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Dexmedetomidine versus propofol for sedation in stereotactic brain biopsy: a comparative study

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Abstract

Background: The aim of this study was to assess the effectiveness of intraoperative dexmedetomidine versus propofol infusions on the sedation and the recovery profiles during stereotactic brain biopsy. A total of 40 patients of American Society of Anesthesiologists (ASA) physical status II were randomly divided to receive either dexmedetomidine hydrochloride (group D) or propofol (group P). The time to reach Ramsay sedation scale of 2–4, as well as the recovery profile by the modified Aldrete score, was recorded.

Results: The heart rate (HR) in group D was significantly lower than that in group P, starting from 2 min after the loading doses and during the whole painful steps of the procedure. The systolic blood pressure (SBP) showed a statistically non-significant decrease over time in both groups except at 2 min after the loading dose in group D, when it was significantly lower than the baseline value. The diastolic blood pressure (DBP) showed a statistically significant decrease over time in group D, starting from 2 min after the loading dose and with skin incision, during burr-hole drilling of the skull and with the dural stitch. The decrease in respiratory rate (RR) recorded 2 min after the loading dose in group P was statistically non-significant to the baseline value; it resulted in a statistically significant decrease in the arterial oxygen saturation (SpO_2) and statistically significant higher end tidal carbon dioxide ($etCO_2$) values that continued till the skin incision. As regards the time to reach Ramsay sedation scale (RSS) of 2–4 and a modified Aldrete score of ≥ 9, they were statistically but not clinically significantly less in group P. However, the time till the first request of analgesia was statistically and clinically significantly more in group D.

Conclusion: Dexmedetomidine offers rapid onset and recovery of sedation, as well as hemodynamic stability with post-operative analgesic effect during day-case stereotactic brain biopsy surgery.

Keywords: Dexmedetomidine, Stereotactic brain biopsy, Propofol, Opioid sparing, Sedation

Background

Anxiety leads to higher sympathetic stimulation; which leads to hypertension, arrhythmia, and increase in myocardial oxygen consumption. So, sedation and pain management for procedures done by local anesthesia is an important issue in anesthesia practice. Sedation aims to provide comfort to the patient, maintain hemodynamic stability, and eliminate anxiety (Mantz et al. 2011).

Propofol is the main safe drug used during interventional techniques that need sedation (Neumann et al. 2009; Mahfouz and Ghali 2010). Also, dexmedetomidine

(dex) causes sedation, analgesia, and sympatholytic properties, without respiratory depression even with day-case sedation. This makes it a safe drug to provide sedation in mini-surgeries and different age groups (Kunisawa et al. 2010; Ok et al. 2013).

Stereotactic brain biopsy under imaging techniques is one of the main procedures in the diagnosis of brain pathology under local anesthesia without craniotomy. But patient discomfort due to drilling a burr hole through the skull and the advancement of the biopsy needle makes the patient in need for good sedation and analgesia (McVey and Tobias 2010).

The study was done to assess the effectiveness of intraoperative dexmedetomidine versus propofol infusions

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on the sedation and recovery profiles during stereotactic brain biopsy.

Patients and methods

After obtaining the approval of Ain-Shams University Hospitals' ethical committee, informed consent was taken from 40 patients of ASA physical status II, aged 20–60 years, scheduled to undergo stereotactic brain biopsy as a day-case procedure in this randomized controlled study at Ain Shams University Hospitals, from January to June 2018.

Preoperative evaluation included a detailed history, physical examination along with neurological assessment and investigations, which included hemoglobin level, liver and kidney function tests, and electrocardiography (ECG). Also, during the pre-anesthetic visit, the procedure was explained to the patients to allay anxiety.

Inclusion criteria

Patients with brain secondaries from the lung/breast/pancreas, tuberculoma, pyogenic abscess, intra-axial supratentorial space occupying lesion with or without hydrocephalus, with an average duration of the procedure 1–2 h, were eligible for participation in the study. Also, patients must have an available caregiver for overnight observation with patient relative proximity to the hospital.

Exclusion criteria

Patients with morbid obesity (body mass index > 35 kg/m^2) or significant comorbidities (a known history of hepatic disease, renal dysfunction, hypertension, and chronic pain), history of drug or alcohol abuse, an allergic reaction to one of the study medications, anticipated difficult airway, uncontrolled epilepsy, poor neurological status, and taking psychotropic drugs were excluded from the study. Patients with brain stem lesions, uncooperative or refusing to participate, patients with ventricular drain, a prior craniotomy, intubated patients, and those who were admitted as inpatients were also excluded. Patients on regular treatment with beta-blocker with heart rate ≤ 50 bpm were also excluded.

