





ORIGINAL RESEARCH

GERIATRIC ANESTHESIA

A comparative randomized study of awareness during two anesthetic induction techniques in old aged patients using isolated forearm technique

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Abstract

Background & Objective: Awareness under anesthesia is defined as intraoperative consciousness and/or postoperative recall of surgical events. The isolated forearm technique (IFT) is a technique that has the ability to assess consciousness of the external world through a verbal command during general anesthesia. It provides live information about the presence of consciousness.

We compared inhalational induction technique versus intravenous induction technique regarding awareness during laryngoscopy and intubation in elderly patients.

Design: A prospective, randomized trial

Methodology: A total of 50 patients scheduled for elective surgery under general anesthesia; aged 60 to 80 years were recruited. Patients were randomized into either Group A (inhalational induction group) or Group B (total intravenous induction group). Awareness reaction using IFT technique was observed during laryngoscopy and intubation phase to identify awareness incidence. A patient was considered a responder if IFT score > 2.

Results: At laryngoscopy and intubation phase, 32% of cases had an awareness reaction in intravenous induction group (Group B): While in the inhalational induction group (Group A), only 8% of cases had an awareness reaction. Additionally, none of the patients, suffered from postoperative explicit recall as detected by modified Brice questionnaire (MBQ).

Conclusions: On the basis of the results of our study, we conclude that intravenous induction of general anesthesia may subject old aged patients to a higher incidence of awareness when compared to inhalational induction technique.

Trial Registration: NCT05019560

Abbreviations: TIVA - Total intravenous anesthesia; IFT - Isolated forearm technique; MBQ - Modified Brice questionnaire; BISTM -Bispectral IndexTM; ETAC - End-tidal anesthetic concentration; MAC – Minimum alveolar concentration

Key words: Awareness; The modified Brice questionnaire; Elderly patients; Isolated forearm technique; Sevoflurane; TIVA

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1. Introduction

Old aged patients are considerably vulnerable and sensitive to the stress of surgery and anesthesia. Standard anesthetic doses can cause more profound clinical effects in the elderly, due to their different pharmacokinetics and pharmacodynamics.¹ This may subject this age category to the possibility of increased incidence of intraoperative awareness ± postoperative recall due to reduced anesthetic doses in the interest of safety.

Regaining consciousness during general anesthesia (“awareness”) is a frightening experience that often causes patients to feel helpless and panicked even when no pain is experienced.² Additionally, it is unethical to operate on a conscious patient.³

Recent studies showed the incidence of intraoperative awareness detected by postoperative recall to be 0.1-0.2% in low-risk surgical procedures; however, it can reach 1% for patients at increased risk.⁴

Isolated forearm technique (IFT) (Appendix 1) is a direct method to detect real-time awareness under general anesthesia; through which the patient either does or does not move his/her isolated forearm after verbal instructions.⁵

This study was conducted to compare the incidence of awareness - during laryngoscopy and intubation phase - between two techniques for induction of general anesthesia; inhalation and intravenous techniques (total intravenous anesthesia) in old aged patients. We hypothesize that intravenous induction technique would subject old aged patients to a higher incidence of awareness when compared to inhalational induction technique.

2. Methodology

2.1. Ethics

This was a prospective randomized parallel-group, non-funded, single-center study (Ain Shams University Hospital) conducted after institutional ethics committee approval. The institutional research committee’s ethical criteria and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics committee of University hospital (FMASU R 153/ 2021) on 4/9/2021, and was registered at Clinical Trial Registry (ClinicalTrials.gov) Identifier: NCT05019560 in accordance with WHO and ICMJE standards. Written informed consent was obtained from all patients. The trial followed the CONSORT statement.

2.2. Study population

The study comprised of 50 American Society of Anesthesiologists- Physical status (ASA-PS) I and II

patients, aged 60 to 80 y, weighing 70-80 kg, both sexes, with intact hearing, undergoing elective day case surgery were included in the study.

The study exclusion criteria were: history of awareness under anesthesia, contraindication to tourniquet use on arm, language barriers, neuromuscular disorders, suspected difficult intubation and more than one attempts of intubation.

2.3 Study groups

The patients were randomly assigned to one of two groups:

Group A: Patients received inhalational induction

Group B: Patients received intravenous induction

2.4 Patients’ recruitment, randomization and control of potential bias

Randomization was performed using a computer-generated random number table in opaque sealed envelopes with 1:1 allocation ratio by an anesthesiologist not directly involved in the trial or patient care. Patients were subsequently followed up by a researcher who was unaware of the group allocation. Thus, the patient and the outcome assessor were blinded to the group allocation.

