Original Research Article

The effects of familiar voices on the level of consciousness among comatose patients: a single-blind randomized controlled trial

ABSTRACT

Background: Brain injury can reduce consciousness and the ability to respond to environmental stimulation.
Objectives: The aim of this study was to investigate the effects of familiar voices on the level of consciousness (LOC) among comatose patients with a brain injury hospitalized in the intensive care unit.
Methods: In this randomized controlled trial, sixty comatose patients with head trauma were conveniently selected from an intensive care unit of a hospital in Rasht, Iran, and randomly allocated to either a control or an intervention group. Participants in the intervention group received auditory stimulation for three consecutive days and the level of consciousness was compared in two groups. The Glasgow Coma Scale was used to assess the patients' level of consciousness. The data were analyzed through the Chi-square, the paired-samples *t*, student's t test, and the repeated-measures analysis of variance.
Results: A significant increase was found in the mean LOC in the intervention group after every daily auditory stimulation ($P<0.05$). However, no significant changes were observed in the control group ($P>0.05$). The repeated-measures analysis of variance revealed that the time and interaction of time and groups were statistically significant ($P<0.001$).

Conclusion: Auditory stimulation with familiar voice was effective in improving levels of consciousness among comatose patients with a brain injury after three days.

Keywords: Coma, Auditory stimulation, Sensory deprivation, Consciousness disorders

1. INTRODUCTION

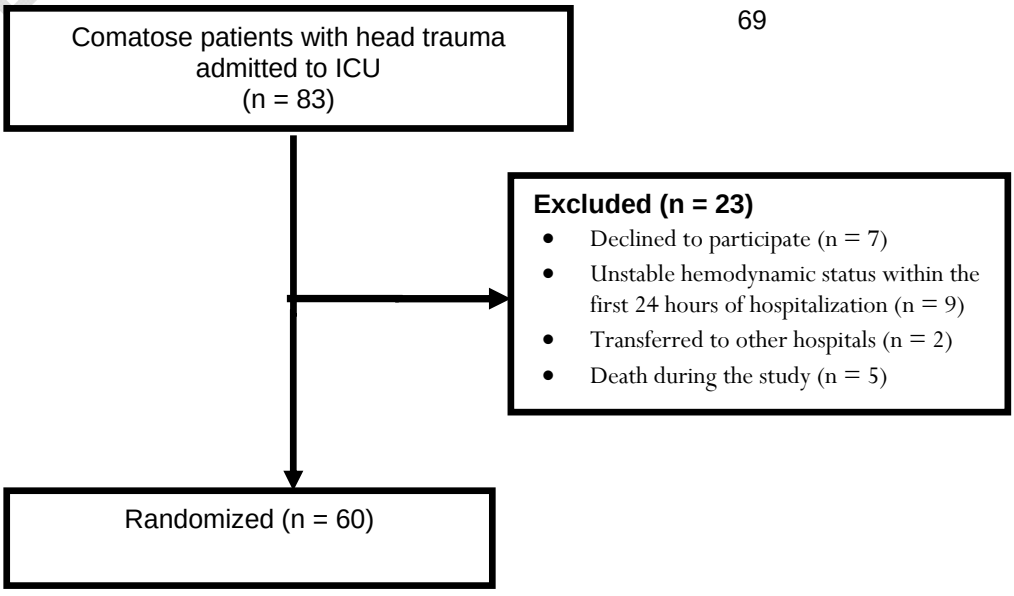
Brain injury (BI) is one of the most common types of trauma (1). Annually, around ten million people experience BI worldwide, of whom five million are from the United States (2). In Iran, BI is the second cause of death (3).
BI is mostly associated with loss of consciousness and coma. Coma, in turn, is the most common cause of hospitalization in intensive care unit (ICU) (4), disabilities, and death (5-8) following accidents. Sensory deprivation is one of the most common aftermaths of coma and hospitalization in ICU. It considerably slows recovery (9). Therefore, strategies are needed to provide comatose patients in ICU with sensory stimulation in order to prevent sensory deprivation.
Sensory stimulation is a therapeutic method which stimulates the reticular activating system in the brain and facilitates the reorganization of brain activities through creating new neural links (10). Auditory stimulation is one of the sensory stimuli which can be provided to patients in ICU by their family members or nurses (11).

