Comparison of Ketamine-Dexmedetomidine Combination with Fentanyl-Dexmedetomidine Combination for Procedural Sedoanalgesia during CT-Guided Interventional Radiology Procedures: A Randomized Controlled Study

Shagun Bhatia Shah[1]*, Akhilesh Pahade[2], Namrata Gupta[1], Deepti Gupta[1], Rajiv Chawla[1], Ajay Kumar Bhargava[1]

[1]Department of Anaesthesia and Critical Care, Rajiv Gandhi Cancer Institute and Research Centre, Delhi, India.

[2]Department of Anaesthesia, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, India.

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ABSTRACT

Background: The quest for an ideal sedoanalgesic-combination exhibiting the triad of efficacy, safety and patient comfort has led to administration of several permutations and combinations of drugs (midazolam, fentanyl, remifentanil, dexmedetomidine, propofol, ketamine, pethidine, pentazocine). The ideal sedoanalgesic for CT-guided core-biopsy of spine, radiofrequency/microwave ablation of hepatic/pulmonary lesions, has hitherto been elusive. In the absence of any guidelines, we compared a ketamine-dexmedetomidine combination (Group-K) with fentanyl-dexmedetomidine (Group-F).

Methods: This prospective, interventional, single-centric, parallel-armed, randomized controlled study included 60 patients (ASA physical state I-II, either gender, aged 18-75y, weighing 35-85kg), undergoing CT-guided core biopsy/radiofrequency/microwave ablation in remote location, allocated to Group-K and Group-F. Independent/paired-sample t-tests were utilized and data expressed as box-whisker plots and trendlines, p-value<0.05 being statistically significant.

Results: There was a significant difference in intraprocedural pain-scores between both groups (p-values 0.0001, 0.0011, 0.0092 and 0.0201 at 0-10mins, 10-20mins, 20-30mins and 30-40mins respectively). More patients in Group-F required rescue-analgesic with reduced interventionist-satisfaction score versus Group-K. In Group-K, mean arterial pressure and heart rate (95.1mmHg;79.6/min) increased after initial ketamine bolus, but were maintained/decreased at intervention-initiation (93.2mmHg;79.4/min) and at 10min and 30min thereafter. In Group-F, MAP and HR decreased after initial fentanyl bolus (83.5mHg;71.9/min), increased with intervention-initiation (90.1mmHg;77/min), progressively decreasing at every time-point thereafter. VAS-scores (resting; on coughing) were lower in Group-K.

Conclusion: A ketamine-dexmedetomidine combination technique demonstrated a superior sedoanalgesic effect with reduced intra-procedural bradypnea, bradycardia, rescue-drug requirement and post-procedural complications with enhanced interventionist-satisfaction and may emerge as the ideal procedural sedoanalgesic for patients undergoing CT-guided core-biopsy, radiofrequency/microwave ablation.

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*Corresponding author.
E-mail address: drshagun_2010@rediffmail.com

Introduction

Non-operating room/office-based anaesthesia requires effective sedative-analgesics with early onset and offset without compromising patient safety. CT-guided core-biopsy and radiofrequency/microwave ablation (RFA/MWA) are interventional radiology procedures frequently undertaken in the CT-scan suite. Prescribed as an alternative therapeutic modality for hepatic/lung cancer patients, RFA involves tissue destruction by high-frequency alternating current, heating tissues beyond 60°C, producing peri-electrode umbral necrosis. RFA efficacy equals surgical resection for solitary malignant lesions measuring ≤ 2cm [1]. Although microwave heats faster than RFA, is better for lesions close to veins, creates a bigger cloud and is better suited for lesions >2.5cm, analgesic requirements for MWA are identical to RFA. These procedures involve synchronized services of an orthopaedician, radiologist and anaesthesiologist who constantly shuttle in and out of the CT-chamber.

While sedation alone suffices during radio-imaging, bone-biopsy coring needle introduction and radio-ablation (thermal tissue necrosis) demand analgesia. Hence, a background sedative-analgesic infusion, superimposed with intermittent analgesic boluses is the preferred technique. There is no consensus/guideline available specifying the ideal combination of sedative-analgesics for these procedures. Dexmedetomidine, a highly selective α2-agonist, is gaining popularity as a sedative-analgesic for procedural sedation. However, short bursts of excruciating pain during CT-guided core bone-biopsy and RFA/MWA mandate profound analgesia where dexmedetomidine monotherapy fails to suffice. Midazolam, propofol, fentanyl, ketamine, pethidine and pentazocine have been used in various permutation-combinations for interventional radiology procedures [2-3]. Fentanyl is a strong short-acting opioid while ketamine is an N-methyl-d-aspartate (NMDA) receptor antagonist with curtailed clinical use attributable to psychomimetic side-effects. Sub-dissociative/analgesic doses of ketamine (≤0.5mg/kg) produce profound analgesia comparable to morphine [4]. Ketamine and dexmedetomidine comprise a symbiotic-pair, complementing each-other and nullifying mutual side-effects. Dexmedetomidine may prevent the tachycardia, hypertension, hypersalivation, and emergence phenomena that characterize ketamine. Dexmedetomidine-associated bradycardia, hypotension, xerostomia and respiratory depression maybe prevented by ketamine [5]. An additional ketamine advantage is to hasten the onset of dexmedetomidine-sedation (slow onset-time when dexmedetomidine is the sole agent). Opioid-free analgesia is coveted as it circumvents the nausea, sedation, constipation and addiction attributable