2.5 Anesthesia

An intravenous (IV) catheter was inserted at the dorsum of the patient’s non-dominant hand. Full monitoring was applied. IFT was explained to each patient before induction. A tourniquet was placed around the dominant arm after placing a cotton bandage; to be inflated later on to 200 mmHg. The headphones of an MP-3 player were placed over the patient’s ears and the following command was presented: ‘Mr/Mrs “Y”, open and close your dominant hand twice. This was repeated at predetermined specific timings (before endotracheal intubation, during laryngoscopy and intubation phase (with the insertion of blade to hypopharynx), one minute after intubation. Relationship between Bispectral Index™ (BIS™) and IFT was investigated regarding classification of responders and non-responders at laryngoscopy phase.

In group A (Inhalational Group)

Patients received inhalational induction using sevoflurane 8%, and fentanyl 2 µg/kg IV, according to previous guidelines. At a constant BIS value of 50 or less, the tourniquet cuff was inflated then atracurium 0.5 mg/kg was given intravenously. After maximum T1-depression, laryngoscopy and intubation were performed.

In group B (TIVA group) Total intravenous anesthesia (TIVA) was used in this group. Propofol 1.5 mg/kg and fentanyl 2 µg/kg IV were given. Then, propofol infusion at 6 mg/kg/h was started. At a constant

BIS value of 50 or less, the tourniquet cuff was inflated and then atracurium 0.5 mg/kg was given intravenously. Once maximum T1- depression was obtained, laryngoscopy and intubation were done. No inhalational agent was used. Patients with awareness reaction to intubation (IFT Score > 2) were assigned to the "Responders" group.

Patients without awareness reaction (IFT Score ≤ 2) were assigned to the "Non-responders" group. One minute after successful intubation, the data collection was stopped and the isolated forearm cuff was deflated. Surgery was then allowed to commence as usual. Two hours and twenty-four hours after extubation, patients were interviewed regarding any experience of dreaming or recall using modified Brice questionnaire (MBQ) (Appendix 2 and 3). Then the principal investigators classified each patient report according to the definitions described in previous literature (Appendices).

2.6 Sample size calculation

Sample size was calculated using PASS program version 15, setting the type-1 error (α) at 0.05 and power at 80%. Results from a previous study showed that 40% of TIVA group cases were aware during intubation. We assumed that, 8% of inhalational group cases will be aware during intubation. Based on this, a sample sizes of 22 in group A and 22 in group B will be needed. However, we included 25 patients per group to take in account for 10% drop out rate.

2.7 Data Management and Analysis

The statistical analysis was performed using SPSS

Table 1: Comparison between the 2 study groups as regard personal data

Parameter	Inhalational Group	TIVA Group	P	Sig
Age (years)	64.48 (3.02)	65.68 (4.79)	0.296*	NS
BMI	24.56 (2.47)	25.20 (1.78)	0.298*	NS
Gender	Male	14 (56.0)	0.571**	NS
	Female	11 (44.0)		
ASA-PS	1	6 (24.0)	0.529**	NS
	2	19 (76.0)		

* Student t test, **Chi-Square Tests

software package version 17 (Chicago, IL). Kolmogorov–Smirnov's test was used to evaluate normal distribution of continuous data. Normally distributed numerical data are presented as mean ± SD, and differences between groups are compared using the Student's t-test. Categorical variables are analyzed using the chi square test or fisher exact test and are presented as numbers and percentages. Kappa statistics was used to compute the measure of agreement between IFT and BIS methods, Kappa's over 0.75 is excellent, 0.40 to 0.75 is fair to good, and below 0.40 is poor. P < 0.05 is considered statistically significant.

3. Results

A total of 50 patients completed the study and were analyzed. There were no differences between the two study groups as regards to age, body mass index, gender, and ASA physical status (Table 1).