Preparation of the study drugs

The loading and infusion doses of propofol (Propofol 1%; Fresenius Kabi Austria GmbH, Graz, Austria) and dexmedetomidine hydrochloride (Precedex 200 μg/2 ml) were calculated according to the patient's body weight and diluted to a 10 ml volume (labeled as loading-1 and loading-2) and a 50 ml volume (labeled as infusion-1 and infusion-2) by an assistant who was not involved in data recording. All syringes and infusion lines were covered by an opaque tape to hide the color of the solution.

The anesthetic technique

On arriving to the operating theater, patients had an 18G intravenous cannula inserted. All patients received 1 mg granitryl (Granisetron 1 mg/ ml; Alex.co in Egypharma) and 1 g paracetamol (Perfalgan vial, 100 ml of 10 mg/ml; Bristol-Myers Squibb Australia Pty Ltd.). Local anesthesia of the scalp was provided by 30 ml of 0.5% bupivacaine (Sunny Pharmaceutical (Egypt) under license of Hamelin Pharmaceuticals (Germany). Then, the stereotactic frame was installed in the sitting position, and the patients were brought to the radiology suite for a magnetic resonance image (MRI).

Almost after an hour, patients returned to the operating room. Intraoperative basic monitors were applied using 3-lead ECG, pulse oximetry, capnography (sample tube inserted under the O_2 mask), and non-invasive blood pressure (NIBP) (Dash 5000; General Electric, Medical Systems Information Technologies, Inc., Tower Ave., Milwaukee, WI, USA). The anesthetic machine used was Datex-Ohmeda, Inc., 3030 Ohmeda Drive, Madison, WI 53707–7550, USA. A simple O_2 mask at 6 l/min was applied. An extension tubing was attached to the IV cannula, as patients get fully draped with limited access. Infusion of Ringer's solution was then started at a rate of 5 ml/kg/h throughout the procedure. A dedicated intravenous line for the sedative drugs was inserted, as an inadvertent bolus of potent sedative can cause apnea or airway obstruction. The stereotactic frame has no mobile face element. Thus, in the case of airway control loss, the screwdrivers are necessary to remove the frame and all airway equipment, like nasal or oral airways, laryngeal mask airway, endotracheal tube, and McCoy laryngoscope must be ready before sedation. All patients received 0.03 mg/kg IV midazolam.

Patients were then randomly divided into 2 equal groups of 20 patients each

Randomization was done by a computer-generated number lists and by using sealed opaque envelopes.

Group D

Patients received dexmedetomidine hydrochloride intravenously as a loading dose of 0.5 μg/kg slowly over 10 min, followed by intravenous infusion of 0.5 μg/kg/h through an infusion pump (B-Braun, Bethlehem, USA) throughout the surgery.

Group P

Patients received propofol intravenously as a loading dose of 0.5 mg/kg slowly over 10 min, followed by intravenous infusion of 5 mg/kg/h through an infusion pump (B-Braun, Bethlehem, USA) throughout the surgery. (Dose of propofol.)

Primary outcome

Our target was an adequately sedated but easily arousable patient. The level of sedation was assessed by the Ramsay sedation scale (RSS), every 2 min after the loading dose then every 2 min until reaching RSS between 2 and 4; (time to reach the desired RSS 2 and 4 was calculated), then reassessed every 10 min.

Ramsay sedation scale: (Ramsay et al. 1974)

1. Patient is anxious and agitated or restless, or both.
2. Patient is cooperative, oriented, and tranquil.
3. Patient responds to commands.
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
5. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient exhibits no response.

Surgery then began after reaching a RSS between 2 and 4.

Secondary outcomes

Hemodynamic parameters (HR, SBP, DBP, RR, etCo$_2$, and SpO$_2$) were recorded at different stages of the procedures; on arrival at the operating room (OR) (baseline) and 2 min after the loading dose, at the painful steps of the procedure; (skin incision, burr hole drilling of the skull, dural stitch closure, skin closure), and after cessation of the study drugs at the end of the surgery.

Intraoperative events, bradypnea (RR < 8 breaths/min) or apnea (respiratory arrest for > 15 s), bradycardia (HR < 45 beats/min), hypotension (SBP decreases > 20% from the baseline or < 80 mmHg), and hypertension (SBP increase > 20% from the baseline or > 150 mmHg), were also recorded. During bradypnea or oxygen desaturation (SpO$_2$ ˂ 94% > 10 s), the infusion of the drugs was discontinued and the patients were requested to breathe deeply, then restarted when the SpO$_2$ increased > 94% with RR > 8 breaths/min. If hypertension occurred, fentanyl 1 μg/kg (Sunny Pharmaceutical Industrial Zone Badr City, Egypt, under license of Hamelin Pharmaceuticals, Hameln, Niedersachsen, 31789 Germany) was administered. If hypotension occurred, drug infusions were discontinued temporarily, and normal saline was infused until the SBP increased > 80 mmHg. At the end of the procedure, the infusions were discontinued, and all the patients were transported to the post-anesthesia care unit (PACU).

