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DEXMEDETOMIDINE VS FENTANYL AS ADJUVANT WITH 0.5% LEVOBUPIVACAINE IN SPINAL ANAESTHESIA. "A CLINICAL STUDY"

Vibhor Rai[1], S. K. Tyagi[2], S. P. Singh[3], Anuj Garg[4]

ABSTRACT

Background: Intrathecal opioids & α2 adrenergic agonists prolong the duration of action of local anesthetics and reduce the required dose. Dexmedetomidine is an α2 adrenergic receptor agonist and its α2/α1 selectivity is 8 times higher than that of clonidine. Intrathecal fentanyl has been widely used as analgesic adjuvant. Its main site of action is the substantia gelatinosa on the dorsal horn of spinal cord. It blocks fiber carrying nociceptive impulses, both pre and postsynaptically.

Aims: In this study, we aimed to investigate the effect of adding dexmedetomidine & fentanyl to intrathecal levobupivacaine on the onset time and duration of motor and sensory blocks.

Methods: Patients were randomly assigned into three groups. Group L (n= 50) patients received 2.5 mL (12.5 mg) of 0.5% levobupivacaine +0.5 mL normal saline, Group LD (n= 50) patients received 2.5 mL (12.5 mg) of 0.5% levobupivacaine + 0.5 mL (5 µg) dexmedetomidine and Group LF (n= 50) patients received 2.5 mL (12.5 mg) of 0.5% levobupivacaine + 0.5 mL (25 µg) fentanyl. Time of onset of block, maximum sensory level, degree of motor block, duration of analgesia were recorded.

Results: Sensory and motor block onset times were shorter in Group LD than in Group LF and Group L ($p<0.001$). The regression of the sensory block to S1 dermatome and Bromage 0 were longer in Group LD than in Group LF and Group L ($p<0.001$). The two dermatome regression time was longer in Group LD than in Group LF and Group L ($p< 0.001$). There were no statistically significant differences between groups in blood pressure and heart rate. There was no statistically significant difference between groups when adverse effects were compared.

Conclusion: We conclude that intrathecal dexmedetomidine addition to levobupivacaine for spinal anaesthesia shortens sensory and motor block onset time and prolongs block duration without any significant adverse effects.

Keywords: Dexmedetomidine; fentanyl; levobupivacaine; spinal

INTRODUCTION

The main disadvantage of spinal anaesthesia is limited duration of action after single injection. Prolongation of spinal anaesthesia using single shot technique has been achieved by the addition of various adjuvants such as adrenaline, neostigmine, benzodiazepines, ketamine and alpha-2 agonists. Intrathecal α2 agonists prolong the duration of action of local anaesthetics and reduce the required dose. The intrathecal use of

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clonidine, a partial α2 adrenoceptor agonist, has been shown as an effective and safe procedure [1,2]. Dexmedetomidine is an α2 receptor agonist and its α2/α1 selectivity is 8 times higher than that of clonidine. In animal models, intrathecal dexmedetomidine has been demonstrated to have an analgesic effect [3].

Intrathecal fentanyl has been widely used as analgesic adjuvant. Its main site of action is the substantia gelatinosa on the dorsal horn of spinal cord. It blocks fiber carrying nociceptive impulses, both pre and post synaptically [4,5,6]

Levobupivacaine is a long-acting local anaesthetic with a pharmacological structure similar to that of bupivacaine. Levobupivacaine has been shown to have a larger safety margin and less neurotoxic and cardiotoxic side effects than bupivacaine[7]. In this study, we aimed to investigate the influences of dexmedetomidine added to levobupivacaine on the time of onset of spinal block and durations of sensory and motor blocks in patients undergoing transurethral endoscopic surgery by spinal anaesthesia.

MATERIAL & METHOD:

The present study was approved by ethical committee of Chaudhary Charan singh university, Merrut India, and was conducted in the department of anaesthesia and critical care, muzaffarnagar medical college & hospital, muzaffarnagar, during the academic year 2013 to 2015 on 150 patients scheduled for lower limb and lower abdominal surgeries.

Patients with known allergy to the study drugs, ASA grading>2 and Suspected Coagulopathy were excluded. Also patients with Infection at the site of spinal block skeletal deformities were excluded. Selected patients were randomly divided into three groups:

- Group LD (*n*=50) – 2.5 ml 0.5% levobupivacaine + 5 mcg dexmedetomidine (0.5 ml)
- Group LF (*n*=50) – 2.5 ml 0.5% levobupivacaine + 25 mcg fentanyl (0.5 ml)
- Group L (*n=50)* – 2.5 ml 0.5% levobupivacaine + 0.5 ml normal saline

Age, body weight and baseline vital parameters of all the patients was recorded. History regarding previous anaesthesia, surgery, any significant medical illness, medications and allergy was recorded. All the patients were informed about the procedure and written consent was taken. Complete physical examination and airway assessment was done. Laboratory investigations was done. An18 G IV cannula was inserted into a peripheral vein and patient was hydrated with Lactated ringer's solution 15 ml/kg. The patient was placed in sitting position on the OT table. With full aseptic precautions part was prepared, painted and draped. Under all aseptic precaution subaracnoid block was performed using 26 G spinal Quincke needle, in sitting position, at L3-L4 inter space and study drug was injected into the subarachnoid space after CSF is freely obtained. Immediately patient was returned to supine position with table in neutral position.

The following observations were made and recorded during peri-operative period:

- Time of onset of blockade (patient ensure when tingling start).
- Maximum sensory level achieved (assessed by pinprick method).
- Degree of motor blockade (according to modified bromage scale).
- Intraoperative hemodynamic monitoring (HR,NIBP,SpO2).
- Sedation (by ramsay sedation scale).
- Any intraoperative side effect (like hypotension, bradycardia, pruritis, sedation, respiratory depression, nausea &vomiting).
- Duration of analgesia (assessed by visual analogue scale)

RESULTS

The three groups were matched for demographic data in regard to group,age and gender (Table 1-3).

Table 1: Group wise Distribution of Subjects

S.No.	Group	Description	No. of patients	Percentage
1.	I	Control Group L	50	33.3
2.	II	Study Group LD	50	33.3
3.	III	Study Group LF	50	33.3

Table 2: Age wise distribution of subjects

S.No	Group	No of cases	Mean	SD
1	Control group (L)	50	38	13
2	Group LF	50	41	14
3	Group LD	50	39	13

Table 3: Gender wise distribution of subjects

Gender	L		LF		LD	
	No	%	No	%	No	%
Female	4	8	4	8	3	6
Male	46	92	46	92	47	94

X^2 0.196 DF=2 P=0.9066

The following conclusions were drawn from the observations made in the present study:

Mean time for onset of sensory block T8 level was 7.8±0.61 minutes in control group L , 5.70±0.50 minutes in study group LD and 5.70±0.53 minutes in study group LF, Showing Statistically significant intergroup difference (p value < 0.001), Onset of sensory block was faster in study group LD.