As regards IFT response; before intubation, no patient followed the command to squeeze the investigator's hand (all were level zero IFT score). On the other hand, there was a significant difference between the 2 study groups as regard incidence of awareness reaction during laryngoscopy and intubation time point. 32% of TIVA

Table 2: Comparison between the 2 study groups as regard IFT response

Response noted		Inhalational Group	TIVA Group	P	Sig
Responders during laryngoscope and intubation by IFT	Non Responder = IFT ≤ 2	23 (92.0)	17 (68.0)	0.03*	S
	Responder = IFT > 2	2 (8.0)	8 (32.0)		
Responders after 1 min from intubation by IFT	Non Responder = IFT ≤ 2	23 (92.0)	21 (84.0)	0.667**	NS
	Responder = IFT > 2	2 (8.0)	4 (16.0)		
Responders during laryngoscopy and intubation by BIS	BIS 40-60	18 (72.0)	18 (72.0)	1.0*	NS
	BIS > 60	7 (28.0)	7 (28.0)		
Responders after 1 min from intubation by BIS	BIS 40-60	24 (96.0)	25 (100.0)	1.0**	NS
	BIS > 60	1 (4.0)	0 (0.0)		

*Chi square test; **Fisher exact test; Data presented as n (%)

Table 3: Agreement between IFT and BIS in detection of responder during laryngoscopy time point and after intubation time point

Response		Responses during laryngoscopy time point by IFT		Kappa	Sig
		Responder	Non Responder		
Response at laryngoscopy by BIS	BIS > 60 = Responder	5 (50.0)	9 (22.5)	0.239	0.118 (NS)
	BIS 40-60 = Non-responder	5 (50.0)	31 (77.5)		
Response at intubation by BIS	BIS > 60 = Responder	0 (0.0)	1 (2.3)	0.036	1.0 (NS)
	BIS 40-60 = Non-responder	6 (100.0)	43 (97.7)		

*Data presented as n (%); *Kappa agreement*

Table 4: Comparative surgical and clinical data of the 2 study groups

Parameter		Inhalational Group	TIVA Group	P	Sig
Duration of surgery		51.56 (6.31)	50.84 (7.51)	0.715 [‡]	NS
Duration of intubation (seconds)		10.28 (3.12)	10.72 (3.22)	0.626 [‡]	NS
Type of surgery	ERCP	13 (52.0)	10 (40.0)	0.777 ^{**}	NS
	Glaucoma	2 (8.0)	3 (12.0)		
	Lipoma excision	4 (16.0)	3 (12.0)		
	Vitrectomy	6 (24.0)	9 (36.0)		
Mallampati score	I	16 (64.0)	16 (64.0)	1.0 [*]	NS
	II	9 (36.0)	9 (36.0)		

*‡ Student t test; *Chi square test; **Fisher exact test
Data presented as Mean ± SD*

Table 5: Comparative hemodynamic parameters in the 2 study groups

Parameter	Inhalational Group	TIVA Group	P	Sig
MAP Baseline	89.28 (12.18)	90.76 (9.90)	0.639	NS
MAP after intubation	93.28 (8.73)	99.40 (11.84)	0.038	S
HR Baseline value	94.00 (10.83)	88.28 (12.81)	0.074	NS
Heart rate after intubation	98.60 (13.53)	95.72 (12.63)	0.440	NS

*Data presented as Mean ± SD, *Student t-test*

group cases were responders (IFT>2) compared to only 8% of inhalational group. Additionally, although there was no significant difference between the 2 study groups after 1 minute of intubation; the incidence was still higher in TIVA group than inhalational group (16% vs. 8%) (Table 2)

Before intubation, mean BIS value was ≤ 50 with no difference between groups. Additionally, there was no significant difference between the 2 study groups as

regard BIS values whether at laryngoscopy phase or after 1 minute from intubation. (Table 2)

There was a poor agreement between BIS and IFT in classifications of responders and non-responders at laryngoscopy phase (kappa = 0.239), as 50% only of responder by IFT were classified as responder by BIS, and 77.5% of non-responders were classified as non-responder by BIS. Also, there was a poor agreement between BIS and IFT in classifications of responders and non-responders after 1 minute from intubation (kappa =

0.0369), as 0% of responders by IFT were classified as responders by BIS, and 97.7% of non-responders were classified as non-responders by BIS (Table 3).

Finally, no patient had postoperative recall, as reported by MBQ, whether within 2 h or 24 h postextubation.

There were no differences between the 2 study groups as regards to surgical and clinical data (Table 4). Regarding hemodynamic data, there was no significant differences (Table 5).