Several studies supported the idea and the practice of regular and organized sensory stimulation for comatose patients; however, some of them reported contradictory results (12-15). For instance, a study showed that familiar sensory stimulation had no significant effects on level of consciousness (LOC) (16), while two other studies reported that music therapy calm comatose patients (12) and direct and indirect auditory stimulation may increase their LOC (14). Thus, while sensory stimulation may potentially accelerate brain plasticity, controversies exist over its effectiveness. Therefore, the present study was designed and conducted to produce clearer evidence regarding the effects of auditory stimulation on patient outcomes.

2. MATERIAL AND METHODS

2.1 Design and participants

As a single-blind randomized controlled trial, this study was carried out on patients with head trauma admitted to the ICU of Poursina Trauma Hospital, Rasht, Iran. During the three-month period of the study, i.e. from 14 July to 19 October, 2014, sixty eligible patients were conveniently selected. Eligibility criteria were head trauma of any cause, comatose state with a Glasgow Coma Scale (GCS) score of 3–8 for 72 hours (as determined by a neurologist), an age of over sixteen, an endotracheal or tracheostomy tube in place, stable hemodynamic status (characterized by a blood pressure of 90 to 160 mm Hg(17), a heart rate of 60–100 beats per minute, a respiratory rate of 12–24 per minute, a body temperature of 35.5–38°C), and no history of previous head trauma, brain pathology, convulsion, hearing loss, cardiac arrest, skull fracture, intracranial hemorrhage, and surgery on the temporal lobe of the brain. Exclusion criteria were patient death or hospital discharge during the study and a sudden significant change in hemodynamic status. During the sampling period, 83 patients with head trauma were admitted to the study setting. The legal guardians of seven patients did not consent for participation, seven patients experienced death or were discharged from ICU during the study, and nine had unstable hemodynamic status. Thus, the remaining sixty patients were included (Figure 1).