In the PACU, patients were monitored, and when they got a modified Aldrete score ≥ 9, they were transferred to the day-case surgery unit, where the time to request first analgesic was recorded and a plain computed tomography (CT) scan of the brain was performed 4 h post-operatively. After six post-operative hours, patients were examined by the surgeon to determine fitness for discharge: normal postoperative CT, wound hemostasis, and a stable neurological status.

Modified Aldrete score (Aldrete 1995)
Activity

2 = Moves all extremities voluntarily or on command
1 = Moves two extremities voluntarily or on command
0 = Unable to move extremities

Respiration

2 = Breathes deeply and coughs freely
1 = Dyspneic, shallow or limited breathing
0 = Apneic

Circulation

2 = BP ± 20 mmHg of pre-anesthetic level
1 = BP ±20–50 mm of pre-anesthetic level
0 = BP ± 50 mm of pre-anesthetic level

Consciousness

2 = Fully awake
1 = Arousable on calling
0 = Not responding

Oxygen saturation

2 = SpO$_2$ > 92% on room air
1 = Supplemental O$_2$ required to maintain SpO$_2$ > 90%
0 = SpO$_2$ < 90% with O$_2$ supplementation

Statistical analysis

Using PASS for sample size calculation, group sample sizes of 18 patients per group achieved 81% power to detect a difference of 3.0 min in time to desired RSS between both groups with estimated group standard deviations (SDs) of 3.0 and 2.0 and with a significance level (α) of 0.05 using a two-sided two-sample t test. Therefore, 20 patients per group were included to replace any dropouts.

The statistical analysis was performed using a standard SPSS software package version 17 (Chicago, IL, USA). Data were expressed as mean values ± SD, numbers (%).For parametric data, Student's t test was used to compare between the two groups and analysis of variance (ANOVA) with post hoc test for comparing with the baseline in each group the changes in hemodynamic and respiratory parameters. Categorical variables were analyzed using the χ^2 test. P value < 0.05 was considered statistically significant.

Table 1 Patient's characteristics

	Group D(n=20)	Group P(n=20)	p-value
Age (yrs)	38.45± 8.35	40.5±9.05	0.461
Weight (kg)	74.6±6.57	73.5± 5.99	0.584
Gender (M/F)	11/ 9	13 /7	0.748

Values are mean ± SD or number. P˃0.05 is considered statistically non-significant

Results

Forty patients undergoing stereotactic brain biopsy were enrolled in the study (20 patients in each group). There were no statistically significant differences in the patients' characteristics (age, weight, and gender) between the two groups ($P = 0.461$, 0.584, and 0.748 respectively) (Table 1).

Regarding the hemodynamic parameters, there were no statistical differences between the two groups with respect to the baseline mean values of HR ($P = 0.552$). In group D, the HR showed statistically significant decrease starting from 2 min after the loading dose and during the whole painful steps of the procedure till the cessation of dex at the end of the procedure ($P < 0.001$). In group P; the mean values of HR showed statistically lower values than the baseline values only after skin incision and after the burr hole drilling of the skull ($P < 0.001$). Also, the mean HR recorded in group P was statistically higher than that recorded in group D; starting from 2 min after the loading doses and during the whole painful steps of the procedure till cessation of the study drugs at the end of the procedure ($P = 0.04$, < 0.001, < 0.001, < 0.001, < 0.001, and < 0.001 respectively) (Fig. 1).

Regarding the SBP, there was no statistically significant difference between the two groups in the mean values of SBP recorded; on arrival to the OR and during the whole painful steps of the procedure till cessation of the study drugs at the end of the procedure ($P = 0.268$,

0.166, 0.26, 0.221, 0.39, and 0.702 respectively). However, the value recorded 2 min after the loading doses was significantly lower in group D than in group P with a P value of 0.03. The mean values of SBP showed statistically non-significant decrease over time in both groups except in group D; the SBP recorded 2 min after the loading dose was significantly lower than the baseline value ($P < 0.05$) (Fig. 2).