Median Level of sensory block was T8 in all the 3 Groups after 8 min of intrathecal injection of drug. Mean time taken to achieve T10 and T8 level was higher in control group L as compared to two study groups. The mean time taken to achieve T10 level in study group LD was slightly lower (3.72±0.50) as compared to that of Study Group LF (5.76±0.66). **Table 4** .

Mean time to achieve sensory block was Faster in dexmedetomidine group.

Median of Maximum level of sensory block (T8) was same in both the study groups. **Table 4,4a,4b.**

Mean time for onset of Grade III Motor block in our study was 9.0±0.00 minutes in control group, 5.76±0.43 minutes in study group LD, and 5.80±0.40 minutes in study group LF. The mean time to achieve Grade III motor blockade was minimum in study group LD, and maximum in control group showing a significant intergroup difference (p value < 0.001). Onset of motor block was faster in study group LD.

Mean time to achieve motor block/bromage-3 was faster in dexmedetomidine group. **Table5,5a.**

There was no statistical significant difference for onset of sensory and motor block in dexmedetomidine and fentanyl group (p value > 0.05).

The sensory and motor block were more prolonged in dexmedetomidine group than fentanyl group showing significant difference among the two groups (p value < 0.001).

Mean time of duration of analgesia was more in study group LD followed by study group LF and then control group L, it means that Dexmedetomidine provided longer duration of analgesia than Fentanyl. Overall duration of analgesia was significantly longer in Dexmedetomidine group (373 minutes) than fentanyl group (302 minutes) showing significant difference among the two groups (p value < 0.001).**Table 7.**

Fall in Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure were more in Fentanyl group which was easily controlled with small bolus dose of Mephentermine.

There was not much difference in cardiovascular stability in all 3 Groups.

Sedation was more in dexmedetomidine group than fentanyl group.

No significant differences were observed among different Groups for any of the side effects **Table 6.**
In our opinion adding Dexmedetomidine 5 mcg to single shot spinal blockade with Levobupivacaine 12.5 mg not only provide rapid onset, profound analgesia with good relaxation for surgery but also prolongs the duration of sensory and motor blockade and extends the duration of post operative analgesia without significant side effect. The overall effect and duration is superior in group LD then in group LF.

DISCUSSION

Table 4: Comparison of Maximum Level of Sensory Blockade achieved in two groups

S.No.	Level of Block	Control Group L (n=50)		Study Group LD (n=50)		Study Group LF (n=50)	
		No.	%	No.	%	No.	%
1.	T8	40	80	50	100	42	84
2.	T6	10	100	0	0	8	16
Median level of sensory block		T8		T8		T8	

X^2=72.773 (df=2); p<0.001 (Kruskall-Wallis Test)

Table 4a: Mean Time taken to achieve sensory blockade at different levels

SN	Level	Control Group L			Study Group LD			Study Group LF			"F"	"p"
		n	Mean	SD	n	Mean	SD	n	Mean	SD		
1.	T10	50	6.14	0.61	50	3.72	0.50	50	3.80	0.53	314.96	<0.001
2.	T8	50	7.84	0.58	50	5.76	0.66	50	5.76	0.66	179.77	<0.001
3.	T6	50	11.36	2.30	50	-	-	50	7.02	0.51	162.96	<0.001

ANOVA

Table 4b: Between Group Comparisons for Mean time taken to achieve sensory blockade at different levels

SN	Level of block	Control vs Study Group LD		Control vs Study Group LF		Study Group LD vs Study Group LF	
		"t"	"p"	"t"	"p"	"t"	"p"
1.	T10	21.833	<0.001	20.469	<0.001	0.775	0.440
2.	T8	16.737	<0.001	16.737	<0.001	0	1
3.	T6	-	-	13.013	<0.001	0.198	0.843

Table 5: Median level of Motor blockade achieved at different time intervals

SN	Time	Control Group L (n=50)			Study Group LD (n=50)			Study Group LF (n=50)			Significance of difference (Kruskall Wallis test)	
		P_{50}	min	max	P_{50}	min	max	P_{50}	min	max	Z	"p"
1.	30s	0	0	0	0	0	0	0	0	0		
2.	1 min	0	0	0	0	0	1	0	0	1	33.468	<0.001
3.	2 min	0	0	0	1	1	1	0	0	1	131.65	<0.001
4.	3 min	0	0	1	1	1	2	1	1	2	35.433	<0.001
5	4 min	1	1	1	2	2	2	2	2	2	149.00	<0.001
6	5 min	1	1	2	2	2	3	2	2	3	102.60	<0.001
7	6 min	2	1	2	3	3	3	3	2	3	143.45	<0.001
8	7 min	2	2	2	3	3	3	3	3	3	149.00	<0.001
9	8 min	2	2	2	3	3	3	3	3	3	149.00	<0.001
10	9 min	3	3	3	3	3	3	3	3	3	–	–
11	10 min	3	3	3	3	3	3	3	3	3	–	–
12	20 min	3	3	3	3	3	3	3	3	3	–	–

Table 5a: Mean Time taken to achieve maximum grade of motor blockade in three groups

S.No.	Group	Time taken to achieve maximum grade of motor blockade		
		N	Mean	SD
1.	Control Group	50	9.00	0.00
2.	Study Group LD	50	5.76	0.43
3.	Study Group LF	50	5.80	0.40

F=1483.967; p<0.001

Table 6: Comparison among three groups for events of side effects

SN	Side Effect	Control Group L (n=50)		Study Group LD (n=50)		Study Group LF (n=50)		Significance of difference	
		No.	%	No.	%	No.	%	χ^2	P
1.	Hypotension	4	8	6	12	10	20	3.231	0.199
2.	Bradycardia	3	6	4	8	5	10	0.543	0.762
3.	Resp. Depression	2	4	0	0	4	8	4.167	0.125
4.	Pruritus	0	0	0	0	0	0	-	-
5.	Sedation	0	0	10	20	6	12	1.190	0.275
6.	Nausea and vomiting	3	6	4	8	6	12	1.179	0.55

Table 7: Mean Time taken to achieve various landmarks (min)

SN	Landmarks	Control Group L			Study Group LD			Study Group LF			"F"	"p"
		n	Mean	SD	N	Mean	SD	N	Mean	SD		
1.	**Duration of analgesia**	50	193.56	12.43	50	373.00	16.26	50	302.40	16.01	1815.495	<0.001
2.	**Duration of surgery**	50	55.00	14.25	50	82.40	14.27	50	82.36	18.75	49.451	<0.001

3.	**Sensory Regression by Level S1**	50	187.94	8.32	50	306.00	13.32	50	206.14	16.69	1153.822	<0.001
4.	**Regression to Bromage -0**	50	160.18	7.44	50	257.70	14.61	50	178.54	14.23	854.421	<0.001

