Comparative Evaluation of Efficacy, Hemodynamic Stability and Recovery during Conscious Sedation with Dexmedetomidine or Propofol in Cardiac Catheterization Laboratory

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Abstract
Background:*Conscious sedation provides calm and cooperative patient for interventional procedures. We compared dexmedetomidineand propofolin combination with fentanylfor conscious sedation during cardiac catheterization of adult patients.*
Methods:*Sixty patients of aged 30-60 years, American society of anaesthesiologist Grade II or III scheduled for cardiac catheterization were randomly divided in two groups of 30 each.*
Group D receiveddexmeditomidine1µg/kg i.v. over 10 mins followed by infusion dose of 0.5µg/kg/hr. Group Preceived propofol 100µg/kg i.v over 1 min followed by infusion dose of 50µg/kg/min. Fentanyl 1µg/kg was given toall patients.Ramsay's sedation score(RSS),intra-operative hemodynamic parameter, modified Aldrete score(MAS), recovery time, patient and cardiologist satisfaction scores andside effects were recorded. The data was analyzed using Microsoft excel 2010 and SPSS v.16 software. Statistical significance was considered at p value <0.05.
Results:*The mean RSS score at 8 min in group D was significantly lower in comparison to group P(3.03±0.49 v/s 3.66±0.47min) (p=0.000).In group D there was significant decrease in heart rate during procedure compared to group P (p<0.05).The fall in mean blood pressurewas significantly more in group P (16.23% vs 3.2%). The oxygen saturation values during sedation were significantly lower in group P(94%) compared to group D(96%) (p<0.05). Thetimeto achieve MAS >8 was less in group Dcompared to group P(5.63±1.40 v/s 13.93±3.11 min., p=0.001).Patient and cardiologist satisfaction scores were more with dexmedetomidine.*
Conclusion: Dexmedetomidine in combination with fentanyl is effective and safe to provide conscious sedation for cardiac catheterization laboratory procedures in adults.
Keywords:*dexmeditomidine, propofol, catheterization laboratory, conscious sedation.*

I. Introduction

The cardiac catheterization laboratory procedures have increased exponentially over the last decade. In adults, the cardiac catheterizations are often performed in awake patient under local anaesthesia. However, now adaysthere is an increasing demand for sedation during diagnostic or interventional cardiac catheterization. Conscious sedation enhances patient comfort and cooperation and facilitates the performance of the procedure.1 Increasing depth ofsedation results in complications such as hypotension and respiratory depression.2,3 Therefore, it is important to selectdrugs that provide adequate anxiolysis,amnesia, analgesia, sedation and immobilityas well as ensure cardiovascular and respiratory stability.

Various anaestheticdrugs such as midazolam, ketamine, propofol, fentanyl,dexmedetomidine, or their combinations have been used for cardiac catheterization with variable degrees of success.4-6Propofol is most frequently and widely used for conscious sedationdue to its pharmacokinetic and pharmacodynamics properties, i.e. fast onset, easy to titrate and rapid wake-up time.7 However, propofol has narrow margin of safety and often causes deep sedationresulting in complications such as hypotension and respiratory depression, especially in patients with advanced age, ASA class>II and prior hypotension.2,7

Dexmedetomidine is a highly selective alpha 2-adrenergic receptor agonist having sedative, hypnotic, anxiolytic and analgesic properties with little effect on ventilation.8Moreover,dexmedetomidine also have

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sympatholytic effect that attenuates stress responses to surgery and provides better hemodynamic stability and protection against myocardial ischemia.[9]These pharmacologic properties combined with a good safety margin, has made dexmedetomidine an attractive choice for anesthesiologists and intensivists for conscious sedation. However, the sympatholytic effects of dexmedetomidine may also cause adverse clinical effects such as hypotension and bradycardia.[10]

Several studies have been conducted for anaesthesia and sedation techniques during cardiac catheterization for paediatric patients but studies in adult patients are very few. Propofol is frequently used for sedation during cardiac catheterization but limited data is available regarding use of dexmedetomidine in cardiac catheterization. This prospective randomized control studywas designed to compare the efficacy, hemodynamic stability and recoverycharacteristics of intravenous (IV) dexmedetomidineandpropofolin combination withfentanyl for conscious sedation during cardiac catheterization in adult patients.