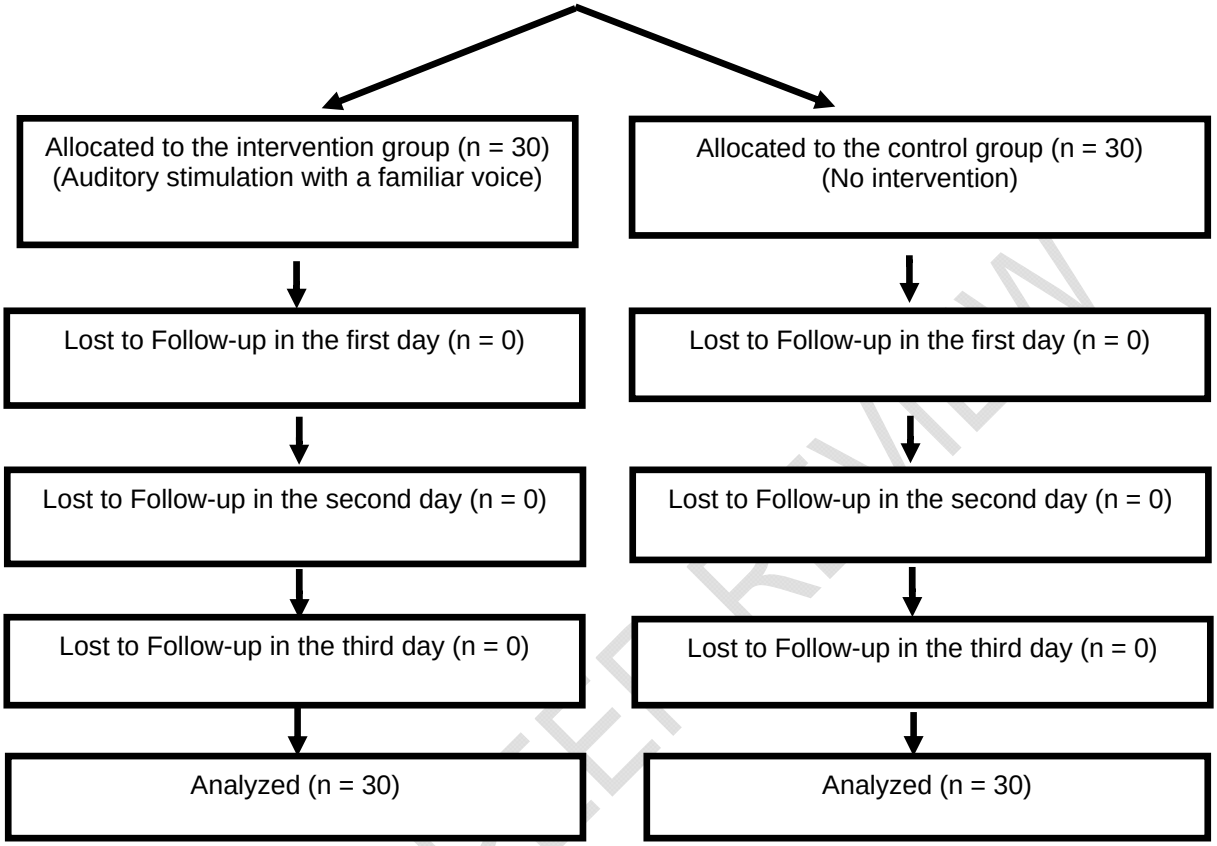


Figure 1. The CONSORT flow diagram of the study

Based on the findings of a previous study (13) and with a type I error of 0.01, a type II error of 0.2, a μ_1 of 7, a μ_2 of 6.2, an S_1 of 0.84, an S_2 of 0.76, and a d of 0.8, sample size was estimated as thirty patients per group based on the following formula.

$$n = \frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 (S_1^2 + S_2^2)}{(\mu_1 - \mu_2)^2}$$

The selected sixty participants were randomly and equally allocated to either a control or an intervention group through block randomization (11). Sampling conducted based on random block process by computer. As the sample size was calculated 60 patients, we used 15 quadruple blocks (with regard to the two existent study groups) and with concealment, 30 patients were allocated to intervention group and 30 individuals to control group.

2.2 Data collection

A four-part instrument was used for data collection. The first part included items on age, gender, marital status, education level, and history of serious illnesses in the past. This part was completed through interviewing participants' family members. The second part included items on participants' clinical characteristics such as the cause of coma, intracranial hemorrhage according to the computed tomography scan findings, surgery for intracranial hematoma management, duration of coma, the need for mechanical ventilation, and medications. The third part contained items on hemodynamic status, namely mean arterial pressure, heart rate, respiratory rate, and body temperature. Data on mean arterial pressure, heart rate, and respiratory rate were obtained from a bedside monitoring device. The monitoring device was also calibrated before measurements. Blood pressure was measured from the right hand through a non-invasive method while the head of bed was elevated by thirty degrees. Body temperature was measured using a mercury-in-glass thermometer. The fourth part was the fifteen-item GCS. The content validity of the first three parts of the instrument was confirmed by ten nursing and medical faculty members.

2.3 Intervention

The study intervention was auditory stimulation through familiar voices. Accordingly, the family of each patient in the intervention group was asked to introduce one of its members who had the closest relationships with the patient. Then, the family members were trained about how to record a ten-minute voice message. The first part of the message was included the information about time and place (thirty seconds) and the accident which had lead to head trauma (thirty seconds).