ANOVA

The present study entitled Dexmedetomidine vs Fentanyl as adjuvant with 0.5% Levobupivacaine in Spinal Anaesthesia. “A Clinical Study” was designed to compare the effects of adding dexmedetomidine or Fentanyl as an adjuvant to Levobupivacaine in Spinal Anaesthesia. The mean time to achieve sensory block upto T8 level was 7.8±0.61 minutes in control group L , 5.70±0.50 minutes in study group LD and 5.70±0.53 minutes in study group LF, Showing Statistically significant intergroup difference (p value < 0.001), but no significant difference between study group LD and LF (p value= 0.440) Though no significant difference between control group and either of study groups was observed for achieving the maximum level of blockade yet it holds no relevance as the levels of block reached in both study groups were much higher as compared to control group While in other studies, ERKAN YAVUZ Akcaboy EY et al[8] did a study on patients undergoing elective transurethral resection of prostate to compare the efficacy of low dose levobupivacaine and bupivacaine with fentanyl. They found that both combinations provided similar haemodynamic effect and sensory blockade to the both group of patients. There was a significant Difference of timing to achieve maximum sensory level in compare to my study because they were used low dose of study drug. Less motor blockade was seen in levobupivacaine with fentanyl group. ALIYE Esaoglu A etal[9] concluded that intrathecal dexmedetomidine addition to levobupivacaine for spinal anaesthesia They found that dexmedetomidine group prolongs block duration without any significant adverse effects in comparison to levobupivacaine alone. block duration was similar to our study.. While in other studies, NESRIN BOZDOGAN **Ozyilkan NM** etal[10] studied the synergistic effect of intrathecal fentanyl and sufentanyl with Levobupivacaine in spinal anesthesia for cesarean section and they suggested that the addition of fentanyl to intrathecal levobupivacaine during caesarean section surgery is more effective than the administration of levobupivacaine alone. Cuvos O etal[11] did a prospective randomized double blinded study on patients undergoing transurethral resection of prostate surgery to compare the efficacy of levobupivacaine alone and fentanyl with levobupivacaine. They found that both combinations were similarly effective but levobupivacaine and fentanyl combination offers shorter duration of motor block in comparison to levobupivacaine alone. Duration of motor block was shorter in cuvas o study because they were used low volume drug as compare to our study.

Duration of sensory block was assessed by time period for sensory regression to S1 level after intrathecal injection of drug. In our study The time period for sensory regression to S1 level were

187.94±8.32, 306.0±13.32, 206.14±16.69 minutes in control group , study group LD, and LF respectively.

Duration of motor block was assessed by time period of regression to motor block/bromage -0 after intrathecal injection of drug. In our study The time period for regression to bromage-0 were 160.18±7.44, 257.70±14.61, 178.54±14.23 minutes in control group , study group LD, and LF respectively.

Cuvos O etal[11] compared the effects of adding 15 mcg Fentanyl to 2.2 ml Levobupivacaine and concluded that duration of Effective analgesia was prolonged to 248 minutes in comparision to 150 minutes when levobupivacaine was used alone. While In our study, The mean duration of effective analgesia was found to be 193.56±12.43, 373.0±16.26 and 302.40±16.01 minutes in the control group, study group LD and LF respectively. The mean time for duration of analgesia was found to be maximum in study group-LD followed by study group-LF and minimum in control group showing a statistically significant intergroup difference (p value < 0.001). It means that in our study the longest duration of analgesia were experienced by the patients receiving Dexmedetomidine, followed by the patients receiving Fentanyl.

For Pulse Rate, There was no statistically significant intergroup difference observed (p value > 0.05. In control group , the mean of SBP ranged from 107.70±6.63 (at 15 minute) to 130.86±8.62 (baseline) mmHg whereas in study group LD, it ranged from 106.80±7.86 (at 15 minute) to 131.88±9.52mmHg (baseline) and in study group LF, the mean value ranged from 105.08±5.93 (15 minute) to 131.10±7.91(baseline) mmHg. There was no statistically significant intergroup difference observed among the three study groups throughout the study period (p value > 0.05).

G. Christian etal[12] was concluded previously that levobupivacaine group was showing least hypotension and better hemodynamic control. In our study, control group, the mean DBP ranged from 60.86±7.05 (at 15 min) to 83.58 ±6.40 mmHg (baseline) whereas in study Group LD, it ranged from 58.18±6.32 (at 20 min) to 84.82±7.25 mm Hg (baseline) and in study Group LF the mean value ranged from 57.02±5.48 (15 min) to 82.88±6.48 (Baseline) mm Hg. There were no statistically significant intergroup difference observed among the three study groups at BL, JAS, and 5 minutes (p value > 0.05), N.K Gergin etal[13] study on intrathecal levobupivacaine and fentanyl, were concluded that fentanyl group shows better hemodynamic control then levobupivacaine alone.

In control group , the mean MAP ranged from 76.32±6.08 (at 15 min) to 102.76±43.89 mmHg (JAS) whereas in study group LD, it ranged from 73.80±6.53 (15 min) to 95.56±8.66 mm Hg (Baseline) and in study group LF the mean value ranged from 73.0±5.36 (15 min) to 98.80±7.21 mmHg (Baseline) . There was no statistically significant intergroup difference observed among the three study groups at 0 minute and 2 minute (p value > 0.05), Statistically significant intergroup differences were observed from 4 min to 35 min time interval (p value < 0.05. It means that fall in MAP was observed maximum in patients receiving Fentanyl followed by patients receiving Dexmedetomidine. Lee YY etal[14] were concluded levobupivacaine and fentanyl combination having more haemodynamic stability and least motor block compare to levobupivacaine alone.

No significant difference was observed among different groups for any of the side effects. Hypotension, bradycardia more in study group LF followed by study group LD (p=0.199 & p=0.762) and then control group. Respiratory depression more in study group LF followed by control group. J.K.Santiago etal[15] concluded that fentanyl group

of there study shows better sensory and motor outcome with least adverse effect.

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A CASE OF WEGNER'S GRANULOMATOSIS WITH PULMONARY TUBERCULOSIS : "A DIAGNOSTIC DIFFICULTY"

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ABSTRACT

Wegner's Granulomatosis is a rare disease of auto immune etiology. The lungs are affected in 90 percent of patients. Wegner's granulomatosis with such presentation both clinically and radiologically is likely to be mistaken for tuberculosis which leads to delayed diagnosis and hence flaring up of the disease

Key-words

Wegner's Granulomatosis, Pulmonary Tuberculosis, c-ANCA

INTRODUCTION

Wegner's Granulomatosis is a disease of unknown etiology, which was described for the first time by Wegner in 1936.[1] Wegner's Granulomatosis usually present as a triad of airway necrotising granulomas, systemic vasculitis and focal necrotising granulomatosis. Classical symptoms and clinical findings together with serology titres positive for anti neutrophil cytoplasmic antibody against proteinase 3 helps to reach at the diagnosis.[2] The lungs are affected in 90 percent of patients. Clinical findings include hematuria, hemoptysis, rhinorrhoea along with constitutional symptoms. In a country like India where tuberculosis is a very common disease, a case of Wegner's granulomatosis with such presentation both clinically and radiologically is likely to be mistaken for tuberculosis which leads to delayed diagnosis and hence flaring up of the disease.