II.   Material & Methods

After institutional ethics committee approval and written informed consent, 60 adult patients of age 30 to 60 years, of either sex, ASA class II or III, who were scheduled for diagnostic cardiac catheterization were included in this prospective, randomized pilot study. Patients with age >60 years, ASA Grade IV, ejection fraction <40% on echocardiography,hemodynamic unstable, baseline oxygen saturation (SpO2) <90%, and known allergy to study drugs were excluded from the study.Using computer generated random number table, patients were randomly allocated to either dexmedetomidine group (Group D, n=30) or Propofol group (Group P, n=30). Allocation concealment was done using sequentially numbered coded sealed envelopes.

All patients were evaluatedone day prior to procedure and were kept fasting for 6 hoursbefore the procedure. On arrival of patient in the cardiac catheterization laboratory,i.v access was secured and i.v fluid started.Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), respiratory rate (RR) and arterial oxygen saturation (SpO2) were recorded.   All patients were premedicated with fentanyl $1\mu g.kg^{-1}$i.v.slowly.Group D patients received dexmedetomidine $1\mu g.kg^{-1}$i.v. over 10 min as a loading dose followed by 0.5 $\mu g.kg^{-1}$ as maintenance infusion.Group P patients receivedPpropofol 100 $\mu g.kg^{-1}$i.v over 1min as a loading followed by 50 $\mu g.kg^{-1}$min-1as maintenance infusion.

After achievingRSS ≥ 3[11],local infiltration with 1% lignocaine was done by cardiologist over femoral vessels to allow cannulation before catheterization procedure. The hemodynamic parameters and RSS were recorded at 0 min(when RSS of ≥ 3), and thereafter at 2min, 5min, 8min, 12min and15min during procedure and continued every 5 min in the recovery period. Intraoperatively when sedation became inadequate (RSS score 1-2),propofol was given as a rescue sedative drug in bolus of 150 $\mu g.kg^{-1}$i.v.aliquots in either of the groups till RSS ≥ 3 achieved.Drug infusion wascontinued till groin bandage had been applied.If any of the following adverse eventswere observed: apnea lasting longer than 30 seconds, decrease of SpO2< 90%, decrease of HR < 50 bpm, MAP<30% of baselinebelow, and sedation that made verbal contact with the patient impossible,drug infusion was discontinued. Bradycardia (HR< 50 bpm), was managed with i.v atropine 0.6 mg and hypotension(MAP<30% of baseline below) was treated with i.v ephedrine 6 mg.RR and SpO2were monitored to assess respiratory depression, which was defined RR≤ 8 breathsper minute or SpO2<90% on room air. SpO2< 90%for more than 1 minute was managed by oxygen supplementation by ventimask. If apnea lasted for >15 second then breathing was assisted manually with Bains circuit.

After completion of the procedure, all patients were initially shifted to catheterization laboratory recovery room and then to high dependency unit (HDU) when MAS>8.[12] The total duration of the procedure, number of patients in which rescue propofol required during the procedure and any adverse effects like nausea/vomiting, bradycardia, hypotension, hypoxia and dry mouth were recorded. At end of procedure patient and cardiologist satisfactions were also assessed using thesatisfaction score (4 = excellent, 3 = good, 2 = fair and 1 = poor).

Statistical analysis:The data were analyzed using Microsoft excel 2010 and SPSS v.16 software. To draw statistical inferences, 'independent sample t test' and 'Chi square test' was applied to compare the ASA score between both the groups. Statistical significance was considered at p value <0.05.A sample size of 30 patients per group was needed to detect intergroup difference of at least 10% in blood pressure and heart rate with a power of 0.80 and α of 0.05.

