Hypnosis for sedation in transesophageal echocardiography: a comparison with midazolam

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BACKGROUND: Transesophageal echocardiography (TEE), being a displeasing intervention, usually entails sedation. We aimed to compare the effects of hypnosis and midazolam for sedation in TEE.

DESIGN AND SETTINGS: A prospective single-blinded study conducted on patients scheduled for TEE between April 2011 and July 2011 at a university in Istanbul, Turkey.

METHODS: A total of 41 patients underwent sedation using midazolam and 45 patients underwent hypnosis. Patients were given the State-Trait Anxiety Inventory (STAI) test for anxiety and continuous performance test (CPT) for alertness before and after the procedure. The difficulty of probing and the overall procedure rated by the cardiologist and satisfaction scores of the patients were also documented.

RESULTS: Anxiety was found to be less and attention more in the hypnosis group, as revealed by STAI and CPT test scores (P < .05 and P < .001, respectively).

CONCLUSION: Hypnosis proved to be associated with positive therapeutic outcomes for TEE with regard to alleviation of anxiety and maintenance of vigilance, thus providing more satisfaction compared to sedation with midazolam.

Transesophageal echocardiography (TEE) is a relatively invasive diagnostic procedure and an unpleasant experience for the patient, as it may cause nausea, pain, and emotional distress unless topical anesthesia and sedation are used. In the cardiology setting, TEE is usually performed with topical anesthesia via spraying the oropharynx with a local anesthetic, with or without sedation. Sedatives, such as midazolam, are commonly used prior to probing to make the procedure more tolerable and comfortable for the patient. Midazolam improves patient comfort during TEE, decreases stress, induces amnesia, and makes it easier for the physician to perform the procedure due to better patient compliance.1,2 However, recovery may be prolonged due to its cumulative hypnotic effect, besides having potential of concurrent adverse effects. However, the effectiveness of stress-reducing strategies has been largely confirmed in published studies. Of these, hypnosis has proven to be a beneficial adjunct to reduce anxiety and pain for many procedures including breast biopsy, general surgery, and plastic surgery.3-5 Most of the reports on hypnosis in published studies have focused on pain control during minor operations. Here, we aimed to evaluate the role of hypnosis on sedation for an unpleasant experience causing distress for the patient, namely TEE, and compare it with a commonly used sedative for this purpose, midazolam.

METHODS
Patients between 18 and 65 years of age scheduled for TEE examination for clinical indications who were in sinus rhythm and not in shock or pulmonary edema were given the choice having the procedure done with hypnosis or intravenous (IV) midazolam sedation. The pros and cons of the 2 methods were explained to the patients. Each patient signed an informed consent form.
Patients with an American Society of Anesthesiology Physical Status I–III were enrolled in the study. Exclusion criteria were a history of mental illness, psychotropic medication use, hypersensitivity to drugs, and a body mass index over 30. The study was approved by the local ethics committee (Ref: 15.12.2010/9-7) and registered with Clinical Trials (Ref: NCT01749475).

Hypnosis was performed by the same anesthesiologist (EKT) certified with a 6-month hypnotherapy training. A first hypnotic induction was carried out the day before the procedure; of the 53 eligible patients undergoing hypnotic induction, 8 were judged as poorly sensitive to hypnosis and not included in the study. The hypnotic state was described to the patient as a state of mental focalization on a pleasant life experience and disattentation to external stimuli. Next day, 15 minutes before the procedure, a new induction was performed and hypnosis was deepened. The hypnosis techniques used were eye fixation, relaxation, and indirect suggestions. Every effort was made to create a state of hypnosis, in which only ideas of complete relaxation and wellness were suggested to patients during the procedure.

Patients in the sedation group were given 0.05 mg/kg IV midazolam (to achieve a Ramsay Sedation Score of 2–3) just before monitoring. During probing, in the case of intolerance to the insertion of the probe, the increments of midazolam with 0.005 mg/kg doses were given.