We report a unique case of dual pathology of pulmonary tuberculosis and Wegner's granulomatosis in a 36 year old male in which the diagnosis of the later was delayed due to concurrent pulmonary tuberculosis.

CASE HISTORY

A 36 year old male presented with a one month history of fever and cough with blood streaked expectoration and worsening of Chest radiograph while on Anti tubercular therapy (ATT) which was started on basis of bronchalveolar lavage (BAL) fluid positive for acid fast bacilli (AFB).

In the past, patient gave history of pain and swelling of right knee joint which was diagnosed as tubercular arthritis five years back and he was given ATT for duration of one year with no improvement of symptoms. Patient also complained of rhinorrhoea and post nasal drip. He was a non smoker and there was no other associated medical history.

Physical examination was unremarkable. The whole blood counts were within normal limits, however urine microscopy showed presence of 10-15 RBC's per HPF with traces of protein. RA factor was negative.

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Figure 1 showing a cavity with air fluid level on left side and a small nodule on right side

CECT chest revealed a cavitatory lesion with thick irregular shaggy walls and air fluid level in left upper lobe and a well defined rounded nodule in posterior segment of right upper lobe. Pus was aspirated from the cavity under CT guidance, Cytology of pus showed necrotizing granulomatous pathology.

Figure 2 Section of Chest on CT with contrast showing a cavity with air fluid level on left side and a solitary nodule on right side

CT PNS suggested pansinusitis with thinning of nasal septum and hypertrophy of bilateral middle and inferior turbinates.

Considering the above mentioned clinical, lab and radiological findings; possibility of non infective multi system pathology was made. Nasal biopsy was done and Serum c-ANCA was sent.

Nasal biopsy revealed necrotizing granulomatous pathology and serum c-ANCA was strongly positive and hence confirming the diagnosis of Wegner's granulomatosis. Treatment was initiated according to BSR and BHPR guideline for the management of adults with ANCA-associated vasculitis CYC was given by i.v. pulses initially at 2-week intervals and then every 3 weeks, along with GCs which were given as daily oral prednisolone, initially at relatively high doses (1 mg/kg up to 60 mg) , with the dose rapidly reduced to 15 mg prednisolone at 12 weeks . Following achievement of successful remission, CYC was withdrawn and substituted with AZA. He responded well and is on maintenance therapy for last 14 months following successful disease remission without any significant episodes of concern.

DISCUSSION

Differential diagnosis of tuberculosis and Wegener's granulomatosis poses a great problem. In both cases, the clinical findings include haemoptysis, low grade fever, weight loss and cough.[3] Radiological presentation can be the same in both diseases. Even histopatologic finding can make confusion, since both diseases have granulomatous changes.[4] We above reported a unique case of two co-existing diseases of pulmonary tuberculosis and wegner's granulomatosis. The diagnosis of the later was delayed due to similar symptoms and radiological findings of the wegner's to pulmonary tuberculosis and also due to high incidence of tuberculosis in this part of the world.

The often rapidly progressive and potentially fatal disease wegner's granulomatosis affects mainly the upper and lower respiratory tracts along with kidneys. The exact etiology remains unclear.

In 1990, the American College of Reumatology (ACR) established the criteria for the diagnosis of WG : nasal or oral inflammation, radiologically demonstrated pulmonary infiltrates, abnormal urinary sediment (red cell cast, haematuria), granulomatous inflammation on biopsy. Patient shall be said to have Wegener's granulomatosis if at least two of these four criteria are present.[5] The disease responds well to immunosuppressive agents and steroids. Diagnosis is usually considered in a patient with classic triad of organ involvement that is upper and lower respiratory tract and kidneys. Outcome is good when treatment is started early using corticosteroids and cytotoxic agents. We came across a patient with this disease who had an atypical presentation and showed clinical as well as radiological response to anti-tuberculosis therapy. This case is reported with the aim of highlighting the importance of keeping a high index of suspicion in patients even with typical profile so that timely diagnosis of this potentially treatable disease could be made. Long term follow up is essential to detect possible relapse suggested by rising ANCA levels. Much literature is not available depicting the effect of other infectious disease like tuberculosis on the course of wegner's granulomatosis.

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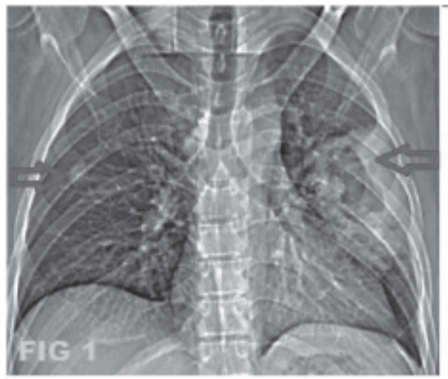

Figure 1 : Cavity with air fluid level on left side and a small nodule on right side

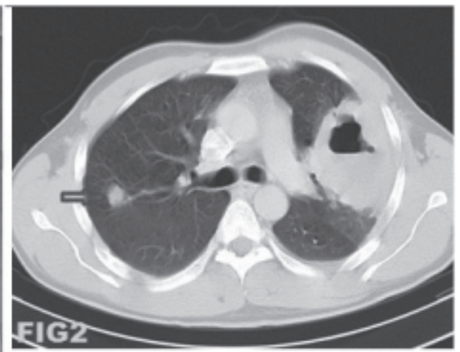

Figure 2: CECT chest : Cavitatory lesion with thick irregular shaggy walls and air fluid level in left upper lobe

EMERGENCY ANAESTHETIC MANAGEMENT OF RUPTURED HEPATOBLASTOMA WITH MASSIVE HEMOPERITONEUM IN PAEDIATRIC PATIENT "A CASE REPORT"

Patel Priti[1], Gosai Nita[2], B. M. Patel[3]

ABSTRACT

This case report describes the emergency anaesthetic management of a male child aged 7 years and weighing 19 kg presented with one day history of sudden onset of abdominal pain with gradual deterioration of general condition progressing to altered sensorium and shock. This case emphasizes the role of anaesthesiologist in the perioperative management of liver resection in a child and includes pre-operative optimization, management of intra and post operative complications.

KEY WORDS

Ruptured hepatoblastoma, Paediatric hepatoblastoma, Emergency anaesthetic management , Liver resection.

INTRODUCTION

Rupture of hepatoblastoma in paediatric patient is a rare life threatening event[1]. Upto 10% may present with tumour rupture with signs and symptoms of a hemoperitonium. The tumour that rupture are not necessarily large and long term survival with complete resection has been reported. Significant perioperative morbidity and mortality have been reported to be as high as 19%[2].

CASE REPORT

A 7 year old male child weighing 19 kg was admitted in emergency department with one day history of sudden onset of abdominal pain. On general examination patient was irritable with altered sensorium and gradual deterioration of general condition. Pulse rate was 140/mi and blood pressure was 70/50 mm of hg.