III.   Results

The study groups were comparable in regard to demographic data, ASA class, baseline vitals and mean duration of procedure.(Table1) In group D, the time to achieve RSS ≥ 3 from start of study drug was (11.46±2.62 minutes) compared to that in Group P (11.93±3.02 minutes). During the procedure at 8 min,patients had significant increase in mean RSS score(3.66±0.47) in group P compared to group D(3.03±0.49)(p<0.05). Number of patients required rescue propofol supplementation were more in group P (11patients) compared to group D (4 patients). (Table 2)

In group D there was significant decrease in HR during procedure compared to group P (p<0.05). The mean HR was 21.63% lower than baseline in group D and was 6.7% increased than baseline in group P(Figure 1a). In group D, four patients had significant bradycardia and were treated with atropine but in group P bradycardia was not seen in any patient.During procedure, fall in MBP from baseline was significantly more in group P(16.23%) compared to group D(3.20%)(Figure 1b). In group P, four patients had significant hypotension and required treatment with ephedrine.The oxygen saturation(Spo2)values during sedation were significantly lowerin groupP(94%) compared to group D(96%)but treatment in form of oxygen supplementation was not required in any patient(Figure 1c).The respiratory rate was comparable in both the groups(Figure 1d).

The time to achieve MAS >8 (recovery time) was significantly lower in group D(5.63±1.40 min) compared to that ingroup P (13.93±3.11 min) (p=0.000).Incidence of adverse events were comparable in both the groups. In group D one patient and in group Ptwo patients experienced nausea/vomiting. Dryness of mouth was found in two patients in group D.Both the patient and cardiologist satisfaction scores were higher in Group D compared to Group P. In Group D median value of patient and cardiologist satisfaction score was 3 and 3 whereas it was 2 and 2 in Group P respectively.

IV.   Discussion

Thisprospective, randomized pilot study was conducted with the aim to compare the efficacy, hemodynamic stability and recovery of i.v.dexmedetomidine and propofol in combination with fentanyl for conscious sedation during cardiac catheterization procedures in adults. The results of the present study showed that compared to propofol, dexmedetomidineprovided more rapidrecovery, better preserved MAP and did not cause any desaturations but was associated with bradycardia. Satisfaction scores of patients as well as cardiologist were more with dexmedetomidine compared to propofol.

Propofol is widely used for cardiac catheterization inpaediatric population and in adults for conscious sedation at remote locations, because of the rapid emergence it produces.[7]However, propofol is also associated with complications such as hypotension, myocardial and respiratory depression, especially in patients with advanced age and in high risk patients(ASA III/IV).[2,7] In contrast to the previous studies where a dose range of 500 to 1000 μg kg^{-1}of propofol had been used,[13-16]we used lower dose of 100 μg.kg^{-1}i.v over 1min as a loading followed by 50 μg.kg^{-1}min^{-1} as maintenance infusion, because the therapeutic window of propofol is very narrow, which makes it easy to move from a moderate level of sedation to deep sedation[17] resulting in cardiac and respiratory depression. Dexmedetomidine, the highly selective alpha-2-adrenoceptors agonist,is a new drug with, sedative, amnestic, anxiolytic, analgesic and sympatholytic properties.[8]It provides conscious sedationand analgesia without respiratory depression.Doses of dexmedetomidine used in our study were in similar range of those used in previous studies for consious sedation.[18-20]

In present study, the depth of sedation was determined according to the RSS and results showed that dexmedetomidine provided better sedation than propofol. Target RSS of ≥3 was achieved at almost similar time with dexmedetomine (11.46±2.62 minutes) andpropofol (11.93±3.02 minutes) after start of study drug. Yavuzdemiraranet al[21] found onset time of sedation with dexmedetomidine as 10 min which was comparable with our study having onset time of 11.46 min showing that induction time in dexmedetomidine sedation are suitable for short surgical procedures. More number of patients requiredrescue propofol supplementation in propofol group compared to dexmedetomidine. Wu Y et al[14] used higher dose of profofol(0.6 mg/kg bolus dose and additional 10-20 mg doses until the OAA/S scores reached 2–4) and found deeper level of sedation with propofolcompared to dexmedetomidine(loading dose of 1μg/kg over 10 min followed by a 0.5 μg/kg/h infusion)

In the present study, HR decreased but comparatively stable MBPand SPO2values were observed with use of dexmedetomidine. In dexmedetomidine group, HR was significantly lower than the baseline values during procedure at all timeintervals. With dexmedetomidine, bradycardia(HR<50bpm) occurred in four patients, which was transient and HR recovered after giving atropine.Our results were similar with other studies in terms ofhemodynamic effects in patients sedated with dexmedetomidine,whichshowsthat HR is significantly lower in dexmedetomidinetreated patients.[22,23] Bradycardia is a major side effect of dexmedetomidine (α2-agonist) that is mediated by the activation of α2-adrenoceptors in the ventrolateral medulla and solitarius nucleus tract.[24]