In the second part that lasted four minutes, they talked about shared sweet memories. In the third part, they spoke promising and encouraging words about the patient's recovery and future subjects (17) (five minutes). This message was recorded in the visitation room of the ICU in the first 24 hours after recruitment to the study and using a voice recorder (LD-73, Lander electronics).The recorded audio files were played for the intended patient in three consecutive days in the afternoon, before the patient's visit time (13).The LOC was assessed using GCS, both five minutes before and five minutes after each auditory stimulation session Moreover, hemodynamic parameters were measured both two minutes before and two minutes after the intervention (17).

Data were collected by the first author who was aware of the allocation sequence. Patients in the control group received no auditory stimulation; but their LOC and hemodynamic parameters were assessed in the same time points as their counterparts in the intervention group.

2.4 Ethical considerations

At the time of sampling, the aim of the study was explained to participants' family members and their informed consent was obtained. They were assured of the confidentiality of their patients' information as well as the voluntariness of participation in and withdrawal from the study. Moreover, we did our best to protect participants' rights according to the Declaration of Helsinki. The study was approved by the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (code: REC.9161.2930162909). It was also registered in the Iranian Registry of Clinical Trials (code: IRCT2014051517693N1).

2.5 Data analysis

The data were analyzed using the SPSS software v. 16.0 (SPSS Inc., Chicago, IL, USA). The Chi-square test was used for between-group comparisons in terms of nominal and ordinal variables such as gender, age, marital status, educational level, mechanism of head trauma, brain tissue injury, and the need for surgery. Moreover, the t-test was used for between-group comparisons in terms of continuous variables such as LOC. The paired-sample *t* test was also used for within-group comparisons in terms of LOC, while the repeated-measures analysis of variance was conducted to compare LOC in both groups

across the three days of the study. The level of statistical significance was set at less than .05

3. RESULTS

Most participants were male (76.6%) and married (61.6%). Age mean in the intervention and the control groups were 35.16 ± 14.1 and 38.13 ± 13.89, respectively. No statistically significant differences were found between the groups in terms of the baseline LOC, clinical characteristics, and hemodynamic parameters (Table 1).

Table 1. Between-group comparisons in terms of participants' demographic and clinical characteristics

Characteristics \ Group		Intervention N (%) or Mean±SD	Control N (%) or Mean±SD	*P* value
Age	16–25	10 (33.3)	5 (16.7)	.807*
	26–35	6 (20)	10 (33.3)	
	36–45	6 (20)	3 (10)	
	46–55	6 (20)	8 (26.7)	
	56–65	1 (3.3)	3 (10)	
	> 65	1 (3.3)	1 (3.3)	
Gender	Male	23 (76.7)	23 (76.7)	.619*
	Female	7 (23.3)	7 (23.3)	
Marital status	Single	12 (40)	10 (33.3)	.49*
	Married	17 (56.7)	20 (66.7)	
	Widowed	1 (3.3)	0 (0)	
Level of Education	Illiterate	5 (16.7)	3 (10)	.141*
	Below diploma	2 (6.7)	8 (26.7)	
	Diploma	12 (40)	7 (23.3)	
	University	11 (36.6)	12 (40)	
Cause of damage	Car accident	15 (50)	16 (53.2)	.508*
	Motorcycle accident	11 (36.7)	7 (23.4)	
	Other	4 (13.3)	7 (23.4)	
LOC (GCS score)		6.1±1.26	5.93±1.33	.658**
Duration of Coma (Hours)		29.76±4.7	32.56±6.72	.102**
Brain tissue injury	Yes	30 (100)	30 (100)	.145*
	No	0 (0)	0 (0)	
Undergoing surgery	Yes	15 (50)	17 (56.7)	.605*
	No	15 (50)	13 (43.3)	

* Chi-square test
** Independent t-test

Within-group comparisons in the intervention group indicated that in each day during the study intervention, posttest value of the LOC was significantly greater than the pretest value (P <.05).Though; the patients were still in coma. No significant changes were observed in the control group in this regard (P >.05; Table 2).

