Results of a moderate sedation program with propofol for transesophageal echocardiography performed by non-anesthesiologist professionals.

Introduction and objectives

The advantages of sedation in patients undergoing transesophageal echocardiography (TEE) are well established, but the increasing number of TEE studies may limit the capacity of Anesthesiology services. In this study we analyze the effectiveness and safety of a moderate sedation program carried out by non-anesthesiologist professionals (NAP).

Methods

Descriptive and prospective study that included all consecutive patients undergoing a TEE procedure under moderate sedation by NAP and by anesthesiologists (AP) from September 2018 to September 2019. Patients were selected according to a specific algorithm agreed upon with the Anesthesiology department. We analyze current indications for TEE, complication rates, and recovery times associated with sedation.

Results

We performed 267 procedures in 252 patients (54% male, 69yo). Main indications were screening or monitoring of surgical and percutaneous cardiac interventions (47.9%), endocarditis (28.5%) and stroke (20.6%). Patients in the NAP group were younger (59 vs 71 yo), less hypertensive (43% vs 61%), with less lung disease (4% vs 24%), lower risk of difficult airway (1% vs 22%) and lower comorbidity (ASA scale ≥III 13% vs 77%). Complications were more frequent in the AP group (26% vs 9%), mainly mild respiratory (19% vs 9%). Multivariate adjustment showed events were associated with

the presence of lung disease and higher ASA degree. Recovery time was longer in the AP sedation group (20min vs 15min).

Conclusions

TEE indications are changing and involve larger and more complex studies. Moderate sedation with propofol performed by NAP is safe in selected patients, with adequate recovery times.

Key words:

Transesophageal echocardiography

Anesthesia

Percutaneous intervention

TEE

Three-dimensional echocardiography

Three dimesional transesophageal echocardiography

Abbreviations:

TEE, transesophageal echocardiography

NAP, non-anesthesiologist professional

AP, anesthesiologist professional

INTRODUCTION

Transesophageal echocardiography (TEE) is an essential diagnostic procedure in cardiology with a low complication rate in the adult population[1]. However, the poor tolerance of the procedure in non-sedated patients made it necessary to carry out studies that were very focused on the pathology being sought, especially when the indications were sources of systemic embolism and suspected endocarditis[2,3]. In the last decade, the clinical profile of patients and the complexity of procedures seem to have changed. The demand for TEE studies has increased in parallel to the rise of interventional percutaneous procedures in Cardiology, usually applied in elderly patients with high comorbidity.

Moderate sedation during TEE provides comfort and amnesia from the procedure and should be available to all patients. This level of sedation also improves the quality of the studies: by creating a state of calm and cooperation, more complex and detailed examinations can be performed.

Midazolam[4] and Propofol[5] are generally used for sedation in these procedures, being the depressant effects on the cardiovascular and respiratory systems the main concern regarding patient safety. Usually, this sedation requires the collaboration of anesthesiologists, familiar with the management of these drugs and their potential adverse effects.

The growing requirement for sedation in outpatient procedures may exceed the capacity of Anesthesiology services, which has led to new approaches in which sedation is performed by non-anesthesiologist professionals (NAP) specifically trained for this purpose. Different Societies of Anesthesiology, aware of this situation, have developed specific recommendations to regulate the training and adequate facilities to carry out NAP sedation[6–8]. Our center has developed a pilot program of training and

support in sedation with Propofol administered by NAP. The objective of this work is to analyze the implementation and safety of this program in patients undergoing TEE.

METHODS

Inclusion criteria

We conducted a descriptive, prospective, non- randomized and single - center study of consecutive patients undergoing TEE in our Cardiac Imaging Unit from September 2018 to September 2019. All patients were aged >18 years and signed informed consents for the procedures. The study was conducted in accordance with the principles of the Declaration of Helsinki.

NA staff training program

Prior to its start, an analysis of the workspace and the necessary material to carry out the program was made. Secondly, the training focused on:

1.- Assessment of the airway and comorbidities that could affect sedation.

2.- Competence in recognizing the different levels of sedation.

3.- Knowledge of the most commonly used drugs in sedation and advanced life support training with special focus on advanced airway management.

4.- Competence in recognizing total recovery of consciousness required to leave the monitoring area.

Finally, practical skills were acquired through supervised live cases.