to opioids. Although ketamine, dexmedetomidine and fentanyl have been used individually, the combination has never been previously studied for procedural sedation for CT-guided core-biopsies and RFA/MWA. Hence, we aimed to compare the quality of anaesthesia provided by two drug combinations, ketamine-dexmedetomidine and fentanyl-dexmedetomidine. The primary outcome measures were the intraprocedural Colorado Behavioural Numerical Pain Scale (CBNPS) [6]. Haemodynamic parameters and respiratory rate. The secondary outcome measures were postoperative Visual Analog Scale (VAS) score, Richmond agitation sedation Score (RASS), adverse events and interventionalist-satisfaction.

Methods

This prospective interventional single-centric parallel-armed, randomised controlled study was conducted according to the Helsinki Protocol after obtaining written informed consent from all patients, approval from the institutional ethics committee and prospective registration (CTRI/2019/11/022038). Sixty ASA physical state I-II patients of either sex, aged 18-75y, weighing 40-85kg, undergoing CT-guided core-biopsy/radiofrequency/microwave ablation in remote location (CT-scan suite of a premiere tertiary care oncology setup) were included in the study. Patients with raised intracranial pressure, glaucoma, opioid dependence and bradycardia (Heart Rate < 60/min) were excluded. The patients were randomised into two groups, Group-K (Ketamine-dexmedetomidine group) and Group-F (Fentanyl-dexmedetomidine group), using computer-generated random number schedule and allocation-concealment was performed using sequentially numbered sealed opaque envelopes.

Sample size calculation

Utilizing a study by Oh et al (2019) [7] with proportion of patients with procedural sedation score 6 at 2min post drug-institution in the two study groups as 50% and 85% with alpha error fixed at 0.05% and power 80% using Medcalc (version 15; MedCalc Software Ltd; Ostend, Belgium) we arrived at a sample size of 27 patients per group. Allowing for dropouts, 30 patients were enrolled in each group.

Statistical Analysis

Continuous variables are presented as mean with standard deviation and 95% confidence intervals as per the Gaussian/non-Gaussian distribution of data in the descriptive summary. Chi-square test/Fisher Exact test was used to find association between two categorical variables portrayed as frequencies and percentages. Independent sample t-test was used for intergroup comparison and paired sample t-test was used for intragroup comparison of continuous variables and significance compared between various time-points. P-value <0.05 was considered statistically significant.

Medcalc statistical software (version 15; MedCalc Software Ltd; Ostend, Belgium) was used for data-analysis and graphical representation as line diagrams, bar charts, forest plots, dot and line box-whisker plots.

Anaesthetic Technique

PAC fitness was determined. After application of standard monitors, all patients in both groups were pre-medicated with intravenous (IV) midazolam (0.03mg/kg), IV glycopyrrolate 0.2mg and loading dose of dexmedetomidine (1µg/kg over 10min) followed by 0.5µg/kg/h maintenance dexmedetomidine infusion. In Group-K, an IV ketamine bolus (0.5mg/kg; analgesic/subanaesthetic dose) was administered 1min prior to local-anaesthetic infiltration by the interventionist. IV ketamine 0.25 mg/kg was repeated at 20min and 40min post biopsy-initiation. An additional bolus of IV ketamine 0.5mg/kg was administered whenever the CBNPS score was ≥ 3. IV morphine 1.5mg bolus was reserved as rescue drug if ketamine dose reached 1.5mg/kg. In Group-F, an IV fentanyl bolus (0.5µg/kg) was administered 1min prior to local anaesthetic infiltration by interventionist. IV fentanyl 0.25 µg/kg was repeated at 20min and 40min post biopsy-initiation. IV fentanyl bolus (0.5µg/kg) was repeated whenever the patient groaned/moved. Morphine 1.5mg bolus was administered as a rescue drug whenever total fentanyl dose reached 1.5 µg/kg. Tachycardia (20% increase in heart rate (HR) above baseline) was treated with 2.5ml (10µg) bolus of dexmedetomidine by activating the bolus-button of the infusion pump [8] while bradycardia (20% decrease in HR below baseline) was treated with 0.6mg atropine in both the groups. Similarly, rescue drug for hypertension (20% decrease in mean arterial pressure (MAP) from baseline) was 2.5ml bolus dexmedetomidine followed 2min later (if hypertension persisted) with IV diltiazem (10mg). Hypotension (20% fall in MAP) was treated with IV ephedrine (3mg).