To set a single-blind design (for the cardiologist performing the intervention), the second hypnotic induction was done in a separate room 15 minutes before the intervention, and IV line was achieved for both groups. The cardiologist was invited just after the administration of midazolam (in the midazolam group) and monitoring. If the patient felt uncomfortable and the cardiologist was aware of this while probing, the patients in both groups were encouraged saying “everything will be alright” in order not to spoil his blindness. This was the only word uttered during the procedure while giving increments of midazolam in the midazolam group and only saline physiologic in the hypnosis group. The patients in the hypnosis group would not be given any placebo right after the hypnotic induction, but they were told that the IV access was performed just in the case of an emergency. While giving the additional doses, patients neither in the midazolam group nor in the hypnosis group were informed. The investigators to give the drug or the placebo (here the hypnotist) and to document the recordings were also different to ensure blindness.

The TEE examination was standard for all patients; pharyngeal topical anesthesia was provided by lidocaine spray; patients lay in the left decubitus position during the examination, and their heart rate (HR) and oxygen saturation were continuously monitored together with noninvasive blood pressure measurements. Bispectral index (BIS) monitoring was started just before midazolam injection in this group and before the probing in the hypnosis group. The baseline recordings of all the parameters (HR, SpO₂, systolic–diastolic, and mean arterial pressures [SAP, DAP, and MAP, respectively] and BIS) were done, and the insertion of the TEE probe was regarded as the onset of the procedure. The recordings were written at the intervals of 1, 3, 5, and 5 minutes thereafter until the end of the procedure.

For each case, the following parameters were recorded: the length of the procedure (in minutes), total dose of midazolam (only for the sedation group), the difficulty of probing, and the overall procedure rated by the cardiologist, both on a visual analog scale (VAS) (0=poor, 10=excellent) and the satisfaction of the patient with the procedure, again on the VAS. Patients were also asked to take the State-Trait Anxiety Inventory (STAI) test for anxiety before and after the procedure. To assess the neuropsychometric performances of the patients, we used continuous performance test (CPT) before and after the procedure (before hypnosis in the hypnosis group and prior to the procedure in the midazolam group). CPT consists of the evaluations of omission errors, commission errors (CEs), and reaction times. Omission errors indicate the number of the target patients missed. High omission rates demonstrate inattention or distractibility of the patient. Commission error score indicates the responses to stimuli but the target. A fast reaction time with a high commission error rate reflects problems with impulsivity, whereas a slow reaction time with high commission and omission errors is associated with inattention.

Statistics

Statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 Statistical Software (UT, USA). Considering the change of the CE domain of CPT (before and after sedation) in the midazolam group as 11 (1.9) in a previous study, the sample size was calculated to be 40-45 for a power of 80% and α=0.05. Results are expressed as mean (standard deviation). Normally distributed data were compared with the paired variance analysis, and the Newman–Keuls test was used to find the group leading to the difference. Independent samples t and paired samples t tests were used for the intergroup and intragroup evaluations, respectively, and the chi-square test was applied to categorical variables. Results
Effects of Hypnosis and Midazolam inTEE

RESULTS

Of the 98 scheduled patients for TEE examination, 45 patients chose medical sedation with IV midazolam and 4 of them could not tolerate probing despite deep sedated with incremental midazolam dosing up to BIS levels of 75 (which we have estimated as to the level that patients are in cooperation with the cardiologist, in a small sample size pilot study with 12 patients, before performing this comparative study). Excluding these 4, 41 patients in the sedation group were compared with 45 patients in the hypnosis group (the number of hypnotizable patients out of 53 patients choosing hypnosis). The total amount of midazolam was 3.76 (0.74) (on average 5.2-2.5). Only 3 patients in the hypnosis group needed to receive placebo for operator blindness.

Groups revealed no statistical significance in any of the demographical or clinical characteristics before the procedure ($P>.05$) (Table 1). BIS levels varied in a range of 72-92 in the midazolam group and 84-98 in the hypnosis group during the intervention ($P<.001$).

There was no significant difference between the groups regarding HR and mean arterial pressures ($P>.05$). Oxygen saturation changes were significant in the midazolam group, but there were no instances of drop of saturation below 90% requiring intervention in any of the groups. Oxygenation parameters were found to be more stable in the hypnosis group throughout the procedure (Table 2).