Regarding the DBP, there were no statistical differences between the two groups regarding the baseline mean values of the DBP, values recorded with skin closure, and after cessation of the study drugs ($P = 0.894$, 0.48, and 0.22 respectively). Whereas the mean values of DBP recorded for group D were statistically lower than that recorded in group P; starting 2 min after the loading doses and with skin incision, during burr hole drilling of the skull and with the dural stitch ($P = 0.046$, 0.001, $< 0.001$and 0.004 respectively). Also, the mean values of DBP showed statistically significant decrease over time in group D; 2 min after the loading dose, with skin incision and closure, and with the burr hole drilling of the skull ($P < 0.05$) (Fig. 3).

Regarding the RR, the changes recorded showed statistically non-significant difference between the two groups; on arrival to the OR, 2 min after the loading doses, with skin incision and closure, burr hole drilling of the skull, dural stitch, and after cessation of the study drugs ($P = 0.15$, 0.18, 0.21, 0.56, 0.46, 0.626, and 0.1 respectively). Also, the changes recorded were statistically non-significant over time within the same group with no patient recording RR ˂ 8 (Fig. 4).

Although the decrease in RR recorded 2 min after the loading dose in group P was statistically non-significant compared to the baseline value and to that recorded at the same time in group D, but it resulted in a statistically significant decrease in the SpO_2
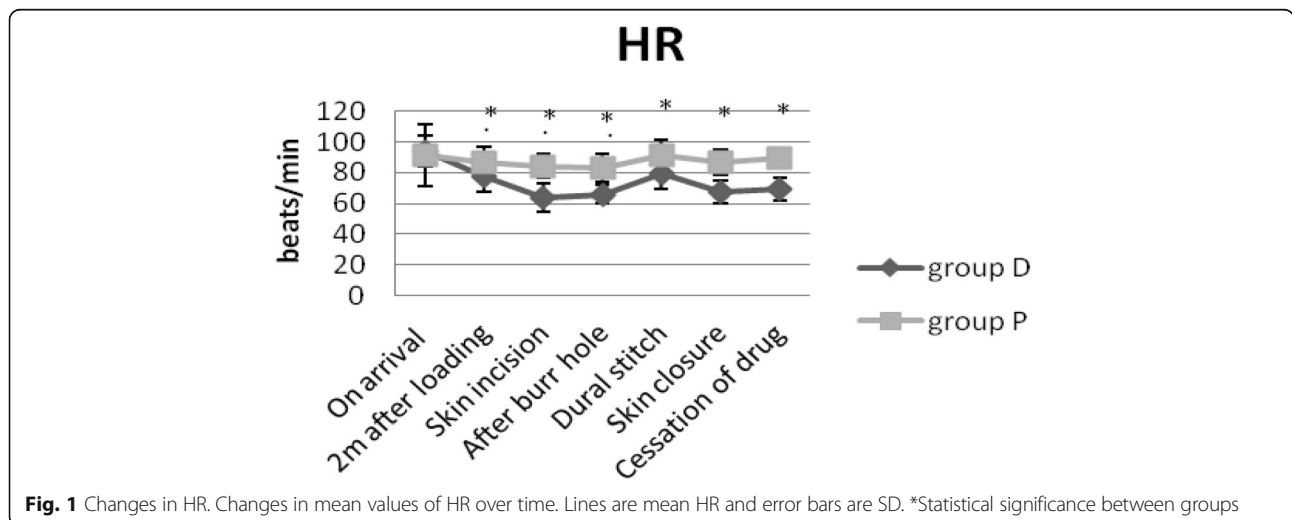

Fig. 1 Changes in HR. Changes in mean values of HR over time. Lines are mean HR and error bars are SD. *Statistical significance between groups
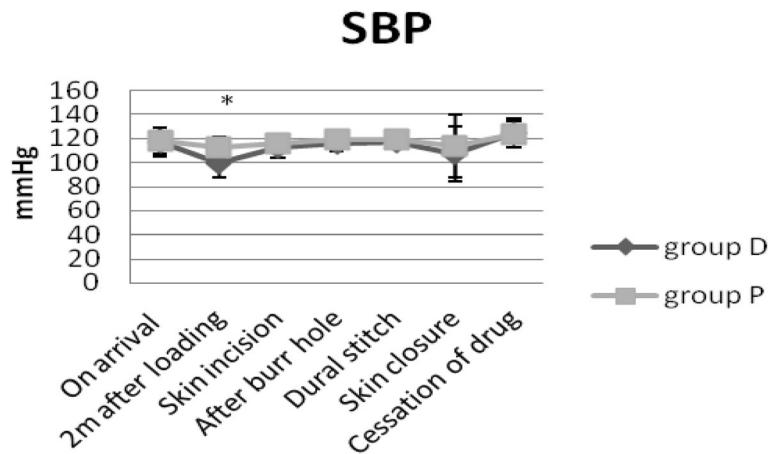
Fig. 2 Changes in SBP. Changes in mean values of SBP over time. Lines are mean SBP and error bars are SD. *Statistical significance between groups

($P < 0.001$) and a statistically significant higher $etCO_2$ values ($P < 0.001$) in group P compared to the baseline, that continued till skin incision ($P < 0.001$), then returned to be statistically non-significant between the two groups and to the baseline value till the end of the procedure (Figs 5 and 6).