PRE-OPERATIVE INVESTIGATIONS

Hb:5 gm%, TC: 21500/cumm, Platelet count: 4,78,000/cumm, S.AFP: 484.24 ng/ml, PT: 12.7 Sec/ 13.0 Sec, INR: 0.98, **CT** abdomen Large heterogenous mass (12cm × 9cm × 9cm) lesion involving segments V,VI,VII and VIII of the liver with intra abdominal fluid accumulation with clots over the right dome of liver suggesting haemoperitoneum.

After initial resuscitation with fluid and packed cell transfusion informed consent of the patient's relative was taken for high risk surgery, anaesthesia and post operative ventilation.

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Prognosis and outcome of anaesthesia and disease were explained to the relatives. After the patient's arrival in the operation theatre all the vital data were recorded. Pulse: 114/min and BP: 130/90 mm of hg. Intravenous (IV) line was secured with 20 G cannula through which an infusion of 25% Dextrose with Ringer lactate was started. IV Ceftriaxone 500mg and Tranexemic acid 250mg were given for prophylaxis. Patient's extremities were wrapped in cotton wool to prevent heat loss. Glycopyrrolate 0.15mg/kg, Ranitidine1mg/kg and Ondansetron 0.2 mg/kg were given IV. After 3 minutes preoxygenation anaesthesia was induced with Thiopentone sodium 5mg/kg and Atracurium hydrochloride 0.5mg/kg, Fentanyl citrate 1.5mcg/kg IV and patient was intubated with endotracheal tube no 5.5. Anaesthesia was maintained with oxygen, nitrous oxide, sevoflurane and atracurium for muscle relaxation. Right subclavian vein cannulation was done for measurement of CVP, drug administration and for infusion.

Monitoring:

During intraoperative period parameters monitored were pulse, BP, CVP, SPO_2, ECG, Temperature, $EtCO_2$, blood loss, urine output, ryle's tube aspiration and concentration of anaesthetic agents.

SURGICAL PROCEDURE

During laparotomy there was a ruptured tumour arising from right lobe of liver with a clot over it. Right hepatectomy with intrahepatic vascular ligation was planned. Intermittent Pringle's maneuver with 15 minute occlusion and 5 minute release was done. The surgical procedure lasted for 5 hours.

All the IV fluid and blood were warmed before infusion. We infused total 700 ml of 25% dextrose with ringer lactate in the ratio of 1:4. Blood loss was 700 ml which was replaced with 400 ml of packed cells and 200ml FFP.

During operative procedure temperature of the patient fell down to 35°C which we tried to maintain with the help of warmer. Immediate environment of patient was also warmed. We also came across frequent alteration in systemic arterial pressure and was corrected by transfusion of packed cells and repositioning of liver.

After the closer of the abdomen caudal epidural catheter was kept for postoperative analgesia and anaesthesia was reversed. Urine output was 700ml at the end of operation. Patient was shifted to ICU and all the vital parameters were monitored.

Postoperative pain relief was provided with 12.5 mg Paracetamol suppository and Bupivacaine 0.125% of 8 ml caudally. Fluid replacement done with 10% dextrose with ringer lactate solution. Rest of the postoperative period was uneventful. Patient was discharged on 15th post operative day.

DISCUSSION

The spontaneous rupture of hepatoblastoma occurs in 2.9% to 8.6% patients affected by hepatoblastoma[3]. This life threatening condition usually presents with acute abdomen with massive internal bleeding which can be associated with tumour rupture. In such emergency situation control of haemorrhage which is life saving can be achieved by transarterial embolization and/or surgical resection[1]. In our case as the patient was deteriorating and also the patient had presented during emergency hours (night) it was not possible to get embolisation done and right hepatectomy with intrahepatic vascular ligation was performed.

In preoperative period arrangements should be made for adequate blood products and rapid infusion system should be immediately available. Need for blood transfusion or vitamin K should be considered. Adequate monitoring for major

laparotomy with possible massive bleeding should be there[4].

Peripheral lines with large bore cannula and central line should be available for CVP measurement and to replace blood rapidly. Clamping of the liver vessels reduces the venous return to the heart and thus decreases CVP. A low CVP between 2 to 5 cm of H_2o while aiming for euvolemia forms the cornerstone of strategies to minimize bleeding which can be achieved by limitations of IV fluids and ensuring diuresis and with the use of vasoactive agents like NTG[5,6,7].

Intraoperative coagulopathy should be monitored and appropriately corrected[7]. Temperature control is critical. Monitoring of intra and postoperative urine output is also very important. In the postoperative period also the patient should be carefully monitored[4,8].

Paediatric patients are known to go into hypoglycemia during hepatic vascular occlusion and after specimen resection[7]. So higher concentration of dextrose in drip should be started and blood glucose should be closely monitored. We also infused 25% dextrose with ringer lactate. Blood volume replacement must be handled with extreme care. Aprotonin and trenexamic acid have been shown to reduce blood requirement in liver resection[6,9]. We infused 400ml packed cells and 200ml FFP and gave Trenexamic acid for prophylaxis.

During surgical procedure on the liver, temporary occlusion of IVC results in marked reduction in cardiac output together with raised SVR and decreased venous volume[4,7], which may lead to hypertension, arrhythmia, cardiac failure and arrest signifying the need to return the liver to its normal anatomical position until the patient is stabilized. We also faced frequent episodes of hypotension due to IVC occlusion and blood loss and was treated by repositioning of liver and blood replacement.

After major liver resection hypoglycemia and hypoalbuminemia are potential problems unless infusion of 10% dextrose and additional albumin is provided[8,10].

Analgesia with caudal or epidural anaesthesia is highly effective and opioids with or without local anaesthesia is indicated keeping in mind preexisting coagulopathy or massive blood loss. Paracetamol is safe in most extensive liver resection. $NSAID_s$ should be used with caution[7,8].

CONCLUSION

Emergency resection of ruptured liver tumours is associated with high mortality because of massive blood loss and shock. An adequate preoperative preparation, selecting appropriate anaesthetics, careful postoperative monitoring and through knowledge of surgical technique goes a long way in successful management of such patients.

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DEXMEDETOMIDINE: "CURRENT PERSPECTIVES"

Sonica Dogra[1]

INTRODUCTION

Effective use of sedative-hypnotic and analgesic agents is an integral part of providing patient comfort and safety. Choosing the appropriate agent is crucial in order to alleviate noxious stimuli, stress and anxiety, while minimizing the risk of adverse events.

Dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with sympatholytic, sedative, amnestic and analgesic properties.[1,2] It is the most recently developed agent in pharmacological class. It provides a unique "conscious sedation" (patients appear to asleep, but are readily roused), analgesia, without respiratory depression. It also has cardioprotection, neuroprotection and renoprotection effects. There is increased evidence of its organ protective effects against hypoxic and ischemic injury. [3]

This article brings the cardioprotective review of current clinical uses, pharmacology, pharmacokinetics, mechanism of action and side effects of dexmedetomidine.