Table 2.patients' daily LOC scores at different times

	Group						P_b	P_c
Group	Intervention (Mean ±SD)			Control (Mean ±SD)				
Day	5 minutes before	5 minutes after	P_a	5 minutes before	minutes after	P_a		

First	5.43±1.1	5.73±1.33	0.005	5.73±1.14	5.76±1.13	< .326	< .305	< .999
Second	5.76±1.19	6.33±1.39	0.001	5.76±1.19	5.8±1.18	< .326	< .908	< .097
Third	6.4±1.32	6.93±1.59	0.001	5.96±1.42	6.03±1.42	< .161	< .224	< .081

a Paired-*t*-test for the comparison of LOC before and after the intervention
b Independent-sample *t*-test for the comparison of LOC in the two groups before the intervention
c Independent-sample *t*-test for the comparison of LOC in the two groups after the intervention

The results of the repeated-measures analysis of variance illustrated significant increase in the posttest mean scores of LOC in intervention group across the three measurement time points ($P < .001$). However, no significant difference was observed in the control group respecting the variations of the posttest mean scores of LOC over time. Also, no statistically significant difference was reported in the effects of the two groups ($P = .141$).There was significant difference in the interaction of time and group ($P < .001$) (Table3).

Table 3: A repeated measures ANOVA to compare mean scores of Glasgow Coma Scale in organized auditory stimulation and control group

Sum of variables	Sum of square	df	Mean square	F	Significant
Within groups					
Time	16.233	.766	9.194	33.075	< .001
Time × groups	6.633	.766	3.757	13.515	< .001
Between groups	11.250	1	11.250	2.226	< .141

No significant differences were observed between the two groups in terms of hemodynamic parameters, namely mean arterial pressure, heart rate, respiratory rate, and body temperature ($P > .05$).

4. DISCUSSION

Findings showed no significant difference between the groups in terms of LOC variations across the three measurement time points. The significant difference was showed to the effects of time in the intervention group, which denotes a significant increase in LOC from the first to the third day in this group. The interaction of time and group was significant that shows LOC of patients in two groups at different stages of the time after the intervention has changed differently.

Moreover, the daily posttest values of LOC in the intervention group were significantly greater than the corresponding pretest values. Consistent with our findings, an earlier study reported significant increase in LOC after auditory stimulation via familiar voices (18). However, the insignificant between-group difference in the present study is inconsistent with the findings of another study which reported higher LOC in the intervention group after a ten-day familiar sensory stimulation (13). Longer duration of intervention in that study compared to the three-day intervention of the present study may account for this discrepancy between these two studies. Moreover, another study into the comparison of the effects of a three-day auditory stimulation intervention reported improvements in patients' LOC(13). The significant effects of sensory stimulation on LOC can be attributed to the high prevalence of sensory

deprivation among patients in ICU as well as the positive effects of sensory stimulation on the reticular activating system.

Study findings also revealed significant improvements in LOC after each daily auditory stimulation with familiar voice in the intervention group. However, it remained unknown whether familiar voice or auditory stimulation accounted for LOC improvements. Considering another group with another type of auditory stimulation could answer this question. Salmani et al., (2017) conducted a study into the effects of affective sensory stimulation including auditory stimulation in comatose patients during the first seven days of their hospitalization. The results of the study showed significant improvements in LOC in the intervention group and no significant changes in the control and the placebo groups (19).

The findings indicated no significant difference between the intervention and the control groups in terms of participants' hemodynamic parameters. This finding may be attributable to the short course of the study intervention and the short period of follow-up assessment. However, some contradictions were seen regarding auditory stimulation effect on hemodynamic changes in comatose patients. Puggina et al.,(2011) showed a significant increase in the hemodynamic responses in the auditory stimulation group(20). Inconsistency in the results could be due to the type of auditory stimulus and different sounds that can have different effects on patient. Also it may be said that the patients in the present study were in a more critical condition than the patients in other studies.

Another finding of the present study was that the study intervention had no adverse effects on participants' brain activities. Similarly, two previous studies reported that due to its non-invasiveness, auditory stimulation can improve brain activities without exerting significant side effects (18, 21).

