 300 seconds post extubation.
- T17- 900 seconds post extubation

Infusion was stopped 300 seconds before the anticipated end of surgery. after patient was put in supine position, any residual neuro muscular block was antagonised with neostigmine 50 microgm /kg and glycopyrrolate 10 microgm /kg and paptient was extubated.

Statistical analysis

The data was entered in the form of a data matrix in Microsoft Excel® and analysed statistically using IBM® SPSS® version 20.0.0. Descriptive statistics were calculated as frequencies for categorical variables and means and standard deviation for continuous variables.

Results

There was no signifiacnt diffrences between the two groups with regard to age, mean height, mean weight, BMI, gender of the patients, baseline HR, MAP, mean duration of surgery.(Table 1) The basal heart rates are comparable between the two groups and the difference is not statistically significant. There is a statistically significant difference between the two groups after starting loading dose infusion and induction, where in statistically significant fall in HR is noted in group DX. But after laryngoscopy and intubation there is increase in heart rate in both groups which more in group NG compared to group DX ($p<0.001$). The intraoperative mean HR during surgery is significantly lower in group DX compared to group NG($p<0.001$). After stopping infusion HR is lower in Group DX compared to Group. Although there is increase in HR after repositioning and extubation, but it is lesser in group DX compared to group N G.
The baseline (MAP) is comparable in both groups and there is no statistical difference in the 2 groups (P=0.228). after starting the loading dose infusion and after induction there is fall in MAP group DX compared to group NG. The MAP increase after laryngoscopy and intubation, but it is significantly low in group D X than group NG. intraoperatively the MAP is significantly low in group D X compared to group N X at T7, T8, T11 but not atT9, T10,T12,T13,T14. The mean MAP values in group S after stopping infusion at the end of surgery, after repositioning and extubation is less compare to group NG.
At 15 min minutes there is no significant difference in the 2 groups with respect to the average surgical field grading of each study population. At 30 min there is significant difference between 2 groups with group DX having average surgical field grade of 1.88 ±0.52, which is less compared to that of group NG, 2.54 ±0.49($p<0.001$). The average intraoperative surgical field grade was 2.18±o.51 in group DX, which was significantly better than 2.41± 0.61 in group NG (p=0.29).

Table 1: Demographic profile of the patients

Parameter	Group A-DX	GroupB- NG	p-value
Age (years)	37.2+/-8.1	40.12+/-7.1	.201(NS)
Gender (male/female)	26/14	23/17	.632(NS)
Mean height (M)	1.611+/-0084	1.602+/-.081	.801
Mean weight (kg)	61.0+/-9.26	61.5+/-10.11	.897
BMI(kg/m2)	22.65+/-2.74	22.34+/-2.77	.934
Baseline heart rate (HR)	93.7+/-9.11	90.1+/-11.32	.356
Baseline Mean arterial pressure (mmhg)	98.65+/-4.81	95.98+/-6.75	.249
Mean duration of surgery (min)	79.1+/-8.97	80.24+/-11.23	.626

Table 2: Heart rate changes in the patients

Heart rate (bpm)	Group DX	Group NG	P value
T1	94.7+/-9.26	90.3±11.79	.382
T2	87.11±8.71	91.27±13.31	.151
T3	70.11±3.81	90.87±13.48	.001
T4	68.87±3.55	92.43±12.49	.001
T5	64.8±3.0	91.6±12.51	.001
T6	103.1±7.17	114.26±12.4	.001
T7	75.65±9.78	100.5±12.84	.001
T8	65.85±2.41	98.71±10.84	.001

T9	62.35±2.48	95.12±9.18	.001
T10	60.87±4.54	97.5±10.31	.001
T11	61.57±3.67	94.92±9.88	.001
T12	63.17±2.44	95.8±9.31	.001
T13	66.52±3.52	93.4±10.11	.001
T14	64.31±1.24	92.54±14.13	.001
T15	66.4±3.17	105.23±7.9	.001
T16	80.7±5.1	117.88±6.67	.001
T 17	73.21±3.64	103.7±7.7	.001

Table 3: Mean arterial pressure changes in patients

Mean arterial pressure (mmhg)	**Group DX**	**Group NG**	**p value**
T1	98.04±4.74	96.54±6.21	.214
T2	95.29±5.36	95.15±6.12	.888
T3	84.74±5.62	95.17±5.52	.001
T4	78.62±5.11	96.31±5.89	.001
T5	71.79±2.74	94.52±4.97	.001
T6	75.88±2.92	113.88±6.25	.001
T7	72.19±2.77	90.82±4.87	.001
T8	69.14±2.47	75.97±3.62	.001
T9	70.42±2.32	69.67±2.74	.221
T10	70.51±2.94	69.42±2.87	.211
T11	70.71±2.17	69.31±3.32	.027
T12	69.89±2.41	69.54±2.97	.624
T13	70.62±2.16	71.77±4.65	.510
T14	70.88±1.89	73.89±4.67	.412
T15	72.2±1.79	77.39± 3.78	.001
T16	77.31±2.51	103.78±12.59	.001
T17	78.42±2.28	94.02±6.18	.001