HISTORY

The first α-2 adrenoceptor agonist was Clonidine and it was synthesized in the early 1960s to be used as nasal decongestant. This new drug showed unexpected side effects, with sedation for 24 hours and symptoms of severe cardiovascular depression. Later on, it was used as an antihypertensive drug in 1966. Over the years, Clonidine gained popularity as a powerful therapy not only for high blood pressure but also for the management of alcohol and drug withdrawl, for adjunctive medication in myocardial ischemia and for pain and intrathecal anesthesia.[4]

At the end of 1999, Dexmedetomidine was approved by FDA in the US for use in humans as a short-term medication (< 24 hours) for analgesia and sedation in the Intensive care unit. Its unique properties make it suitable for sedation, analgesia during the whole perioperative period and also in diagnostic and procedure units. They decrease sympathetic tone, with attenuation of neuroendocrine and hemodynamic responses to anesthesia and surgery, reduce anesthetic and opoid requirements. α-1 to α-2 ratio of 1:1600 makes it a highly selective α-2 agonist compared to clonidine, thus decreasing the unwanted side effects involving α-1 receptors. It is also used as a supplement to anesthesia in patients undergoing cardiac procedures and also for withdrawl / detoxification amelioration in adult and pediatric patients.[5,6]

MECHANISM OF ACTION

Dexmedetomidine, an Imidazole compound, is the pharmacologically active dextroisomer of medetomidine that displays specific and selective α-2 adrenoceptor agonism.

The hypnotic and supraspinal analgesic effects of dexmedetomidine are mediated by the hyperpolarization of noradrenergic neurons,

which suppresses neuronal firing in the locus ceruleus along with inhibition of norepinephrine release and activity in the descending medullospinal noradrenergic pathway, secondary to activation of central α-2 adrenergic receptors.[1,7,8] This suppression of inhibitory control triggers neurotransmitters that decrease histamine secretion producing hypnosis similar to normal sleep, without ventilator depression, making dexmedetomidine a good sedative.[9,1,10] Suppression of activity in the descending noradrenergic pathway, which modulates nociceptive neurotransmission, terminates propagation of pain signals leading to analgesia.[8] In the spinal cord, activation of both α2-C and α2-Adrenergic receptors (AR), situated in the neurons of superficial dorsal horn especially lamina II [7,11,12] directly reduces pain transmission by decreasing the release of pro-nociceptive transmitter,substance P and glutamate from primary afferent terminals and by hyperpolarizing spinal interneurons via G-protein mediated activation of K+ channels[7]. Post synaptic activation of central α-2 AR results in sympatholytic effect leading to hypotension and bradycardia, this effect is used to attenuate the stress response of surgery.[13,14]

Other effects of activation of α-2 AR include decreased salivation, increased glomerular filteration, decreased intraocular pressure, decreased shivering threshold [15].

PHARMACOLOGY

Dexmedetomidine is chemically described as (+)-4-(S)-[1-(2,3-dimethylphenyl)ethyl]-1 H-imidazole monohydrochloride. It has a molecular weight of 236.7. It has a pH in the range of 4.5-7. It is water soluble, has a pKa of 7.1. Its partition coefficient in octanol:water at pH 7.4 is 2.89.[16]

Dexmedetomidine is the pharmacologically active dextroenantiomer of medetomidine, a substance that has been used for sedation and analgesia in veterinary medicine for many years.[17]

It is chemically related to clonidine, but is approximately eight times more specific for α-2 adrenoceptors with α-2:α-1 selectivity ratio of 1620:1, compared with 200:1 for clonidine, especially for 2a subtype, which makes it more effective for sedation and analgesia as compared to clonidine 16. Its effects are reversed by selective α-2 antagonist, such as atipamezole.[18]

PHARMACOKINETICS

Dexmedetomidine exhibits linear pharmacokinetics in the dosage range of 0.2 to 0.7 mcg/kg/hr when administred by intravenous infusion for upto 24 hrs. It has onset of action after 15 mins. Peak concentrations are achieved with 1 hr after continuous intravenous infusion. It is also absorbed systemically through transdermal, oral or intramuscular routes.

Dexmedetomidine undergoes almost complete biotransformation with very little unchanged dexmedetomidine excreted in urine and feces. Biotransformation involves both direct glucuronidation as well as cytochrome P450 mediated metabolism. There are no known active or toxic metabolites. However, hepatic clearance may be decreased by as much as 50% of normal with severe liver disease. No differences have been seen between healthy patients and those with renal impairment. The metabolites are eliminated in urine (about 95%) and in feces (about 4%). The elimination half-life is approximately 2 hrs. As majority of metabolites are excreted in urine, there is theoretical risk that accumulation may result with prolonged administration.[19]

Dexmedetomidine has a rapid distribution phase. Its steady state volume of distribution is 118 L and distribution half-life is 6 mins with elimination half-life is between 2.0 to 2.5 hrs [20] and a clearance of 39 lt/hr.

Protein binding to serum albumin and α1-glycoprotein is approximately 94% and it remains constant despite varied concentrations of the drug. The bound fraction is decreased signifacntly in patients with hepatic dysfunction, which requires dose reduction in these patients.
There have been no significant age or sex based differences in pharmacokinetic profile.

PHARMACODYNAMICS
Dexmedetomidine is a non-selective α-2 agonist. Alpha 2 adrenoceptors are membrane stabilizing G proteins. Intracellular pathways include inhibition of adenylate cyclase and modulation of ion channels. Three subtypes of α-2 adrenoceptors have been described in humans: α-2A, α-2B, α-2C. The α-2A are distributed in the periphery whereas α-2B and α-2c are in brain and spinal cord. Postsynaptic located α-2 adrenoceptors in peripheral blood vessels produce vasoconstriction where as presynaptic α-2 adrenoceptors inhibit the release of norepinehrine, attenuating the vasoconstriction. The stimulation of α-2 adrenoceptors located in CNS and spinal cord produces sympatolysis, sedation and antinociception effects.

HEMODYNAMIC EFFECTS
The basic effects are decreased heart rate (HR), decreased systemic vascular resistance (SVR) and indirectly decreased myocardial contractility, CO and systemic BP.

A biphasic, dose dependent response has been shown after administration of dexmedetomidine. An acute intravascular injection of 1ug/kg resulted in an initial increase in BP (22%) and decrease in HR (27%) from baseline that occurred at 5 mins and lasts for 10 mins after injection. The initial increase in BP is due to vasoconstrictive effects of dexmedetomidine when stimulating peripheral α-2 receptors. HR returned to baseline by 15 mins and BP gradually decrease to approximately 15% below baseline by 1 hr **21**. The decrease in BP is mainly due to the inhibition of central sympathetic outflow. Another reason for decrease in HR and BP is stimulation of presynaptic α-2 receptors, thereby decreasing norepinephrine release. The baroreceptor reflex is well preserved in patients receiving dexmedetomidine and the reflex HR response to a pressor stimulation is augmented. [22]

The rise in BP can be attenuated by the slow infusion and by avoiding bolus administration of drug. [23] This also prevents reflex bradycardia. [24]

CNS EFFECTS
Dexmedetomidine produces sedation, hypnosis, anxiolysis, amnesia and analgesia.