Hypnosis reduced anxiety more effectively compared with midazolam as was revealed by the STAI test ($P=.027$). Moreover, CPT domains displayed that attention remained intact in the hypnosis group at the end of the procedure ($P<.001$) (Table 3). One patient in the midazolam group could not complete the CPT after the procedure because of profound sedation, and we omitted his initial CPT result from the analysis. Moreover, satisfaction scores of both the patients and the cardiologist were also higher in the hypnosis group ($P<.05$) (Table 4).

DISCUSSION

Hypnosis has been employed clinically for both medical and psychotherapeutic purposes. By far, the most outstanding of these has been hypnotic analgesia for the relief of pain. Clinical studies indicate that hypnosis can effectively relieve pain in surgery, childbirth, and dental procedures.5-11 But studies comparing it with drug-induced sedation techniques are scarce. To our knowledge, there is only 1 research12 comparing hypnosis with

Table 1. Demographical data, educational background, and baseline clinical characteristics of patients before transesophageal echocardiography.

|              | Midazolam (n=41) (%) | Hypnosis (n=45) (%) | $P$  |
|--------------|----------------------|---------------------|------|
| Age (yr)     | 36.1 (14.0)          | 38.1 (13.7)         | .393 |
| Gender       |                       |                     |      |
| Male         | 21 (51.2)            | 20 (44.4)           | .530 |
| Female       | 20 (48.8)            | 25 (55.6)           |      |
| Educational level |                   |                     |      |
| Primary school | 26 (63.4)         | 25 (55.6)           | .683 |
| High school  | 11 (26.8)            | 16 (35.6)           |      |
| University   | 4 (9.8)              | 4 (8.9)             |      |
| Height (cm)  | 168.5 (9)            | 166 (8.2)           | .170 |
| Weight (kg)  | 71.2 (9.4)           | 72.1 (8.9)          | .645 |
| Heart rate (beats/min) | 85.0 (13.2) | 86.2 (16.4)         | .722 |
| Systolic BP (mm Hg) | 124.7 (21.3) | 126.9 (18.8)        | .612 |
| Diastolic BP (mm Hg) | 71.7 (12.4) | 76.4 (13.3)         | .095 |
| $\text{SpO}_2$ (%) | 95.8 (2.3)    | 96.4 (1.9)          | .252 |
| BIS (min-max) | (98-94)             | (98-89)             |      |
| Mean value throughout procedure | (92-72) | (98-84)             | .0001|

Data are presented as n (%), mean (standard deviation [Sd]) and minimum-maximum. BIS: bispectral index. Levels of hypnotosedation throughout the procedure, indicated by BIS values, are also provided.

Table 2. Change of vital parameters throughout TEE procedure.

|              | Midazolam | Hypnosis | $P$  |
|--------------|-----------|----------|------|
| MAP          |           |          |      |
| Baseline     | 88.7 (17.6) | 92.6 (15.9) | .265 |
| 1 min        | 102.0 (18.8) | 100.6 (18.1) | .725 |
| 3 min        | 95.4 (16.8) | 96.7 (19.4) | .746 |
| 5 min        | 91.8 (16.3) | 93.5 (17.8) | .656 |
| 10 min       | 91.7 (16.7) | 92.3 (15.7) | .857 |
| $P^*$        | .0001     | .0001    |      |
| Baseline     | 85.0 (13.2) | 86.2 (16.4) | .722 |
| 1 min        | 97.3 (16.4) | 96.2 (18.8) | .771 |
| 3 min        | 97.1 (20.2) | 91.9 (16.1) | .189 |
| 5 min        | 93.1 (17.6) | 90.5 (14.8) | .450 |
| 10 min       | 91.4 (14.8) | 91.5 (16.0) | .960 |
| $P^*$        | .0001     | .0001    |      |
| HR           |           |          |      |
| Baseline     | 96.8 (2.3) | 97.4 (1.9) | .252 |
| 1 min        | 95.8 (3.3) | 97.0 (1.8) | .032 |
| 3 min        | 95.5 (2.9) | 96.0 (1.9) | .013 |
| 5 min        | 95.8 (2.9) | 96.0 (2.1) | .448 |
| 10 min       | 96.0 (2.4) | 97.0 (1.8) | .03 |
| $P^*$        | .0001     | .144     |      |

Data presented as mean (standard deviation). MAP: mean arterial pressure; HR: heart rate; $\text{SpO}_2$: peripheral oxygen saturation. $^*P$: one-way ANOVA, $P$: independent-samples t-test, $P<.05$: statistically significant.
midazolam, which is the most frequently used drug for sedation in transoesophageal echocardiography. The present study replicates that hypnotic induction prior to TEE produces alleviation of anxiety comparable to midazolam. It renders the procedure more comfortable for both the operator and the patient. Satisfaction scores provided by both the cardiologist and the patient were significantly better in the hypnosis group than in the midazolam group.