Among the limitations of the present study were our uncertainty about the patients' favorite family members as well as the short course of the study intervention. Moreover, GCS is a general LOC assessment tool (22) which is not sensitive enough to the small changes in LOC. The impossibility of performing the study using a double-blind design as well as the differences in participants' medical treatment regimens might also have affected the study results. Future studies are recommended to use double-blind designs and provide auditory stimulation with familiar voices for longer periods of time and with more than one auditory stimulation session per day.

5. CONCLUSION

This study indicates that auditory stimulation with the familiar voices of patients' family members may improve LOC among patients with head trauma after three days. Thus, this technique can be used to improve the LOC of these patients during their ICU stay. Of course, longer auditory stimulation with familiar voices may produce more significant effects on the LOC.

CONSENT AND ETHICAL APPROVAL

This study was conducted after receiving the written approval of the Ethics Committee of Guilan University of Medical Sciences with ethics code (No: REC.9161.2930162909).Before starting the sampling, we explained to the participants in terms of the objectives of the research and the data collection process. Also, written informed consent was obtained from all of samples.

COMPETING INTERESTS

The authors have no conflict of interest.

ETHICAL APPROVAL

This study was conducted after obtaining the approval of the Ethics Committee of deputy of research and technology of Guilan University of Medical Sciences with Ethical code number REC.9161.2930162909) and the Iranian Center for Clinical Practice ID(code: IRCT2014051 517693N1). Before performing the sampling, the participants received descriptions in terms of the aims of the study, the method of study and their rights and their expectations at each stage of the research, and in case of willingness they sign the written inform consent for participation in the study.

References

1. Parveen Y, Dhandapani M, Dhandapani S, Gupta SK. A randomized controlled trial to assess the efficacy of auditory stimulation on selected parameters of comatose patients with traumatic brain injury. Indian Journal of Neurotrauma. 2015;12(02):128-34.

2. Ahmed S, Venigalla H, Mekala HM, Dar S, Hassan M, Ayub S. Traumatic brain injury and neuropsychiatric complications. Indian J Psychol Med. 2017;39(2):114.http://dx.doi.org/10.4103/0253-7176.203129. [PMID: 28 515545].

3. Saatian M, Ahmadpoor J, Mohammadi Y, Mazloumi E. Epidemiology and pattern of traumatic brain injury in a developing country regional trauma center. Bull Emerg Trauma. 2018;6(1):45. http://dx.doi.org/10.29252/beat-060107. [PMID: 29379809].

4. Liew B, Zainab K, Cecilia A, Zarina Y, Clement T. Early management of head injury in adults in primary care. Malays Fam Physician 2017;12(1):22.[PMID: 28503270].

5. Dash HH, Chavali S. Management of traumatic brain injury patients. Korean J Anesthesiol. 2018;71(1):12-21. http://dx.doi.org/10.4097/kjae. 20 18. 71.1.12. [PMID: 29441170].

6. Algattas H, Huang JH. Traumatic brain injury pathophysiology and treatments: early, intermediate ,and late phases post-injury. nt J Mol Sci. 2013;15(1):309-41. http://dx.doi.org/10.3390/ijms15010309. [PMID: 24381049].

7. Andrews PJ, Sinclair HL, Rodriguez A, Harris BA, Battison CG, Rhodes JK, et al. Hypothermia for intracranial hypertension after traumatic brain injury. NEJM. 2015;373(25):2403-12. http://dx.doi.org/10.1056/ NEJMoa1507581. [PMID: 26444221].

8. Prince C, Bruhns ME. Evaluation and treatment of mild traumatic brain injury: The role of neuropsychology. Brain Sci. 2017;7(8):105. http://dx.doi.org/10.3390/brainsci7080105. [PMID:28817065].

9. Moattari M, Shirazi FA, Sharifi N, Zareh N. Effects of a sensory stimulation by nurses and families on level of cognitive function, and basic cognitive sensory recovery of

comatose patients with severe traumatic brain injury: a randomized control trial. Trauma Mon. 2016;21(4):http://dx.doi.org/10.5812/traumamon. 23531. [PMID: 28180120] .