The HR, MAP, respiratory rate (RR) and CBNPS-score were monitored, recorded and analysed at baseline, after dexmedetomidine loading dose, 1min post ketamine/fentanyl bolus, at intervention-initiation, at 10-minute intervals thereafter till the end of procedure.

CBNPS-score (0-5) was assigned: Restful patient with no facial expression (0), moaning, frowning, restless (1), facial grimacing, protective body positioning (2), resistive, crying out/vocalizing patient (3), yelling, tossing (4) and combative patient (5). Oxygen therapy involved face mask (for supine position) or nasal prongs (prone position). Oxygen saturation was monitored using a pulse oximeter and a side-stream capnography tubing monitored ventilation and respiratory rate. RASS and recovery in both the groups were assessed. Adverse events (airway obstruction, nausea-vomiting, dry mouth/hypersalivation, hallucinations) were recorded for the first post-operative hour. Interventionalists were requested to rate their satisfaction with the quality of sedoanalgesia (binary yes/no response).

Results

The flow of participants in both arms is depicted by the CONSORT flow-diagram (Figure 1).

The demographic profile of patients in both groups pertaining to age, sex and body weight was comparable (Table 1).

CBNPS scores at baseline and the highest CBNPS-score in first 10min, 10-20min, 20-30min and 30-40min of initiation of intervention are plotted in (Table 2).

The baseline CBNPS-score in both groups was comparable (p=0.88) while difference in pain-scores during all following time-periods throughout the intervention was statistically and clinically significant (p-values 0.0001, 0.0011, 0.0092 and 0.0201 at 0-10min, 10-20min, 20-30min and 30-40min respectively).

9/30 patients required rescue analgesic and 3/30 required bradycardia rescue in Group-F whereas no rescue drugs were required in group-K. All patients in both groups, maintained airway patency throughout the procedure.

The baseline and 10min post-dexmedetomidine infusion values of HR, MAP, RR in both groups were comparable (Table 3).

All three parameters decreased from baseline in both groups after dexmedetomidine loading. Thereafter, in Group-K, HR increased from baseline (82.8 beats/min) after initial ketamine bolus (79.6), but did not increase further at the time of intervention (79.4), or at 10mins (75.8) and 30min (74.0) post intervention-initiation. Whenever a ketamine bolus was instituted (at 20mins (78.3) and 40 mins (76.0) post intervention-initiation) HR rise accompanied. In Group-F, HR decreased from baseline after initial fentanyl bolus (76.4 beats/min), increased at intervention-initiation (77 beats/min) and progressively decreased at every time-point thereafter (74.7, 69.9, 69.8, 67.5/min at 10, 20, 30 and 40mins post intervention-initiation respectively; Figure 2).

Atropine rescue was instituted in 3 patients for bradycardia.

In Group-K, MAP increased (95.1 mmHg) after administration of initial ketamine bolus, but was maintained/decreased at the time of intervention (93.2mmHg), or at 10min (87.9mmHg) and 30min (91.4mmHg) post intervention-initiation. Whenever a bolus of ketamine was instituted (at 20min (94.0mmHg) and 40min (91.2mmHg) post intervention-initiation) MAP rise accompanied. In Group-F, MAP decreased after initial fentanyl bolus (83.5 mmHg) increased at intervention-initiation (90.1mmHg), and decreased at every time-point thereafter (88.6, 86.0, 87.1, 83mmHg at 10, 20, 30 and 40min post intervention-initiation respectively). Hemodynamic changes in both groups are depicted as forest plots (Figure 3).

Paired sample t-tests for HR and MAP at two time points (post initial ketamine bolus; intervention) in group-K gave a p-value of 0.566 and 0.0041 respectively. The mean±SD for HR and MAP post initial ketamine bolus were 79.63±11.47/min and 95.1±12.01mmHg

respectively, whereas mean±SD at time of intervention decreased to 79.37±10.89 and 93.2±11.16 respectively. In Group-F corresponding p-values for HR and MAP at two time points (post initial fentanyl bolus; intervention-initiation) were 0.0001 and 0.0001 respectively. The mean±SD for HR and MAP post initial fentanyl bolus were 71.93±11.13 and 83.5±8.42 respectively whereas mean±SD at the time of intervention increased to 77±12.72 and 90.1±10.18 respectively. This is depicted in the dot and line box-whisker plots (Figure 2) showing a downslope from left to right in most patients of Group-K and upslope in most patients of Group-F between the above two time-points plotted on x-axis.

(Table 4) displays mean RR for both groups over various time-points. Seventeen patients in Group-F had a RR of 12 breaths/min at minimum one time-point during the procedure out of which 3 patients had a RR of 10 and one had a RR of 11 breaths/min at minimum one time-point. None of the patients in Group-K had a RR ≤12 breaths/min. One patient in Group-F had a baseline RR of 26 breaths/min while at no other time point in any patient in both groups did the RR exceed 25.