Study variables

The baseline characteristics of the patients and the presence of a priori pathologies associated with events during sedation, such as underlying lung disease (asthma, COPD or sleep-apnea) or severe valvular disease were recorded. Adverse events throughout the sedation procedure until recovery were recorded on a sedation form. These events were classified as respiratory (pulse oximetry oxygen saturation <90%, need for endotracheal intubation: EI), hemodynamic (hypotension <90 mmHg, need for cardiopulmonary

resuscitation: CPR), arrhythmic (bradycardia <40bpm or sustained new tachyarrhythmia), digestive (non-self-limited digestive bleeding) and neurological events (new-onset focal neurological deficits). The monitoring of the procedure and its complications were recorded in a *Sedation in TEE register* for publication in the patient's medical history.

Study protocol

With the objective of planning sedation, this program designed a decision-making algorithm (Figure) to perform a pre-anesthetic evaluation. This could be done by anesthesiologists (AP) or by NAP depending on the patient's personal history. At the end of the visit, it was established whether the patient would be sedated by AP or by NAP (Annex).

For the sedation procedure the use of propofol was prioritized. The target was to keep patients in a moderate degree of sedation, also called conscious sedation, which enables spontaneous ventilation with preserved cardiovascular function [9]. In all cases of NAP sedation an anesthesiologist was previously advised and available to provide support or switch to AP sedation if needed.

After the TEE, patients were transferred to a recovery area. The modified Aldrete[10] post-anesthetic recovery score was used to authorize discharge, considering a score > 9/10 points in hospitalized patients and> 17/18 points in outpatients to finish the procedure. The time to reach the adequate Aldrete score was recorded as recovery time.

Statistical analysis

Categorical variables are expressed as absolute frequencies and percentages. Quantitative variables are expressed as mean ± interquartile range (IQR; 25-75%). Quantitative variables distribution assessed using the Shapiro-Wilk test showed a significant violation of normality assumption. To compare variables between the two groups, Chi-square and Fisher test were performed for categorical variables and Wilcoxon test for quantitative variables. Multivariate analysis was performed with

logistic regression to control confounding variables. An alpha error level of 0.05 was established and Stata 12.1 software was used for all analysis.

RESULTS

Between September 2018 and September 2019, 267 TEE were performed under sedation in 252 patients (Table 1). 54% were men and median age was 69yo. Main indications were percutaneous or surgical intervention (45.3%), endocarditis screening (28.5%) and stroke study (20.6%). Repeated TEE were mainly performed in endocarditis monitoring (55.2%), planning and follow up of structural procedures (31%) and thrombosis (10.3%).

Out of the total study sample, 75 participants met criteria for NAP sedation (28.09 %) and 75 were sedated by NAP. However, 28 of these patients with NAP sedation criteria were sedated by AP (discordant AP sedation) and conversely, 28 of the patients with AP sedation criteria were sedated by NAP (discordant NAP sedation), as detailed in table 2. The multivariate analysis of baseline characteristics (Table 1) showed a statistically significant classificatory weight for all the variables used in the algorithm (Figure 1), except for BMI> 40 (present in 2 subjects, both sedated by AP) and study of severe valvular disease.

Procedure sedation results are summarized in Table 3. Baseline vital signs were similar in both groups. Propofol was the main drug used (85% NAP, 98% AP) at a similar mean dose of 1.71mg / kg and combined with midazolam in 68% of cases.

The event rate was higher in the AP sedated group. The overall event rate was 21% and respiratory and global hemodynamics events were 16.5 % and 4.5 %, respectively. EI or CPR maneuvers were not necessary in any case. The rate of digestive or neurological events in both groups was 0%. After adjusting for patient characteristics, no significant differences in the event rate between the two groups were shown (Table 4), neither in the event rate of discordant NAP sedation.

An additional analysis was performed to determine which variables could be related to the occurrence of events. The multivariate analysis showed that both the presence of previous lung disease, as well as an ASA grade III were related to a higher risk of events (Table 4).

Urgent Anesthesiology support was required in only one case, due to difficulty in the introduction of the TEE probe. Recovery time after sedation was 20 min in the AP group, and 15 min in the NAP group.

DISCUSSION

Most relevant findings of the study

1.- Update in the TEE indications

The results of our study confirm a change in the indication for TEE studies, with a high demand for those aimed at planning and evaluating percutaneous and surgical interventional procedures (45.3% of all studies). These studies are usually more extensive and detailed, as they require a methodical and careful assessment that should not depend on the patient's tolerance. Moreover, many of these patients would need follow-up studies; in this sense, a pleasant memory by means of sedation facilitates this continuity.