10. Shaffer J. Neuroplasticity and clinical practice: building brain power for health. Front Psychol. 2016;7:1118. http://dx.doi.org/10.3389/fpsyg. 2016.01118. [PMID: 27507957] .

11. Grap MJ, Munro CL, Wetzel PA, Ketchum JM, Ketchum JS, Anderson WL, et al. Stimulation of critically ill patients: relationship to sedation. Am J Crit Care. 2016;25(3):e48-e55. http://dx.doi.org/10.4037/ajcc2016269. [PMID: 27134238] .

12. Dijkstra BM, Gamel C, Van Der Bijl JJ, Bots ML, Kesecioglu J. The effects of music on physiological responses and sedation scores in sedated, mechanically ventilated patients. J Clin Nurs. 2010;19(7-8):1030-9. http://dx.doi.org/10.111/j.365-2702.009.02968.x. [PMID: 20492047].

13. Hosseinzadeh E, Mahmoodi SGR, Vakili MA, Kazemnejad K, Mohammadi MR, Taziki MH, et al. The Effect Of Voice Auditory Stimulation On The Consciousness Of The Coma Patients Suffering From Head Injury. Journal of research development in Nursing & Midwifery. 2013;10:1-9.[persian].

14. Park S, Davis AE. Effectiveness of direct and non□direct auditory stimulation on coma arousal after traumatic brain injury. Int J Nurs Pract. 2016;22(4):391-6. http://dx.doi.org/10.1111/ijn.12448. [PMID: 27241789].

15. Tavangar H, Shahriary-Kalantary M, Salimi T, Jarahzadeh M, Sarebanhassanabadi M. Effect of family members' voice on level of consciousness of comatose patients admitted to the intensive care unit: A single-blind randomized controlled trial. Adv Biomed Res. 4;2015. http://dx.doi.org/10.4103/2277-9175.157806. [PMID: 26261808].

16. Hasanzadeh F, Hoseini AT, Esmaily H, Ehsaee MR. THE Impact of Familiar Sensory stimulation On Level of Consciousness in Patient with Head Injury in Icu. Journal of north khorasan university of medical sciences. 2012;4(1):121-33.[persian].

17. Haddad SH, Arabi YM. Critical care management of severe traumatic brain injury in adults. Scand J Trauma Resusc Emerg Med. 2012;20(1):12.

18. Gorji MAH, Araghiyansc F, Jafari H, Gorgi AMH, Yazdani J .Effect of auditory stimulation on traumatic coma duration in intensive care unit of Medical Sciences University of Mazandarn, Iran. Saudi J Anaesth. 2014;8(1):69. http://dx.doi.org/10.4103/1658-354X.125940. [PMID: 24665243] .

19. Salmani F ,Mohammadi E, Rezvani M, Kazemnezhad A. The effects of family-centered affective stimulation on brain-injured comatose patients' level of consciousness: A randomized controlled trial. Int J Nurs Stud. 2017;74:44-52. http://dx.doi.org/10.1016/j.ijnurstu. [PMID: 28601692] .

20. Puggina ACG, da Silva MJP, Santos JLF. Use of music and voice stimulus on patients with disorders of consciousness. J Neurosurg Nurs. 2011;43(1):E8-E16.

21. Schnakers C, Magee WL, Harris B. Sensory stimulation and music therapy programs for treating disorders of consciousness. Front Psycho. 2016;7:297. http://dx.doi.org/10.3389/fpsyg.2016.00297. [PMID: 27014119] .

22. Yeganeh MR, Gholami S, Tabari R, Atrkar Roshan Z, Rimaz S. The effect of controlled sedation based on the Richmond scale on the duration of mechanical ventilation and the changes of blood pressure in patients following coronary artery bypass graft surgery: A randomized clinical trial. Journal of hayat. 2018;23(4):372-86.[persian].