The sedative-hypnotic effect is produced by an action on α-2 receptors in the locus caeruleus and an analgesic action at α-2 receptors within the locus caeruleus and within the spinal cord. [25]

Patients receiving dexmedetomidine infusions as part of their sedation regimen in postoperative ICU have been described as being very easy to wake up and have the ability to follow commands while being tracheally intubated. Undisturbed patients were noted to fall asleep right away.[26] It can produce prolonged sedation with increasing doses (10 times than normal), thus can be used as a total IV. [27]

Dexmedetomidine has some similarity with natural sleep. It has been shown to induce non-rapid eye movement sleeping pattern (NREM). The stimulation of locus caeruleus releases the inhibition the locus caeruleus has over the ventrolateral preoptic nucleus (VLPO). The VLPO subsequently releases GABA onto the tuberomaxillary nucleus thus inhibiting the release of Arousal promoting histamine on the cortex and forebrain, inducing the loss of consciousness. [28]

Amnesia with dexmedetomidine is achieved at high plasma levels (≥ 1.9 ng/ml), without retrograde amnesia. [29]

The analgesic effects of dexmedetomidine are complex. Alpha-2 agonists do have an analgesic effect when injected via the intrathecal or epidural route.[30] The primary site of analgesic action is thought to be the spinal cord. [31] Systemic use of dexmedetomidine shows narcotic sparing. In the post operative ICU setting, narcotic requirements were reduced by 50% when patients were receiving a dexmedetomidine drip compared with placebo. [32]

RESPIRATORY EFFECTS
In spite of profound sedative properties, dexmedetomidine is associated with only limited respiratory effects at clinical doses.[33] Increasing the concentrations to 15 ng/ml in spontaneously breathing volunteers, showed no change in arterial oxygenation or pH 29. PaCo2 increased by 20%, respiratory rate increased with increasing concentration from 14 breaths/min to 25 breaths/min 29. Hypercapnic arousal phenomenon is preserved and apnoea threshold is decreased. When dexmedetomidine and propofol were titrated to equal sedative end points (BIS of 85), both resulted in no change in respiratory rate 13.

In a study comparing the effects of remifentanil and dexmedetomidine on respiratory parameters[34], the hypercapnic ventilator response was unaffected even at doses that produced unresponsiveness to vigorous stimulation. PaCo2 increased mildly with dexmedetomidine but reached a plateau after the 1st increment.

METABOLIC EFFECTS
It suppresses shivering by their activity at α-2b receptors in the hypothalamic thermoregulatory center of the brain. Easley etal [35], in an prospective pediatric study, found that a single intravenous bolus of dexmedetomidine, 0.5 mcg/kg over 3-5 mins, was effective in the treatment of postaneasthesia shivering. [35,36]

ORGAN PROTECTIVE EFFECTS
MYOCARDIAL ISCHEMIA AND CARDIOPROTECTION
Alpha-2 agonists ameliorate the hemodynamic profile during the perioperative period by attenuating sympathetically mediated hyperdynamic responses. In animal models, dexmedetomidine showed some beneficial effects on the ischemic heart through decreased oxygen consumption and redistribution of coronary flow from non ischemic zones to ischemic zones after acute brief occlusion. [37]

The perioperative use of α-2 agonists reduces the incidence of perioperative myocardial ischemia. [38] At present, a reduction in myocardial ischemia and improved outcomes for patients at risk of cardiac events has only been documented for clonidine. The only available data for dexmedetomidine showed that perioperative infusion appeared to benefit the perioperative hemodynamic management of surgical patients undergoing vascular surgery. [39]

NEUROPROTECTION
It possesses neuroprotective properties. It attenuates hypoxic-ischemic brain injury in developing brains, highly susceptible to neuronal damage.[40] A significant improvement in functional neurogical outcomes after brain injury was demonstrated.[40] The exact mechanism of neuroprotection is not clear, but catecholamine pathways play an important role. α-2 adrenoceptors modulate neurotransmitter release in the central and peripheral sympathetic nervous system, thus offering a possible explanation for the neuroprotective properties of dexmedetomidine.

TOXICOLOGY AND SIDE EFFECTS
The teratogenic effects of dexmedetomine have not been studied during pregnancy only if the benefits justify the risk to fetus.The adverse effects include hypotension, hypertension,

bradycardia, nausea, AF and hypoxia.[29]

The incidence of bradycardia has been reported to be as high as 40% in healthy patients. These effects can be managed with atropine, ephedrine and volume infusion. Severe bradycardia leading to cardiac arrest has been reported with the use of dexmedetomidine. [41,42]

CLINICAL USES
ANAESTHESIA
1.PREMEDICATION
Dexmedetomidine at IV doses of 0.33 to 0.67 mcg/kg, given 15 mins before surgery, seems efficacious, while minimizing the cardiovascular side effects of hypotension and bradycardia[43]. It reduces thiopental requirements (by ±30%) for short procedures [43], reduces the requirements of volatile anesthetics (by around 25%). It efectively attenuates the hemodynamic responses to endotracheal intubation, provides analgesia, anxiolysis and sedation. [1]

Dexmedetomidine has high bioavailability when administred by the non invasive buccal or nasal route.[44] The buccal route ensures more compliance and better absorption in younger children than IV route. [1,44] Studies evaluating the efficacy, safety, optimal dosage for buccal dexmedetomidine in children have found a dose of 3-4 mcg/kg, 1 hr before the operation to be safe and effective. [45]

Various other studies[46,47] also report better sedation with 1mcg/kg intranasal dexmedetomidine when given 30-45 mins prior to surgical procedure as compared to oral midazolam. The technique causes no discomfort during administration [48], is simple and quick.

2. MAC: Dexmedetomidine is used for sedation for MAC. It has minimum alveolar concentration and has opiate sparing properties, which helps in decreasing the inhalational anesthetic and opoid requirements by upto 90%. [1,49,50] This is very helpful in situations where high anesthetic concentrations are not tolerated and undesirable.

3. Dexmedetomidine reduces rocuronium requirements during sevoflurane anesthesia, by altering the pharmacokinetic profile of rocuronium.[51] This effect **decreases muscle relaxant** requirement during surgery, thereby decreasing the risk of residual muscle weakness during emergence.