Regarding the time taken till reaching RSS of 2–4, it was statistically significant less in group P ($p < 0.001$). Also, the time to reach a modified Aldrete score of ≥ 9 was statistically significant less in group P ($P < 0.001$). However, the time till the first request of analgesia was statistically significant more in group D ($P < 0.001$) (Table 2).

Discussion

Stereotactic brain biopsy is one of the low-risk day-case surgeries. It allows three-dimensional localization of certain sites of the brain by MRI scan (Balakrishnan et al. 2000). The procedure can be performed under analgesia-based sedation, to alleviate the pain in periods of intense stimulation (scalp incision and closure, burr hole drilling, and the dural stitch) (Dorairaj and Hancock 2008). However, the partial arterial pressure of carbon dioxide and oxygen should be maintained to avoid any increase in the cerebral blood volume, with secondary increase of intra-cranial pressure (ICP) (Johnson 2002). Thus, the ideal technique should provide adequate analgesia, stable level of sedation, and ICP with rapid recovery without significant cardio-respiratory depression; this can be achieved by continuous infusion technique of sedatives, short-acting anesthetics, and analgesics than intermittent bolus techniques (White et al. 1986; White and Negus 1991; Bilgin et al. 2006).

Although propofol is commonly used due to its favorable effect on the ICP, along with rapid recovery (Bone and Bristow 1991; Baker and Sert 1997; Bhade et al. 2002), due to its short context-sensitive half-times (3 min for a very short infusion time to 18 min after a 12-h
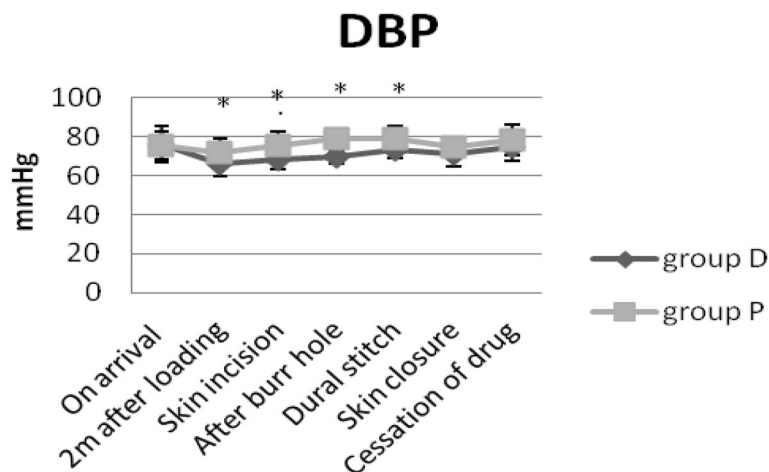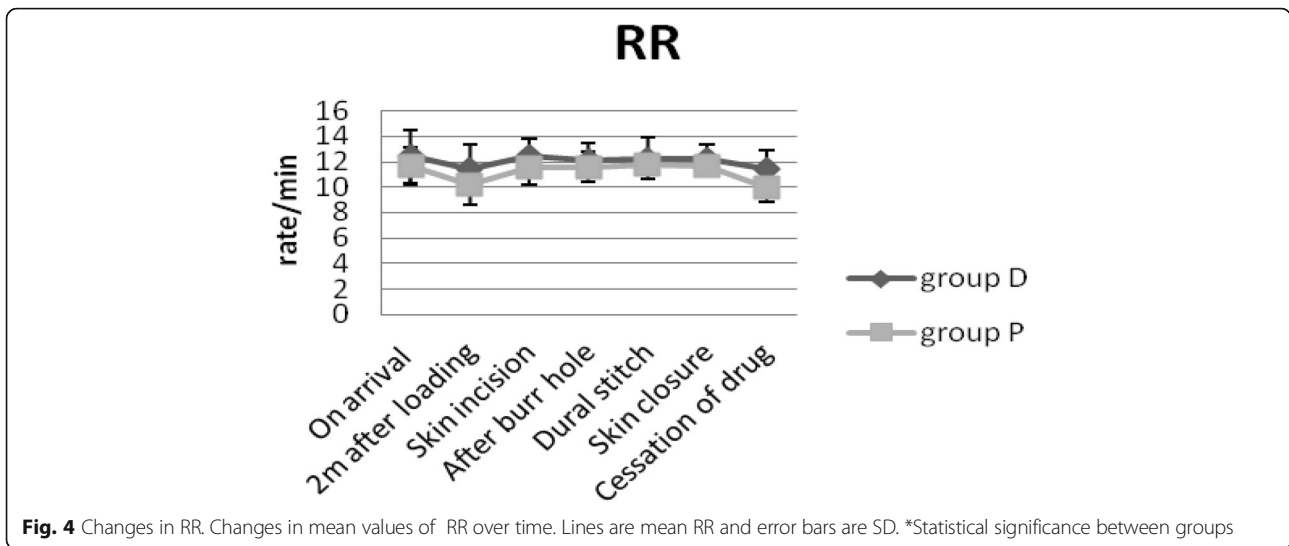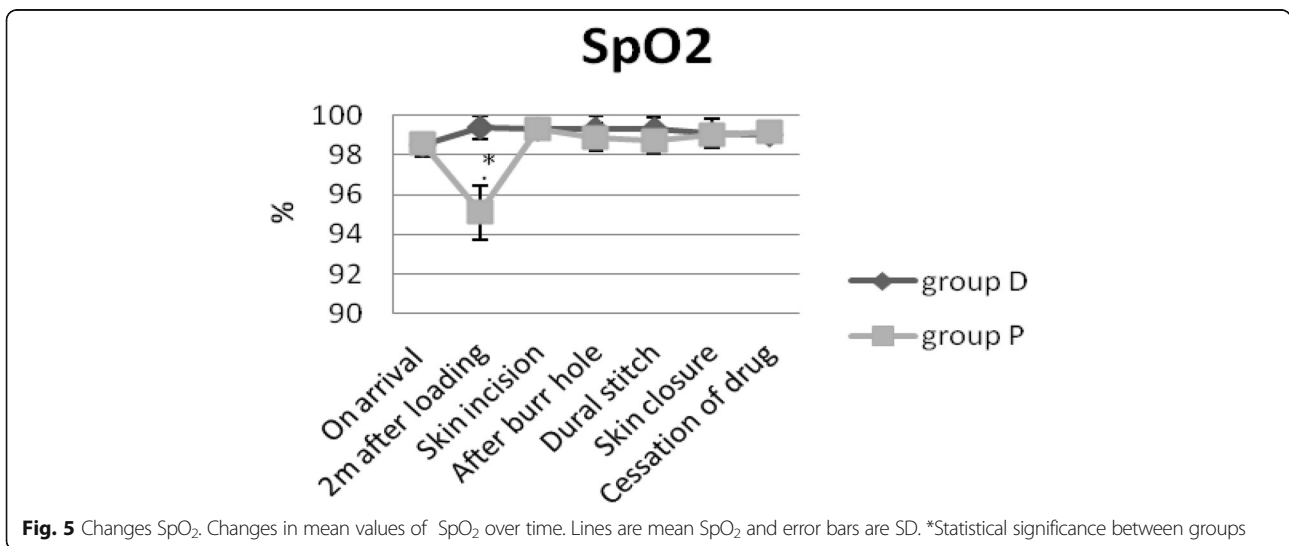

Fig. 3 Changes in DBP. Changes in mean values of DBP over time. Lines are mean DBP and error bars are SD. *Statistical significance between groups