4. Discussion

In this study, we aimed primarily, to compare inhalational induction technique versus intravenous induction technique (TIVA), in old aged patients, regarding awareness reaction incidence. The techniques and the doses were used according to the previous studies.⁶⁻¹³ We chose laryngoscopy and intubation time point, as it is associated with more profound stimulation than surgical incision.¹⁴ Additionally, induction phase of anesthesia usually accounts for half the cases of awareness.¹⁵

From the 50 patients that completed the study, the number of IFT responders at laryngoscopy time point was 10. The majority of cases were in TIVA Group: 8 cases out of 25 cases (32%). While in the inhalational group, only 2 (8%) cases were IFT responders. We also found that, during laryngoscopy and intubation phase, the differences between hemodynamic variations as well as BIS values were insignificant between the two groups, which may indicate their limited predictive value. Finally, none of the patients, suffered from postoperative explicit recall as assessed by MBQ.¹¹

4.1 Old age and awareness

The variability in pharmacodynamics and kinetics is high in old aged population. Usually, smaller doses of anesthetics are needed for clinical effect, and the duration of action of medications is prolonged. Therefore dosing should be carefully titrated by the principle: “start low – go slow”.¹⁶ Unfortunately, it might lead to the probability of under dosing with subsequent intraoperative awareness, especially due the unavailability of accurate continuous monitoring. Very few studies, with conflicting results, had investigated the incidence of awareness according to age.^{12, 17, 18} Only one study had used IFT to detect awareness after intubation.¹⁷

Supporting our results, Pollard and their colleagues¹⁸ analyzed around 87 thousands patients undergoing general anesthesia, for postoperative awareness using MBQ. Only six patients reported instances of recall configuring an awareness incidence of 0.0068%, which is very low than that reported in the recent literature.⁴ All confirmed cases of recall in that study were due to light anesthesia. The reported patients were found to be of

older age (55.5 ± 12.5 y). The very low awareness incidence could be attributed to: the method of data collection that might have missed some subtle cases of awareness as it was a retrospective study, the frequency of patient interviews, and the anesthetics given mostly as per balanced anesthesia protocols, that rely heavily on the use of halogenated anesthetic compounds combined with intravenous narcotics. Balanced anesthesia protocols were assumed by some authors to have a very low incidence of awareness.¹⁴

On the other hand, other researchers, using MBQ, identified a total of 25 awareness cases out of 19000 patients undergoing general anesthesia through a prospective cohort study (0.13% incidence). They stated that age did not influence the incidence of awareness.¹² Similarly, Sanders and their colleagues through a prospective cohort study on the incidence of connected consciousness after tracheal intubation, reported an incidence of 4.6% (12 out of 260 patients). Responders were younger than non-responders (39 ± 17 vs. 51 ± 16 y).¹⁷

4.2 Awareness during laryngoscopy and intubation phase

Generally, our results agree with the reported incidence range of real-time awareness reaction – as detected by IFT, during laryngoscopy and intubation in previous literature; whether intubation and laryngoscopy were done after rapid sequence induction, giving an incidence of 36%, or using TIVA, reporting variable incidences of 24%, 40%, 65% in different studies.^{13, 19, 20, 21}

Surprisingly, three studies reported an incidence of awareness reaction either: 100%,²² or zero%.^{14, 23}

Russel and colleagues, conducted their study on 12 women undergoing gynecological surgeries using TIVA. IFT responses occurred in all the 12 patients at some time during surgery.²² Baraka and their colleagues on the other hand, observed a negative IFT response in all of the 13 full term patients that had undergone cesarean section with an induction to delivery time < 10 min.²³ Ketamine and succinylcholine were used for rapid sequence induction. They attributed their results that ketamine decreased maternal intraoperative awareness. Finally, Parate and colleagues used inhalational based balanced anesthesia, and reported zero incidence of awareness reaction.¹⁴ They stated that after intravenous induction, commencing inhalational agent before laryngoscopy could be a potential solution to reduce awareness reaction. Additionally, the genetic and ethnic impact could be another factor.