2.- Safety of moderate sedation with propofol by non-anesthesiologists

Our work shows the safety of a TEE program with moderate **propofol** sedation designed in collaboration with the Anesthesiology department and carried out by NAP, based on the appropriate selection of patients and identification of those with a higher risk of complications.

The safety of **midazolam** in TEE studies is well known from two randomized trials. The first, by the group by Aeschbacher[11] et al. and including 200 patients, demonstrated the safety of midazolam with only 3% of desaturation episodes (SpO2 <90%). The other was performed by Blondheim[12] et al. on 62 patients, showing an incidence of respiratory events of 23%. None of the patients in these studies required EI and in both there were

statistically significant differences in terms of tolerance to the procedure facilitated by sedation.

Safety with the use of **propofol** in TEE has been less well characterized. There are two studies with few patients. The first, from Ferson[13] et al., compared 8 patients with midazolam administered by NAP and 34 patients with propofol administered by AP. It identified a rate of respiratory events (SpO2 <90%) between the midazolam and the propofol group of 12.5% vs. 17.6% and a striking rate of incomplete studies of 37.5% vs. 0%. The second study, by Toman[5] et al., compared three therapies: midazolam (M), midazolam-alfentanil (MA), and propofol (P), and observed a respiratory event rate (SpO2 <90%) of 13.3% vs. 0.03% vs. 16.7% in M, MA and P, respectively, without statistically significant differences.

In this line, our work provides information on the incidence of events with the use of **midazolam + propofol** for TEE procedures, which was found to be around 21% globally, 16.5% for respiratory events and 4.5% for hemodynamic events. All complications were mild and did not require invasive rescue procedures such as EI, nor hospitalization. Events were mainly related to the presence of previous **lung disease** and higher comorbidity, as reflected by an **ASA** degree **III**. Therefore, our findings underscore that patient selection is key to achieving a low complication rate when sedation is performed by non-anesthesiologists.

Protocol safety and efficacy

There was a crossover of 56 patients between the two initially defined groups, probably due to errors in the functioning of the circuit in its first year. Characteristics of the discordant patients are detailed in Table 2. Safety in the group of 56 discordant patients, and particularly in the subgroup of 28 patients assigned to AP sedation but sedated by NAP was tested. The global prevalence of complications in the 56-patients discordant group was 3%, whereas the prevalence of complications in the discordant subgroup sedated by NAP was 1.87%. We did not detect a significant increase in complications in misclassified patients.

Clinical implications

The results of this study show the expansion of TEE in cardiac imaging units, with a new profile of patients with advanced heart disease directed to percutaneous or surgical intervention. This may require the reorganization of the units to respond to new demands, including the establishment of collaboration circuits between medical specialties as well as the incorporation of cardiac imaging specialists trained in the interventionist field. Also, our safety data support the expansion of propofol sedation in TEE procedures performed by non - anesthesiologists professionals in selected patients.

LIMITATIONS

Our work is a registry of patients included in a pilot sedation program with a selection algorithm that results in two clearly differentiated groups. This may limit the comparability of results between the two groups. However, safety data, events and recovery time are similar to previously published work.

Moreover, a standardized definition and classification of adverse events has not been used, thus limiting the comparison with other studies.

CONCLUSIONS

Moderate propofol sedation in transesophageal echocardiography procedures performed by trained non-anesthesiologist personnel is safe after adequate patient selection. The creation of these collaboration agreements between specialists could serve to extend sedation to all patients undergoing TEE in a safe and protocolized manner, increasing the efficiency of available resources and reducing waiting lists and healthcare pressure on Cardiology and Anesthesiology services.

CONFLICT OF INTERESTS

Nothing to disclose.

WHAT IS KNOWN?

- The main indications for TEE are stroke and endocarditis studies.
- Sedation with midazolam for TEE is safe but shallow.
- Propofol sedation is more profound albeit with higher complication rates.
- The safety of propofol for sedation by non-anesthesiologists for TEE studies is not known.

WHAT DOES THIS STUDY CONTRIBUTE?

- The main indications for TEE in our center are planning and follow-up studies of percutaneous and surgical cardiac interventions.
- Sedation with propofol performed by non-anesthesiologists for TEE studies is safe with adequate patient selection, including those with advanced heart disease.
- Collaboration agreements for non-anesthesiologist sedation could help to extend moderate sedation with propofol to all TEE procedures, without increasing the healthcare pressure on the Anesthesiology services.

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