Hypnosis is a clinical practice in which suggestions are used to change patients’ experience in sensation, perception, thought, and behavior to achieve specific therapeutic goals such as alleviation of anxiety and pain. It is a state of relaxation and concentration, where the subject’s awareness of the surroundings is feasible, but he can tailor induced inattention to external stimuli.

Before the technology era, it was thought that hypnosis itself might be of the placebo effect, a phenomenon that was also attributable to all active analgesic agents. We now know that we can activate the frontal lobe by simply applying focused attention to it, and thereby we can begin to modify our emotional and chemical responses, as the frontal lobes are considered our emotional control center. Positron emission tomography revealed that the anterior cingulate cortex (ACC) is one of the sites in the brain affected by hypnotic modulation of pain. Mitigation of both affective and sensory responses has been provided by hypnosedation through ACC activation.

Conscious sedation through midazolam induces relaxation and abates the pre-procedural anxiety, but it can result in a number of potential complications. Oversedation, disorientation, confusion, dizziness, discoordination, and dyspraxia are the neurologic side effects. All psychomotor functions can be compromised. Actions requiring attention and alertness, such as driving and running gear, should be postponed until full recovery. Moreover, it is recommended that patients should not give medical decisions and even get health care information while under the sedation effect. A 24-hour recovery waiting period is usually a common practice.

CPTs are frequently used to measure quantitatively the individual’s ability to sustain attention over time. The initial CPT was developed by Rosvold et al in 1956 to study attention and vigilance. Since then, it has been used for researches related to attention, and various components of the CPT tasks have been found to be associated with neural substrates that are associated with attention. Here in this study, the CPT scores explicitly revealed that hypnosis does not curb attention and vigilance, whereas those for midazolam replicated the fact that midazolam sedation may attenuate alertness.

During endoscopic interventions, sedation with midazolam is prone to a couple of deleterious effects. Respiratory complications related to midazolam sedation are depicted as a decrease in the respiratory drive caused by respiratory depression as a result of the drug occupying brainstem benzodiazepine receptor sites. Unless treated properly, the evolving apnea may even lead to hypoxic brain injury. Sedation with midazolam before TEE causes significant hemodynamic deterioration with more prominent tachycardia, hypotension, and oxygen desaturation compared with the TEE probe insertion alone. Therefore, alternative methods have been sought, especially nonpharmacologic, with the hope of being devoid of possible complications.

**Table 3. Anxiety scores of patients revealed by STAI test before and after echocardiography together with CPT results prior to and after the procedure.**

|                  | Midazolam | Hypnosis | P    |
|------------------|-----------|----------|------|
| STAI (prior)     | 41.1 (6.5) | 41.2 (5.5) | .922 |
| STAI (after)     | 41.0 (7.6) | 39.1 (6.3) | .202 |
| P<             | .977     | .027     |      |
| CPT (prior)      |           |          |      |
| CE score         | 6.1 (4.5) | 6.5 (4.7) | .698 |
| OE score         | 7.9 (4.8) | 7.6 (4.3) | .723 |
| RT (ms)          | 398.7 (51.2) | 411.6 (42.5) | .205 |
| CPT (after)      |           |          |      |
| CE score         | 14.2 (4.7) | 8.4 (4.3) | .0001 |
| OE score         | 23.3 (7.2) | 11.9 (4.0) | .0001 |
| RT (ms)          | 493.8 (29.2) | 489.7 (31.8) | .532 |
| Difference of CPT scores (after-prior) | | | |
| CE              | 9 (9)     | 4 (3)    | .0001* |
| OE              | 14 (13)   | 5 (4)    | .0001* |
| RT              | 87 (60)   | 70 (52)  | .041*  |

Data are presented as mean (standard deviation [SD]) and median (interquartile [IQR]), as appropriate. STAI: State-Trait Anxiety Inventory; CPT: continuous performance test; CE: commission error (false hit); OE: omission error (missed target); RT: reaction time in milliseconds (time between presentation of the stimulus and the patient’s response); P<.05: statistically significant; independent-samples t test, and a Mann–Whitney U test.