The mean duration of anaesthesia was 46.5min in Group-K and 51min in Group-F (Table 1)

Post-operative RASS-score was ≥1 in 3 patients in Group-K (all with RASS=1) and none in Group-F. RASS-score was ≤ -1 in 6 patients in Group-F (4 with

RASS= -1; 2 with RASS=-2) and none in Group-K. The remaining patients (87.6% and 80% in Group-K and Group-F respectively) had RASS-score of zero (Table-1). Post-procedure resting VAS-score was 0 (no pain) in 30 Group-K and 20 Group-F patients. Resting VAS was between 1-3 (mild pain) in none of the patients in Group-K and in 10 Group-F patients. Moderate (VAS 4-7) and severe (VAS 7-10) pain was not observed in any patient at rest. Post-operative VAS-scores on coughing are plotted in (Table 5).

Post-operatively, hallucinations (resolving spontaneously within an hour) in 3/30 (10%) and hypersalivation in 2/30 (6.7%) patients were observed in Group-K but none in Group-F. Post-operative nausea-vomiting, sedation and xerostomia were the postoperative complications observed in 7/30 (23.3%), 6/30 (20%) and 5/30 (16.7%) patients respectively in Group-F versus none in Group-K patients.

Mean dexmedetomidine consumption in Group-K was 87.4µg versus 86.3µg in Group-F (Table-1) Mean total drug consumption was 51.3mg of ketamine and 59µg of fentanyl in their respective groups (Table-1). Interventionalists were satisfied with the quality of analgesia in all Group-K patients while they expressed concern about procedural interruptions pertaining to patient movement/groaning in nine Group-F patients and bradycardia in another three.
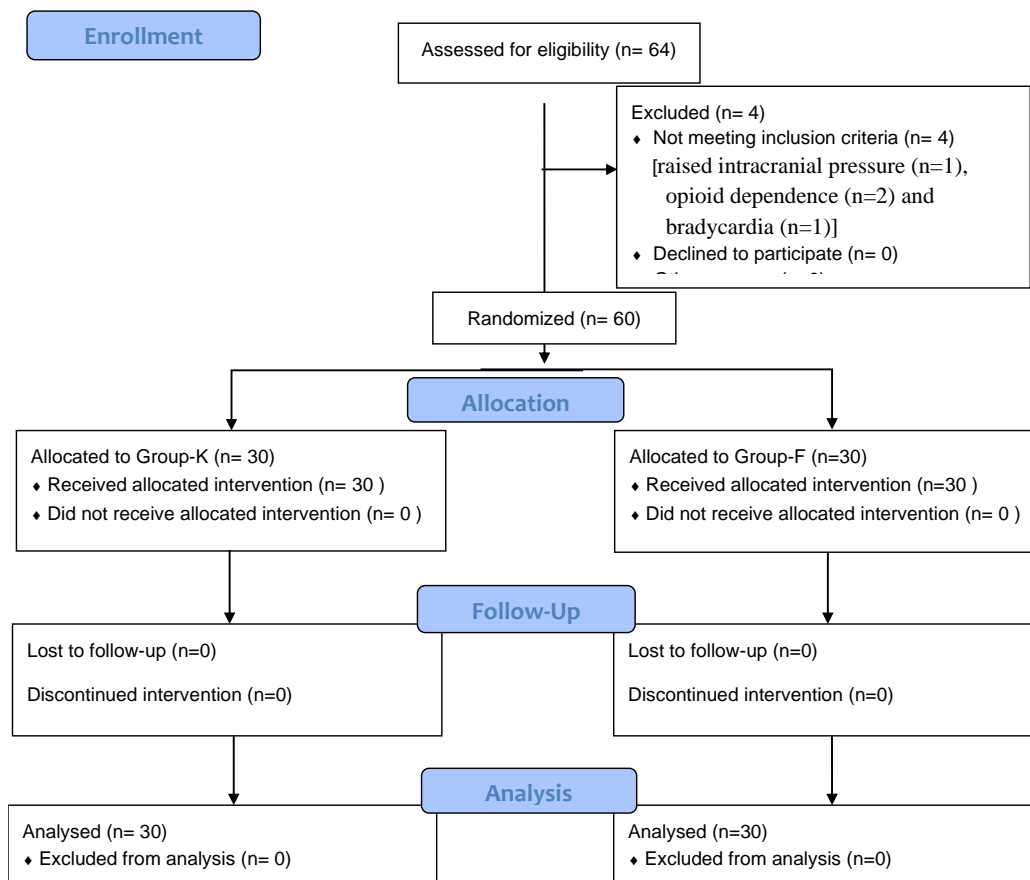