Table 4: Fromme-Boezaart surgical field grade

	Group DX 15 min (T9)	30 min (T10)	45 min (T11)	**Group NG** 15 min (T9)	30 min (T10)	45 min (T11)	**P value** 15 min (T9)	30 min (T10)	45 min (T11)
Grade 0	0	0	0	0	0	0			
Grade I	0	7	4	0	0	0			
Grade II	27	27	32	18	20	32			
Grade III	13	6	4	22	20	8	127	.001	.581
Grade IV	0	0	0	0	0	0			
Grade V	0	0	0	0	0	0			
Average FBG	2.30±.48	1.88±.52	2.11±35	2.55±0.51	2.54±0.49	2.09±0.52			
Average intraoperative FBG	2.18±0.51			2.41±0.61			.029		

Discussion

During surgeries it is important to reduce bleeding to allow a better view of the surgical field there by increasing the surgeon's control and shortening surgical time which in turn reduces the bleeding.[17,18] By decreasing intraoperative blood pressure bleeding from surgically injured arteries and arterioles can be reduced. Venous dilatation in turn reduces the venous bleeding, especially from cancellous bony sinuses that do not collapse when transected. In various types of surgeries, including spine surgery, for reduction of intraoperative blood loss as well as providing better surgical field for the operating surgeon controlled hypotension is most commonly used technique.[17,19] Contolled hypotension has been widely advocated to reduce blood loss, but it may be associated with risk of neurological deficit because of reduced spinal cord perfusion.[17,20] The lower limit of human autoregulation can be considered in determing the range of target autoregulation, the target MAP have been derived by various studies. In the studies Ozcan AA et al [21], Akkaya et al and Bhatnagar V et al [22], the target MAP used was 65-75mmhg. Therefore in our study MAP of 70 - 75mmhg was adopted which was effectively reached in both groups before skin incision. The ideal hypotensive drug for inducing hypotensive anaesthesia should be easy to administer, with a short onset time, easy titratability; its dose can be meticulously controlled; its effects disappears quickly when its administration is discontinued; it has a rapid elimination and causes no unwanted or adverse effects.[9,23] Many agents can be used to produce hypotensive anaesthesia; out of those in our study the nitroglycerine and dexmedetomidine was used.

The minimum dose of nitroglycerine infusion was 0.5µg/kg/min found to be effective dose by many authors,[24,25] hence same was used in our study. Khalifa OS et al [26] used 10µg/kg/min as maximum dose of nitroglycerin infusion for controlled hypotesion, and the same used in our studies. For the purpose of blinding, 10ml of plain normal saline was infused over 10 min before induction in participants in Group NG in our study followed by intraoperative infusion of Nitroglycerin at 0.5- 10µg/kg/min using syringe pump, titrated to the target MAP. Many authors[25-27] used loading dose of dexmedetomidine 1µg/kg was given over 10 min before induction. The minimum dose of dexmedetomidine infusion intraoperatively is 0.2µg/ kh/hr [21,26,27] and the maximum dose of dexmedetomidine used was 0.7µg/kg/hr.[21,26] Hence the intraoperative infusion of dexmeditomidine in our study was given between 0.2-0.7µg/kg/hr in group DX.

The basal heart rates are comparable between the two groups and the difference is not statistically significant. There is a statistically significant difference between the two groups after starting loading dose infusion and induction, where in statistically significant fall in HR is noted in group Dx. But after laryngoscopy and intubation there is increase in heart rate in both groups which more in group NG compared to group DX ($p<0.001$). So our concurs with the findings of Scheinin H et al[28] and Jaakola ML et al.[29] The intraoperative mean HR during surgery is significantly lower in group DX compared to group N G($p<0.001$). After stopping infusion HR is lower in Group DX compared to Group NG. Although there is increase in HR after repositioning and extubation, but it is lesser in group DX compared to group NG.[30] The baseline (MAP) is comparable in both groups and there is no statistical difference in the 2 groups ($P=0.228$). After starting the loading dose infusion and after induction there is fall in MAP group DX compared to group N G. The MAP increase after laryngoscopy and intubation, but it is significantly low in group DX than group N G.[31,24] Intraoperatively the MAP is significantly low in group DX compared to group N G at T7, T8, T11.[26,32] The mean MAP values in group DX after stopping infusion at the end of surgery , after repositioning and extubation is less compare to group NG.[28] Many authors[28,29] used the quality scale proposed by fromme – Boezaart. Fromme – Boezaart surgical field grading at 15 min minutes was comparable in both group. At 30 min there is significant difference between 2 groups with group DX having average surgical field grade of 1.88±0.52, which is less compared to that of group N G, 2.54±0.49(p<0.001). The average intraoperative surgical field grade was 2.18±o.51 in group DX , which was significantly better than 2.41±0.61 in group NG (p=0.29)

Conclusion

Dexmedetomidine and Nitroglycerine both can be used with great safety profile to achieve controlled hypotension during spine surgerie.

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