Fig. 4 Changes in RR. Changes in mean values of RR over time. Lines are mean RR and error bars are SD. *Statistical significance between groups
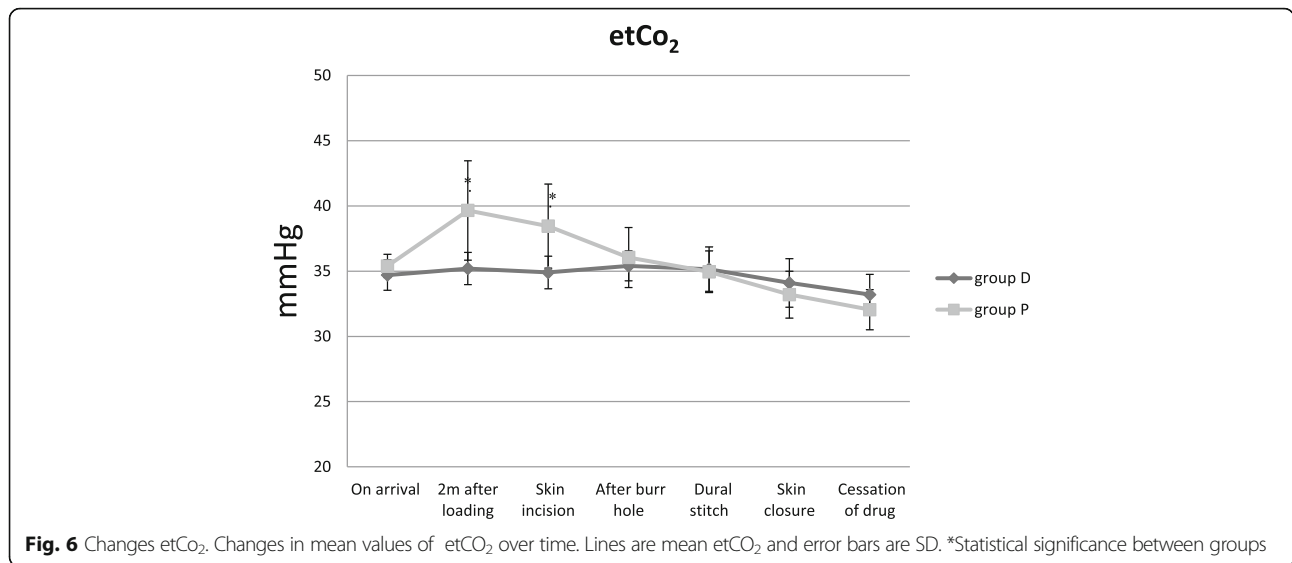
infusion) (Hill 2004), its depth of sedation should be balanced to avoid airway obstruction, respiratory depression, hypercarbia, and hypotension (Piccioni and Fanzio 2008; Mack et al. 2004), especially in advanced age patients (Arain and Ebert 2002). In our study, stereotactic brain biopsies were also performed with dex; a highly selective α2 adrenoceptor agonist on the locus coeruleus (LC). Dex is a good sedative analgesic with no respiratory depression even at high-infusion rates with deep levels of sedation, along with no significant effect on ICP (Ebert et al. 2000). In 2001, Doyle and his colleagues reported a case of awake craniotomy managed using dex infusion, which proved its good hemodynamic stability (Doyle et al. 2001).

In 1981, De Jonge and his colleagues stated that dex is associated with a decrease in HR, because of its sympatholytic effects and vagal mimetic effect (De Jonge et al. 1981). In our study, the statistically significant

decrease in HR in patients of group D showed beneficial clinically significant lower SBP values than that recorded in group P patients at all the painful steps of the operation, also, showed beneficial statistically significant decrease in the DBP values at most of the painful steps of the operation. This decrease in HR, SBP, and DBP values in group D patients indicates the analgesic effect of dex; also, it did not result in severe bradycardia or hypotension that required discontinuation of the infusion to any patient denoting its hemodynamic stable effect. The hemodynamic stability of dex could be explained by the direct postsynaptic vascular smooth muscle effect causing vasoconstriction (α2 mediated) (Jie et al. 1984; Link et al. 1996) antagonizing the central sympatholysis demonstrated by Talke and his colleagues in 1997 and 2000 (Talke et al. 1997; Talke et al. 2000). Whereas for propofol, it has no direct effects on the vascular smooth muscle (Robinson et al. 1997) to

Fig. 5 Changes SpO_2. Changes in mean values of SpO_2 over time. Lines are mean SpO_2 and error bars are SD. *Statistical significance between groups

Fig. 6 Changes etCo$_2$. Changes in mean values of etCO$_2$ over time. Lines are mean etCO$_2$ and error bars are SD. *Statistical significance between groups

antagonize its powerful inhibitory effect on the sympathetic outflow (Ebert et al. 1992).

Both propofol and dex have minimal respiratory depression when used as sedative agents which is evident from our results, 2 min after propofol loading, group P patients showed statistically non-significant decrease in the RR along with statistically significant decrease in the SpO$_2$ and increase in the etCO$_2$ that continued till skin incision, and then started to improve by asking the patient to take a deep breath. This decrease in the RR and SpO$_2$ was not defined to be significant according to Shahbaz and Thomas in 2002 (Shahbaz and Thomas 2002), who defined significant respiratory depression during infusions of propofol for sedation as a decrease in respiratory rate more than 25% or a decrease in SpO$_2$ ≥ 90%. In 2012, Ryu and his colleagues observed that dex was associated with fewer incidents of oxygen desaturation (Ryu et al. 2012).