Figure 1- CONSORT flow diagram

Table 1- Demographic parameters and drug consumption

Parameter	N	Mean	95% CI	SD	Min	Max	P value
Age (Y) Group-K)	30	51.6	46.9 to 56.4	12.7	18	71	0.79
Age (Y) Group-F)	30	52.5	47.4 to 57.7	13.8	18	72	
Sex (M:F) (Group-K)	30	15:15					0.60
Sex (M:F) (Group-F)	30	18:12					
Weight (Group-K)	30	65.6	61.5 to 69.8	11.1	40	85	0.96
Weight (Group-F)	30	65.8	61.8 to 69.7	10.7	42	85	
Duration (Group-K)	30	46.5	41.5 to 51.6	13.5	29	82	0.12
Duration (Group-F)	30	51.0	48.0 to 54.1	8.1	39	72	
Total Dexmed (Group-K)	30	87.4	81.7 to 93.1	15.3	54	113	0.80
Total Dexmed (Group-F)	30	86.3	79.9 to 92.8	17.4	46	124	
Tot Ket (Group-K)	30	51.3	45.1 to 57.6	16.8	25.0	80.0	
Tot Fent (Group-F)	30	59.0	54.1 to 63.9	13.1	35.0	80.0	

Table 2- Comparison of Colorado Behavioural Numerical Pain Scale (CBNPS) score

Time point	n	CNBPS (Mean ±SD)	Range	P value
Baseline (Grp-K)	30	0.33 ± 0.92	0-3	0.88
Baseline (Grp-F)	30	0.3 ± 0.84	0-3	(t-test)
0-10 (Grp-K)	30	0.37± 0.72	0-3	0.00
0-10 (Grp-F)	30	1.73± 1.05	0-4	
10-20 (Grp-K)	30	0.27±0.74	0-3	0.00
10-20 (Grp-F)	30	1.17±1.23	0-4	
20-30 (Grp-K)	29	0.14±0.44	0-2	0.01
20-30 (Grp-F)	30	0.63±0.89	0-4	
30-40 (Grp-K)	22	0.18±0.40	0-1	0.02
30-40 (Grp-F)	30	0.70±0.95	0-4	

Table 3- Trends in heart rate (HR), mean arterial pressure (MAP) and respiratory rate (RR) over time (Bx=Biopsy; CI = Confidence Interval; d10m= 10 min after start of Dexmedetomidine; p= p value; SD = Standard Deviation)