4. The **narcotic sparing** effects of dexmedetomidine were evident intraoperatively and postoperatively in morbidly obese patients. [52] It attenuates postoperative pain, decrease volatile anesthetic requirements without causing cardio-respiratory depression nad ensures faster neuromuscular recovery and smooth emergence. [53]

5. Use of dexmedetomidine for **sedation** during vascular and cardiac surgery has been reported due to its cardio-protective modulation of sympathetic tone and maintenance of myocardial oxygen supply/demand ratio with less perioperative ischemia. [1,54]

6. Dexmedetomidine has a important role in facilitating **Awake fiber-optic intubation** (AFOI) in difficult airway situations. [55, 56] AFOI in patients with difficult airway requires maintenance of clear dry airway, with spontaneous ventilation to avoid complications of respiratory depression, upperairway obstruction and pulmonary aspiration. Dexmedetomidine provides an ideal solution to this problem especially in critical airways compromised due to anatomical distortions and infections. [57]

7. Dexmedetomidine has a role in **neurosurgery** also. Many neurosurgical procedures require a hemodynamically stable, comfortable, sedated patient who is awake and cooperative enough to perform neuromotor and neurocognitive tests on

dexmedetomidine. In a dose of 0.2 to 0.5 mcg/kg/hr provides desirable neurophysiologic profile in procedures like craniotomies, deep brain stimulation etc. [1,58-61]

7. ICU: The importance of patient orientation and rousability is well established in ICU care.[61] Dexmedetomidine is well suited for use in intensive care , allowing sedated patients to be quickly aroused and oriented upon demand.[62] Dexmedetomidine is approved by FDA for sedation in initially intubated patients for a period of 24 hrs. This time limitation is probably due to lack of data regarding adverse events for its use for more than 24 hrs. Various studies are now focusing on the safety and efficacy of dexmedetomidine beyond 24 hrs. [1,63,64] In a phase IV study, dexmedetomidine was safe in dosages upto 1.4 mcg/kg/hr for greater than 24 hrs and did not produce rebound tachycardia and hypertension when abruptly discontinued. [64,65] Dexmedetomidine has demonstrated advantages over propofol for sedation in mechanically ventilated postoperative patients. When both drugs were titrated to equal sedation, as assessed by BIS (appx.50) and Ramsey sedation score (5), dexmedetomidine patients require significantly less Alfentanil (2.5 vs 0.8 mg/hr). HR was slower in dexmedetomidine group, whereas MAP was similar. The time to extubation after discontinuation of the infusion was similar in both the groups. Patient receiving dexmedetomidine have greater recall of their stay in ICU, but all described this as pleasant overall. [66] Several other studies have confirmed the decreased requirements for opoids(>50%), when dexmedetomidine is used for sedation compared with propofol or BZD. Most studies also describe more stable hemodynamics during weaning.[67] This is very beneficial in patients with high risk of myocardial ischemia. For sedation in ICU, loading dose of 0.5 to 1 mcg/kg have been used. Omitting the bolus or giving the lower dose has been associated with fewer episodes of severe bradycardia and other hemodynamic perturbations. Infusion rates of 0 to 1 mcg/kg/hr are needed to maintain adequate sedation.

In a double-blind, randomized controlled trial of sedation in ventilated patients with dexmedetomidine versus lorazepam (MENDS), it was found that dexmedetomidine infusions provided more days alive without delirium or coma and a greater amount of time spent at the appropriate sedation level compared with lorazepam.[68] This study also reported an earlier return to a delirium free cognitive state and more ventilator free days with dexmedetomidine when used for more 24 to 120 hrs.

Another important advantage of dexmedetomidine is that it provides adequate sedation with minimal respiratory depression, can be used when weaning patients from ventilator. [69]
In the pediatric population, several studies (prospective and retrospective) have evaluated its usefulness in ICU. [70] Tobias etal [71], in a prospective randomized trial, found that dexmedetomidine at a dose of 0.5 mcg/kg/hr provided more effective sedation than midazolam at 0.22 mg/kg/hr . Another retrospective study [72] of 38 spontaneosly breathing and mechanically ventilated children undergoing cardiothoracic surgery, found that dexmedetomidine provide adequate sedation 93% and adequate analgesia 83%. Side effects included hypotension (15%) and transient bradycardia in one patient.

8. PROCEDURAL SEDATION : Dexmedetomidine has a role in procedural sedation due to its faster onset of action, faster recovery and discharge times. It is safe alternative to BZP/opoid combinations in patients undergoing MAC for multitude of procedures because of its analgesic, 'cooperative sedation' and lack of respiratory depression properties. [73-78] Its use has been reported in a 24 week gestation neonate treated for refractory agitation while on

mechanical ventilation.[79,80]

9.TREATMENT OF WITHDRAWL: Dexmedetomidine has been successfully used in the treatment of withdrawl of narcotics, BZD, alcohol and recreational drugs.[81]

10. FOR ACUTE AND CHRONIC PAIN: The α-2 AR selectivity of dexmedetomidine makes it useful in the treatment of pain.[82] Its opiate sparing properties are beneficial in the management of acute postoperative pain and chronic pain states, including disorders like spasticity/myofacial pain, neuropathic pain, sympathetically maintainted pain (CRPS) and chronic daily headaches. It is evolving as an adjuvant analgesic, both as IV and intrathecal infusion, in cancer pain refractory to multitude treatment modalities.[83,84]

11. REGIONAL ANESTHESIA: Dexmedetomidine when used intravenously prolongs the duration of sensory block of LA during spinal anesthesia [85], and peripheral nerve block.[86]

Due to its effects on spinal α-2 receptors, dexmedetomidine mediates its analgesic effects. It has been found to prolong analgesia when used as an adjuvant to LA for SAB, epidural and caudal epidural blocks. There is no proper consensus regarding the dose of drug to be used for neuraxial blocks. Doses varying from 3 to 15 mcg have been used as adjuvant for spinal anesthesia. There has been dose dependent prolongation of analgesia. However the incidence of side effects due to dexmedetomidine is difficult to assess as different doses of bupivacine were used in different studies.[87,88]

12. OBSTETRICS : Its role in obstretric analgesia is being explored in view of high lipophilicity. It is retained in placental tissue, resulting in less fetal transfer and decreased incidence of fetal bradycardia. Continuous IV dexmedetomidine infusion has been successfully used as an adjuvant to systemic opoids in laboring parturients who could not benefit from epidural analgesia.[89,90]

Dexmedetomidine also improve block quality, prolong post-deflation analgesia and decrease tourniquet pain when used as an additive to lignocaine in IVRA.[91]

CONCLUSION

Dexmedetomidine is a potent, highly selective α-2 adrenoceptor agonist, with sedative, analgesic, anxiolytic, sympatholytic and opoid-sparing properties. It provides a unique type od sedation,"conscious sedation". It has a quick onset and short duration of action, that makes it suitable for a critical care unit, for post operative cardiac and non cardiac patients and for selective invasive and non-invasive procedures. Hypotension and bradycardia are the most significant side effects. It appears to have minimal respiratory depression. It can be used safely in both mechanically ventilated and spontaneously breathing patients. These properties make dexmedetomidine a useful agent in the current era of early extubation and fast track of postoperative cardiac patients. It does not decrease gut motility, prevents post operative nausea, vomiting, shivering and at the same time, offers benefit towards neuroprotection, cardioprotection and renoprotection.

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