In our study, both dex and propofol achieved a RSS of 2–4 as targeted; however, the time required was statistically significantly less for propofol (1.362 ± 0.425) min than for dex (3.187 ± 0.62) min. Also, the time required to achieve a modified Aldrete score of 9 or more after ending of the infusions was statistically significantly less

for propofol (9.85 ± 3.5) min than for dex (19.9 ± 15.58) min. Although both times were statistically significant, they were clinically non-significant to delay the start of surgery or to discharge the patient from the PACU. Venn and his colleagues in 1999 and Hall and his colleagues in 2000 (Venn et al. 1999; Hall et al. 2000) stated that dex has an interesting ability to achieve sedation but with preserving patient arousability. Our findings correlate well with the results of previous studies by Arain and Ebert in 2002 (Arain and Ebert 2002), Kaya and his colleagues in 2010 (Kaya et al. 2010), Hoy and Keating in 2011 (Hoy and Keating 2011), and Abdelkareim and his colleagues in 2012 (Abdelkareim et al. 2011). However, in 2002, Shahbaz and Thomas (Shahbaz and Thomas 2002) recorded more delayed onset and offset times of sedation than ours; as they used higher doses with longer durations of elective surgeries and postoperative patient hospitalization for 24 h. Also, Muller and his colleagues in 2008 (Muller et al. 2008) and Pratibha and his colleagues in 2016 (Pratibha et al. 2016) recorded more prolonged recovery time for dex compared to propofol (long duration of sedative action). In 2009, Khurana and his colleague (Khurana et al. 2009) related the early onset time of sedation for propofol to the high lipophilicity and rapid distribution into the central nervous system. However, Techanivate and his colleagues in 2012 (Techanivate et al. 2012) found a rapid recovery time for dex as they used a single injection of dex with no infusion. The persistent effects of dex in the recovery room resulted in significantly more sedation when compared with the short-acting propofol.

In our study, the time passed until the patient requested analgesia was statistically significant prolonged for dex (112 ± 39.24) min than for propofol (35.75 ± 18.91) min. The finding of our study is well supported

Table 2 Time to RSS 2-4, Modified Aldrete score ≥9 and first analgesic request

	Group D (n=20)	Group P (n=20)	p-value
Time to RSS 2-4 (min)	3.187 ± 0.62	1.362 ± 0.425	<0.001*
Time to Modified Aldrete score ≥9 (min)	19.9 ± 15.58	9.85 ± 3.5	<0.001*
Time to first analgesic (min)	112 ± 39.24	35.75 ± 18.91	<0.001*

Values are mean ± SD. $P < 0.05$ is considered statistically significant

with other studies (Talke et al. 2000; Pratibha et al. 2016; Chernik et al. 1990). In 1993, Jorm and Stamford (Jorm and Stamford 1993) stated that dex produces analgesia by binding to adrenoreceptors in the spinal cord, and they observed the inhibitory effect (membrane hyperpolarization) of dex on the pontine LC (A6 group) which could explain the supraspinal prolongation of analgesia after iv administration of dex. In 1999, Khan and his colleagues (Khan et al. 1999) described the half-life of dex as 2 h; thus, the analgesic-sparing properties are likely to persist in the recovery period.

In summary, dex achieved similar levels of sedation to propofol, albeit with a slower onset and offset, without respiratory depression, with intraoperative analgesic effect favoring hemodynamic stability. In the post-operative period, dex was associated with an analgesia-sparing effect, slightly increased sedation, but with no compromise of the cardio-respiratory function.

Conclusion

Compared with propofol, dexmedetomidine is a useful alternative for stereotactic brain biopsy sedation; dex proved to be a potent sedative with respiratory and analgesia-sparing properties.

Abbreviations
ANOVA: Analysis of variance; ASA: American Society of Anesthesiologists; CT: Computed tomography; DBP: Diastolic blood pressure; dex: Dexmedetomidine; ECG: Electrocardiography; etCO$_2$: End tidal carbon dioxide; HR: Heart rate; ICP: Intra-cranial pressure; LC: Locus coeruleus; MRI: Magnetic resonance image; NIBP: Non-invasive blood pressure; OR: Operating room; PACU: Post-anesthesia care unit; RR: Respiratory rate; RSS: Ramsay sedation scale; SBP: Systolic blood pressure; SDs: Standard deviations; SpO$_2$: Arterial oxygen saturation

Availability of data and materials
The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
Idea, data collection, data analysis, and manuscript editing was done by the two authors. Both authors read and approved the final manuscript.

Ethics approval and consent to participate
The study was done after institutional ethical committee approval from Ain-Shams University with the committee's reference number (R44/2017). Consent to participate was obtained from the patient or next of kin for inclusion in this study/requirement for consent was waived by the ethical committee. Please amend as appropriate.

Consent for publication
A consent to publish has been obtained from the participant to report individual patient data.

Competing interests
The authors declare that they have no competing interests.

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