| Time point	n	HR Mean±SD	HR 95%CI	p	MAP Mean ±SD	MAP 95% CI	P value
Grp-K (Base)	30	82.80 ±15.97	76.8-88.7	0.64	98.03 ±10.80	94-102.1	0.87
Grp-F (Base)	30	84.53 ±12.44	79.9-89.2		98.5 ±11.61	94.2-102.8	
Grp-K (d10m)	30	73.67±14.73	68.2- 79.2	0.43	88.27 ±9.87	84.6-92	0.65
Grp-F (d10m)	30	76.40 ±11.60	72.1- 80.7		89.4 ±9.38	85.9-92.9	
Grp-K (Post Ket)	30	79.63 ±11.47	75.4- 83.9	0.01	95.1±12.01	90.6-99.6	0.00
Grp-F (Post Fent)	30	71.93 ±11.13	67.8- 76.1		83.53±8.42	80.4-86.7	
Grp-K (Bx-0)	30	79.37 ±10.89	75.3-83.4	0.44	93.17±11.16	89- 97.3	0.27
Grp-F (Bx-0)	30	77.00 ±12.72	72.3-81.8		90.1±10.18	86.3- 93.9	
Grp-K(Bx10)	30	75.83 ±10.06	72.1-79.6	0.71	87.93 ±9.85	84.3- 91.6	0.82
Grp-F (Bx10)	30	74.73 ±12.94	69.9- 79.6		88.6±12.34	84- 93.2	
Grp-K (Bx20)	29	78.28 ±11.48	73.9- 82.6	0.01	94.04±11.8	89.6- 98.5	0.01
Grp-F (Bx20)	30	69.87 ±13.41	64.7- 74.9		86±11.97	81.5- 90.5	
Grp-K (Bx30)	22	74 ±10.06	69.5- 78.5	0.27	91.41±10.6	86.7- 96.1	0.24
Grp-F (Bx30)	30	69.8 ±15.18	64.1- 75.5		87.07±14.51	81.7- 92.5	
Grp-K (Bx40)	12	76.0 ±9.79	69.8- 82.2	0.05	91.15±9.13	85.9- 96.5	0.05
Grp-F (Bx40)	26	67.5 ±13.06	62.2- 72.8		83.04±13.17	77.7- 88.4	
Grp-K (End)	30	75.83 ±9.44	72.3- 79.4	0.02	90±10.30	86.2- 93.9	0.04
Grp-F (End)	30	69.10 ±12.34	64.5-73.7		84.3±10.34	80.4- 88.2	
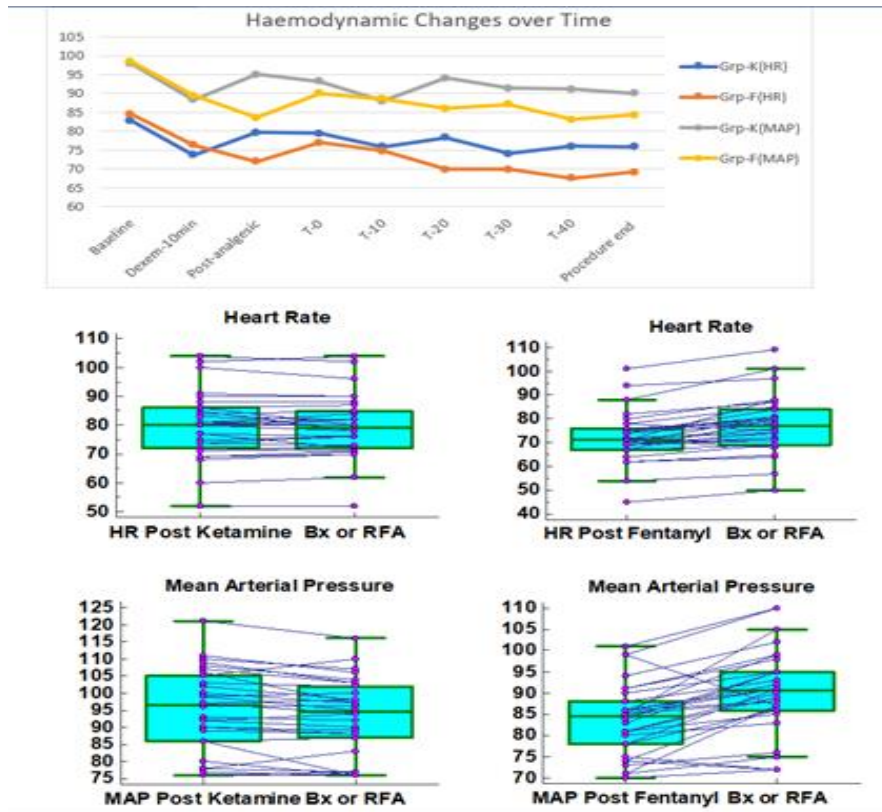
Figure 2- Line diagram with hemodynamic trends over time and Dotted box-whisker plots depicting comparison of Intragroup variation in hemodynamic parameters at two time points- Ketamine/Fentanyl administration and intervention-initiation
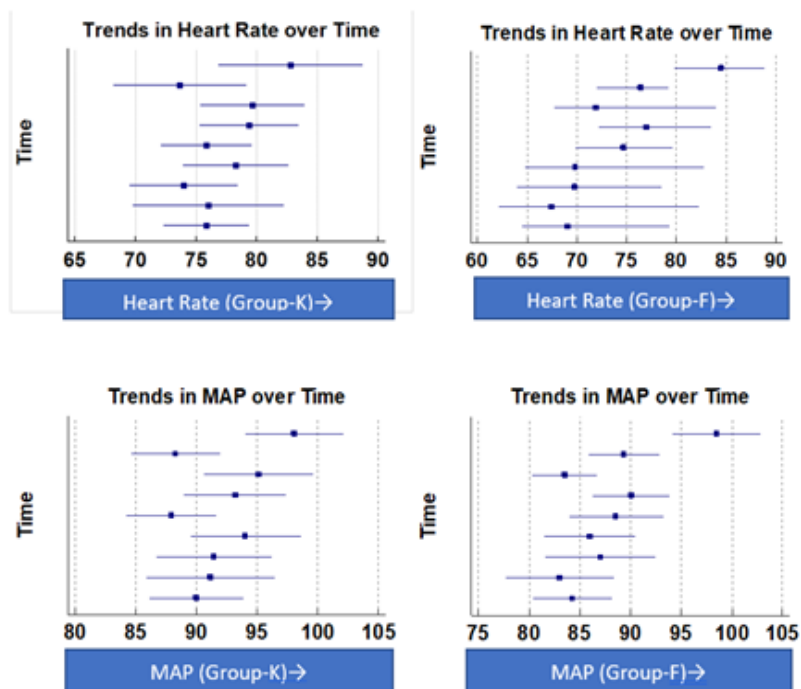