4.3 TIVA versus Inhalational technique

TIVA-based technique carries more risk of awareness than end-tidal anesthetic concentration (ETAC)-based inhalational agent technique.²⁴ It could be attributed to

multiple factors. First; propofol has wider interpatient variability in adequate dose requirement and at present, we still lacks easy and rapid monitoring technique for it. Secondly; propofol dose required to make the patient unresponsive may not be adequate to attain unconsciousness.¹⁴ On the other hand, the MAC requirement for movement suppression is usually higher than MAC for suppression of consciousness (i.e., MAC-awake).²⁵ Thirdly, use of inhalation agents with low blood solubility (e.g., sevoflurane and desflurane) allows relatively rapid adjustments in anesthetic concentration and corresponding anesthetic depth.²⁶

In our study, we found a higher incidence of awareness reaction using IFT in TIVA group during laryngoscopy and intubation phase. Similarly, researchers detected awareness reaction using IFT in all 40 to 100% of the patients with TIVA.^{13, 22} A study used the LMA-Fastrach™ insertion technique and remifentanyl/propofol anesthesia (titrated to a BIS of 40 to 65 using TIVA).²⁷ Number of IFT responders was 7/51 (13.5%). This low percentage of awareness reaction could be attributed to the fact that the stimulus of laryngoscopy and intubation might be greater than that of LMA-Fastrach™ intubation.

4.4. Postoperative recall using MBQ

In our study, using MBQ at 2 and 24 h postoperatively, no patient had evidence of explicit recall of intraoperative events. This could be explained that the highest IFT response score in our patients was “level 3”, and it is known that level 4 or 5 responses, usually are associated with a higher rate of recall.⁹ Our results are in concordant with the findings of many previous studies.^{14, 17, 19} Opposed to our data, a large study diagnosed 25 awareness cases out of 19 thousands patients.¹² The researchers interviewed the patients twice. In their study, approximately one third of the cases of awareness were detected in the second interview. They followed previous literature which demonstrated that approximately 35% of postoperative recall cases, are usually detected at a delayed postoperative interview.²⁸

5. Limitation

IFT provides real-time information about the presence of consciousness. But this valuable tool is not without limitations. For one, the patients with connected consciousness may not be able to respond to the command, despite hearing it (for example, due to impaired motivation or anesthetic actions on motor responses). As such, the IFT is a modest estimate of connected consciousness. Moreover, this technique does not allow for the prediction of return of consciousness and prevention of inadequate anesthesia. Finally, with increased duration of cuff inflation (less than 20 min is suggested), the method becomes less reliable, because

anaerobic metabolism impairs neuromuscular function. Finally, rather than conducting the postoperative interview three times as advised, we only did it twice. It is possible to have a delayed recall of events 1-3 weeks after surgery.

6. Conclusion

Intravenous induction technique might subject the patients to a higher incidence of awareness when compared to inhalational induction technique, when isolated forearm technique is used to identify it.

7. Conflicts of Interest

The authors declare that there were no conflicts of interest.

8. Authors' contribution

THI: Study supervision, Drafting

AHA: Conception and design, Drafting

RHM: Drafting, Analysis and interpretation of data

IMI: Acquisition of data. Statistical analysis

MAAI: Conception and design, Statistical analysis

All authors critically revised and reviewed submitted manuscript.

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Appendix 1: Isolated forearm technique response scale proposed by Pandit⁹

Level 0: No response or spontaneous movement

Level 1: Random, spontaneous movement, not associated with any stimulus, where the movement does not localize a stimulus; difficult to identify as a meaningful attempt at communication and is possibly even a reflex

Level 2: Movement in response to tactile stimulus, including painful stimulus (2a, non-localizing movement; 2b, movement that localizes the stimulus)

Level 3: Movement response to direct verbal commands (e.g. 'squeeze hand', 'move your fingers')

Level 4: Movement response to choice questions or conversation (e.g. 'Do you want to be more/less asleep?', 'Are you comfortable?')

Level 5: Spontaneous, purposeful movement initiated by the patient that indicates a desire to communicate; associated with Level 3 or 4 responses when the appropriate questions are asked (e.g. waving arm or hand to indicate distress or seek attention to initiate questioning as above)

Appendix 2: Modified Brice questionnaire¹¹

- 1- What is the last thing you remember before going to sleep?
- 2- What is the first thing you remember waking up?
- 3- Do you remember anything between going to sleep and waking up?
- 4- Did you dream during your procedure?
- 5- What was the worst thing about your operation?

Appendix 3: Modified Brice questionnaire interpretation and awareness categorization¹²

- 1- No awareness: no reported awareness or a vague description, or what had been reported had a high probability of occurring in the immediate pre- or postoperative period; i.e., music, people talking, dressing application
- 2- Dreaming, possibly associated with awareness
- 3- Possible awareness: patient unable to recall any event definitely indicative of awareness
- 4- Awareness: recalled event was confirmed by attending personnel, or the investigators were convinced that the memory was real, but no confirmation could be obtained