**Table 4. Procedural ratings of the cardiologist and the patients regarding the quality and satisfaction.**

|                  | Midazolam | Hypnosis | P    |
|------------------|-----------|----------|------|
| Duration of procedure (min) | 11.6 (1.5) | 11.6 (1.5) | .904 |
| Evaluation by cardiologist probing | 6.2 (1.6) | 8.0 (1.6) | .0001 |
| Procedure        | 7.2 (1.4) | 8.2 (1.5) | .003 |
| Patient satisfaction | 6.4 (1.8) | 7.3 (1.6) | .016 |

Probing and overall procedure was rated by cardiologist over a scale of 0 to 10 (0=poor and 10=excellent). Patients also rated their experiences by VAS (0=very bad and 10=very good).
these, hypnosis has been tried mainly in gastroscopy and colonoscopy. However, in 1 of these trials, hypnosis was found inferior to the comparative, midazolam group, and the authors mounted this finding to insufficient time to full induction of the patients, as the mean time for the sole induction of hypnosis was only 4.52 minutes. Differing from this, we conducted 2 episodes of hypnosis: (1) the day before the procedure and (2) 15 minutes prior to TEE, to deepen the hypnosis. This might have assured success for hypnosis, in all aspects, in our study.

BIS is used to assess the depth of anesthesia and sedation through global brain electrical activity. To simplify, BIS monitors convert several parameters of electroencephalographic (EEG) sample into a single variable (BIS index). Painful stimuli and anxiety alter the electrical activity of the brain. Cortical arousal can be lowered by hypnosis and sedation. Congruently, there is a decrease in EEG amplitudes, in highly hypnotizable individuals, both during painful awake and hypnotized states. In their report, Burkle et al described BIS values in a patient who performed self-hypnosis for mastectomy. The patient tolerated the procedure under local anesthesia and self-hypnosis without any pharmacological sedation. Her BIS values remained at approximately 90 throughout the operation, and it occurred as low as 59 in 1 instance. Hypnosis is a complex dynamic cerebral process, and significant sustained drops in the BIS monitor are not expected, rather it may oscillate up and down from time to time as seen in this unique example. This was the case in our study also. Baseline BIS readings in the hypnosis group were as low as 89 and were significantly lower than in the midazolam group (P = .0001). This was not a fair comparison because the BIS recording in the midazolam group was done as soon as midazolam was given. However, in the hypnosis group, the baseline BIS was corresponding to the time of hypnosis impact when the monitoring began, as the time interval between the hypnotic induction and the TEE intervention was at least 15 minutes. This can be regarded as a methodological limitation. But the following recordings were fairly comparable, and BIS levels were lower in the midazolam group than in the hypnosis group; nonetheless, low levels were recorded up to 84 even with hypnosis.

Another limitation of this study was the lack of double blindness. It is compulsorily impossible to undertake a double-blind comparative trial of hypnosis, because the individual has to be informed of the therapy involved. Nevertheless, every effort was made to undertake at least single-blind comparative trial.

Whether conscious sedation increases or decreases the percentage of aborted procedures remains still controversial. Conlong and Rees documented difficult gastroscopies in 26% of patients in the midazolam group and 9% in the hypnosis group, most of which were probing related. There was no intolerance in the hypnosis group in the current study; however, 4 out of 45 patients receiving midazolam could not tolerate probing at all, and they were excluded from the study. De Lima et al declared in their comparative study that hypnosis facilitates TEE increasing the satisfaction of both the cardiologist and the patient better compared to midazolam. These results are totally consistent with our findings, except that we measured the level of anxiety and vigilance on a more objective basis through scales like STAI and CPT, which probably renders our study powerful against the study by De Lima et al.

In conclusion, hypnosis proved to be associated with positive therapeutic outcomes for TEE in regard to alleviation of anxiety and maintenance of vigilance. When compared to midazolam, hypnotic intervention for sedation provides a safer and more satisfactory experience for TEE.
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