Figure 3- Forest plots depicting hemodynamic changes at various time points

Table 4- Comparison of respiratory rates (RR) over time

Time point	n	RR Mean±SD	RR 95%CI	P value
Grp-K (Base)	30	19.13 ±2.21	18.31 to 19.96	0.22
Grp-F (Base)	30	19.83 ±2.14	19.04 to 20.63	
Grp-K (d10m)	30	16.23± 2.08	15.46 to 17.01	0.27
Grp-F (d10m)	30	16.83± 2.19	16.04 to 17.62	
Grp-K (Post Ket)	30	18.07± 2.95	16.97 to 19.17	0.00
Grp-F(Post Fent)	30	14.5± 2.15	13.7 to 15.30	
Grp-K (Bx-0)	30	17.93±2.7	16.92 to 18.94	0.01
Grp-F (Bx-0)	30	16.03±3.0	14.93 to 17.14	
Grp-K (Bx10)	30	17.0±2.36	16.09 to 17.85	0.02
Grp-F (Bx10)	30	15.43±2.46	14.52 to 16.35	
Grp-K (Bx20)	29	18.35±3.0	17.22 to 19.47	0.00
Grp-F (Bx20)	30	14.27±2.2	13.46 to 15.08	
Grp-K (Bx30)	22	18.14±2.2	17.13 to 19.15	0.00
Grp-F (Bx30)	30	14.27±2.5	13.35 to 15.18	
Grp-K (Bx40)	12	19.92±1.6	18.92 to 20.91	0.00
Grp-F (Bx40)	26	13.31±2.3	12.37 to 14.25	
Grp-K (End)	30	17.73±2.15	16.93 to 18.54	0.00
Grp-F (End)	30	13.97±1.85	13.28 to 14.66	

Table 5- Comparison of Richmond agitation sedation score (RASS) and Visual Analog Score (VAS); CST=Chi squared test; FET=Fisher Exact Test

RASS	<1	0	>1	P value
(Grp-K)	1 (3.3%)	26 (86.7%)	3 (10%)	0.56 (Chi-sq. test)
(Grp-F)	6 (20%)	24 (80%)	0	
VAS-r	0	1-3	4-7	P
(Grp-K)	30	0	0	0.10 (CST)
(Grp-F)	20	10	0	
VAS-c	0	1-3	4-7	P
(Grp-K)	0	0	0	0.00 (CST)
(Grp-F)	11	18	1	
Surg. Sat. (Grp-K)	Yes/No: 30/0			0.00 (FET)
Surg. Sat. (Grp-F)	Yes/No: 18/12			

Discussion

Valid and reliable ICU sedation scales (Observers Assessment of Alertness/Sedation score), behavioural numerical pain scales (Payen behavioural pain scale for mechanically ventilated patients; Finks-Wilda pain measurement score) are largely unsuitable for objective pain measurement in patients who are unable to effectively provide a self-report of pain (including our subset of patients undergoing painful bone biopsy and RFA/MWA) [9]. Hence, we utilized the CBNPS for sedated adult patients [6,10]. Our results found the low-dose ketamine-dexmedetomidine combination to be more effective than fentanyl-dexmedetomidine combination for pain relief in interventional radiology procedures reflected by a superior CBNPS-score (ketamine-dexmedetomidine group) and reduced rescue analgesic requirement (9/30 Group-F patients versus none in Group-K). This is supported by the multipronged

antinociceptive effects of ketamine like nitric oxide synthesis [11] mu-opioid receptor potentiation [12] and anti-inflammatory effect [13] besides NMDA-antagonism. Tahiri et al reported equal rescue analgesic requirement for low-dose ketamine (0.5mg/kg) and fentanyl (1µg/kg) for post-adenotonsillectomy pain relief [14]. Messenger et al utilized 0.3mg/kg ketamine and 1.5µg/kg fentanyl for orthopaedic reduction/abscess drainage in 63 ED-patients and reported that patients administered fentanyl had 5.1 times the odds of having a serious intrasedation-event rating score with 83.9% witnessing a cardiopulmonary event in fentanyl group versus 46.9% in the ketamine arm [15]. Serious intrasedation-events were not encountered in our patients attributable to lower fentanyl doses. The greater incidence of post-procedure sedation hypotension, bradycardia and bradypnoea in fentanyl arm corroborates with our findings. Majidinejad et al compared low-dose (0.5mg/kg) IV ketamine and IV morphine (0.1mg/kg) in 126 trauma patients with long-bone fractures and found

both to be equianalgesic [16]. Motov et al in their prospective randomised trial comparing intravenous sub-dissociative (0.3mg/kg) ketamine and morphine (0.1mg/kg) for emergency sedation found both to be equianalgesic [17]. Miller et al used the same drugs in same doses for pain relief in ED-patients and found that although reduction in NRS was comparable in both groups, low-dose ketamine produced maximum analgesia at 5min (moderate analgesia lasting 2h) versus morphine(100mins) [18]. Hence, in the interventional radiology milieu the analgesic profile of ketamine is better suited than morphine/fentanyl. Analgesic efficacy within 60min post-administration and safety profiles were similar for low-dose ketamine and morphine during ED procedural sedation in a metanalysis by Balzer et al [19]. Lee et al found low-dose ketamine group provided superior analgesia with fewer cardiorespiratory events versus the opioid group (risk ratio 2.2) [20].