In our study, MBPand SPO2 was more stable in the dexmedetomidine group compared to propofol showing that dexmedetomidine has clinical advantages in controlling hemodynamic variabilityand respiration.Inpropofol group, there was a higher incidence of decrease in MBP, and SpO2 compared to baseline during sedation. However, these episodes were clinically insignificant and required no therapeutic interventions. The possibility for decreases in SpO2 was due to hypotension and additive effect of fentanyl.Our results were similar to study byTosun z et al,[15]Taniyama et al[25]and Ali NP et al[26]in which statistically significant lower HR was found in the dexmedetomidine group and lower MBP and SpO2 was seen in the propofol group.

Recovery time, as assessed by modified AldreteScorewas significantly longer in propofolgroup(13.93±3.11 minutes) compared to dexmedetomidine group (5.63±1.40 minutes). The results were in contrast to other studies byWu Y et al,14Tosun z et al,15 and Ali NP et al,26where recovery was delayed in dexmedetomidine group compared to propofol group. This discrepancymay result from the more adverse events like dizziness, nausea andvomiting seen in their study with use of dexmedetomidine resulting in delayed recovery and hospital discharge. In our study minimum adverse events like nausea,vomiting and dry mouth were seen with use of both dexmedetomidine and propofol.Similarly, Abdellatif et al27 and Arain and Ebert28 found no intra-operative or postoperative adverse effects in the dexmedetomidine group

In present study, higher satisfaction scores both for patients and cardiologist was seen in dexmedetomidine as compared to propofol. Better patient and cardiologist satisfaction may be related to early recovery and minimum adverse effects seen with dexmedetomidine. Moreover dexmedetomidine also have analgesic properties resulting in better pain relief in patients as indicated by less requirement of rescue sedative (propofol) during procedure. Our results were in agreement to that ofArain and Ebert28, Takimoto et al29where patients were more satisfied with dexmedetomine than propofol for sedation.

There are certain limitations in our study.The main limitation is that it is prospective randomizedpilot study so there is always risk of bias toward intervention group. In present study, the depth of sedation was determined according to the Ramsey sedation score. Intraoperative bispectral index (BIS) monitoring would have been definitely a more objective method in deciding the depth of sedation and the requirement of rescue propofol.

In conclusion, this study demonstrates that dexmedetomidine is a safe drug with good hemodynamic and recovery profile. Dexmedetomidine better preserved MBP and SpO2. Moreover, degree of satisfaction experienced by patients and cardiologist was better with dexmedetomidineTherefore, dexmedetomidine in combination with fentanyl is useful to provide conscious sedation for cardiac catheterization laboratory procedures in adults and it may be a valuable alternative to propofol.

Legends
Figure 1: Graphical representation of (a) HR, (b) MBP, (c) SpO2 & (d) RR.
Table 1: Demographic characteristics and pre-operative data
Table2: Other study variables

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Table 1: Demographic characteristics and pre-operative data

Variables	Group D	Group P	P value
Age(yrs) Mean±SD	51.63±3.76	51.50±4.90	0.906
Weight(Kg) Mean±SD	64.40±2.73	62.80±5.01	0.130
ASA II/III	26/4	26/4	1.00
HR	80.90±5.66	78.40±5.68	0.093
MEAN BP	99.26±5.21	98.63±6.40	0.67
SPO2	99.36±0.88	99.20±0.20	0.480
RR	14.66±0.62	14.33±1.53	0.421

Table2- Other study variables

Variables	Group D	Group P	P value
Duration of procedure(min)	10.63±1.93	11.30±1.60	0.152
Time to achieve ≥3 RSS(min)	11.46±2.62	11.93±3.02	0.412
Mean RSS at 8min	3.03±0.49	3.66±0.47	< 0.001
Time to achieve MAS >8(min.)	5.63±1.40	13.93±3.11	< 0.001

Table 3- Median Satisfaction score

Variables	Group D	Group P
Patient satisfaction score(Median)	3	2
Cardiologist satisfaction score(Median)	3	2