The baseline HR was comparable and declined to a similar extent post dexmedetomidine-loading, despite glycopyrrolate administration, in both groups. It was better maintained post-ketamine owing to the nullification of negative chronotropic effect of dexmedetomidine with positive chronotropic effect of ketamine. HR dropped below 60/min in 3/30 (10%) patients in Group-F post initial fentanyl-bolus attributable to additive/synergistic negative chronotropic effect of dexmedetomidine and fentanyl. Yuan et al [21] compared the fentanyl-dexmedetomidine combination with propofol-dexmedetomidine combination for elective flexible fiberoptic bronchoscopy in 100 patients and reported significantly lower HR, SBP and DBP and higher incidence of bradycardia (26% patients; P=0.037) with fentanyl-dexmedetomidine.

Although baseline MAP was similar, it progressively declined in Group-F except at intervention-initiation when MAP rose abruptly attributable to painful stimulus. Clinically, HR and MAP recorded at intervention was comparable in both groups. This is a deceptive picture, misleading us into believing that both ketamine and fentanyl are equianalgesic. Analysis of haemodynamic changes reveals that in Group-F, it is the sympathetic response to pain driving the HR and MAP upwards, whereas in Group-K the upward haemodynamic trends are attributable to positive chronotropic and ionotropic effects of ketamine (blunted under influence of dexmedetomidine) without any contribution from pain stimuli. This statement is strengthened by two facts. Firstly, a statistically highly significant p-value, when haemodynamic parameters at two time points (1min post-fentanyl and intervention-initiation) were subjected to paired sample t-test in Group-F. In group-K, a statistically insignificant change was observed in HR and a small but statistically significant fall in MAP was observed as compared to pre-biopsy (post initial ketamine bolus) values. Secondly, rescue analgesic requirement was much higher in Group-F as compared to group-K. At 20min and 40min post-intervention (timepoints for scheduled ketamine/fentanyl bolus) difference in HR and MAP between both groups was statistically significant because ketamine and fentanyl have diametrically opposite effects on HR and MAP. At 10min and 30min post intervention-initiation, although HR and MAP were lower in Group-F versus Group-K, there was no statistically significant difference in haemodynamics, because morphine (9/30 patients) and glycopyrrolate (3/30 patients) were used as rescue drugs in Group-F.

Although average duration of surgery was marginally longer in Group-F, no statistically significant difference in the dexmedetomidine consumption between both groups was observed. This is explained by slightly higher requirement of dexmedetomidine boluses in Group-K to bring HR/MAP down.

Only three group-K patients (10%), experienced mild post-procedure psychosis (RASS=1), much less than the reported incidence for ketamine. Lahti et al meticulously studied subanaesthetic ketamine boluses (as sole medication) in healthy and schizophrenic volunteers and reported psychosis occurrence in 70% individuals, which was short-lived (20–30min), with mental status of all volunteers reverting to baseline levels by 90min, with minimal distress to the patients (unaltered anxiety-score) [22]. Lee et al reported a higher incidence of post-procedure psychological events with low-dose ketamine versus low-dose morphine (RR 13.86) [20]. This may be attributed to the fact that ketamine was not accompanied by dexmedetomidine which had a major role in prevention of ketamine-related psychomimetic effects in our patients.

Nearly one-fourth Group-F patients developed nausea, causing significant patient discomfort. Mauermann et al place the incidence of PONV at 45% despite employing propofol based total intravenous anaesthesia and prophylactic antiemetics in 80% and 66% of their cohort respectively [23]. Our incidence is lower despite not utilizing propofol/antiemetics because of lower average fentanyl consumption, 1-1.5 µg.kg-1 versus 2-3 µg.kg−1 fentanyl used by them.

One-fifth of Group-F patients had a RASS-score of -1/-2 at procedure completion, an undesirable tenet for office-based procedures. Differences in post-procedural VAS-scores, especially on coughing, were significant with most patients in Group-F experiencing mild post-procedural pain versus pain-free Group-K patients (Table 5).

Satisfaction of interventional radiologist, gauged by a binary yes/no scale was 30/30 and 18/30 in Group-K and Group-F respectively, which conclusively highlights their preference for ketamine-based sedation despite being blinded to the combination used (P=0.00; Fisher Exact Test).

The ketamine-dexmedetomidine sedoanalgesic combination has been successfully employed for burns dressings [24], analgesia post cleft-palate surgery [25], muscle biopsies in Duchenne muscular dystrophy patients [26], acute CPRS pain [27] and cardiac-catheterization [28]. Current literature lacks sedoanalgesia data for CT-guided interventional radiology procedures and our study fills this knowledge gap. Our limitation is that we have clubbed CT-guided core bone biopsy with RFA and MWA since they are interventional radiological procedures of similar invasiveness.

Conclusion

A ketamine-dexmedetomidine combination may prove to be the ideal procedural sedoanalgesic technique for patients undergoing CT-guided core biopsy, RFA/MWA of lesions taking into account the superior analgesic effect, less intra-procedural bradypnea/bradycardia and rescue drug requirement, reduced post-procedural complications and enhanced interventionist satisfaction.

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