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The Value of Using Amantadine Upon Improving Conscious Level in Isolated Head Trauma Patients Guided by Glasgow Coma Scale and Bispectral Index

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Abstract

Background: We performed the current study to find out the effect of Amantadine upon rate of improvement of conscious level in patients with isolated head injuries undergoing surgical intervention.

Aim of the Study: Finding out the value of using Amantadine upon improving of consciousness in head trauma patients.

Patients and Methods: Patients in group 1 (n=20) were given amantadine intraoperative at a dose of 100mg IV infusion over 3 hours, then amantadine were given at a dose of 100mg IV infusion over 3 hours every 12 hours for 7 days then was switched to tablet form at a dose of 300mg per day divided into 3 equal doses, the 1 st was given in the morning and the last before 5 o'clock PM.

Patients in group 2 (n=20) were given placebo instead at the same form and intervals.

Glasgow coma scale and bispectral index readings were recorded at time of arrival, immediate post operative, 3 days and 2 weeks post operative.

Results: We found that Glasgow coma scale rate of improvement in group 1 was 4.53±2.61 and in group 2 was 2.11 ±2.81 which is statistically significant p-value 0.014.

Conclusion: We conclude from this study that the rate of improvement of patients given amantadine was significantly higher than those given placebo.

Key Words: *Amantadine – Glasgow coma scale – Bispectral index.*

Introduction

TRAUMATIC brain injury (TBI) is the leading cause of death among adults younger than 45 yr and in children (1-15 yr). The majority of TBI is classified as mild, and around 8-10% is classified as moderate or severe **[1]**.

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TBI has been divided into two distinct periods: Primary and secondary brain injury. The primary injury is the result of the initial, mechanical forces, resulting in shearing and compression of neuronal, glial, and vascular tissue. Axonal tissue is more susceptible to the injury than vascular tissue. Thus, focal injuries are usually superimposed upon more diffuse neuronal injury. The consequences of the initial injury include physical disruption of cell membranes and infrastructure, and disturbance of ionic homeostasis secondary to increased membrane permeability **[2]**.

The decision to use pharmacological intervention should be the result of multidisciplinary collaboration and made with the patient or his or her substitute decision maker. Goals of therapy should be clarified, and outcomes and adverse events should be reliably tracked, particularly so medications that are ineffective or cause adverse events can be discontinued and unnecessary poly pharmacy can be avoided **[3]**.

Selecting the most appropriate agent requires careful analysis of the neurological disabilities present, the nature of the underlying lesion, and the time elapsed since the injury **[4]**.

Amantadine is a weak antagonist of the NMDA-type glutamate receptor, increases dopamine release, and blocks dopamine reuptake **[я]**. This makes it a weak therapy for Parkinson's disease. As an antiparkinsonian, it can be used as monotherapy, or together with L-DOPA to treat L-DOPA-related motor fluctuations (i.e., shortening of L-DOPA duration of clinical effect, probably related to progressive neuronal loss) and L-DOPA-related dyskinesias (choreiform movements associated

with long-term L-DOPA use, probably related to chronic pulsatile stimulation of dopamine receptors).

The first study of the use of amino-adamantane as an NMDA antagonist for influencing vigilance was published by Wallnfter and Schiller in 1974 [6]. In comatose conditions, very good results were achieved in 41.6%. In a further study in 1975 [7] in which 1 6 patients with severe disturbances of consciousness were treated with amantadine infusions 400mg daily, 6 patients responded very well and 4 responded well. In 1989 the results for 30 brain injured patients [8] who received 50 to 400 mg amantadine sulfate daily were presented, 19 of whom had very good to good results in respect of arousal, attention and drive. A significant elevation in cognitive performance was demonstrated in 1992 [9] in 20 patients. The electroencephalogram showed a significant effect in 20 patients in a further study in 1992 [10]. These effects were chiefly temporo-occipital, fronto-temporal and temporal and were accompanied by a psychometrically differentiable improvement in brain function 6 hours after administration of the drug (200mg amantadine infusion). Also, in a clinical study [11] in 1993 it was demonstrated in 52 patients that amantadine was effective in 92% of patients, very good to good results being achieved in 71% of cases. Since numerous experimental studies of the action mechanism have demonstrated that amantadine acts as a non-competitive NMDA receptor antagonist and increases vigilance by modulating the glutamatergic system [12].

Patients and Methods

The study has been approved by the Department of Anaesthesia at Kasr El-Aini Hospital, Cairo University and the local ethics and research committee. Written informed consent was obtained from the relatives of each patient before operation.

This study had enrolled 40 patients with moderate to severe isolated head injury undergoing emergency head surgical procedure at Cairo University Hospital, in 2014 and 2015.

Inclusion criteria: Patients with ASA physical status I or II with age from 1 6 to 65 years old, having isolated head injury undergoing surgical intervention and with Glasgow coma scale 12 or less.

Exclusion criteria: Patient with ASA III and IV, Patients younger than 1 6 years old, patients older than 65, Patients with history of epilepsy, Patients with renal impairment, Patients with Glasgow coma scale more than 12, Patients with polytrauma, patients with history of schizophrenia.

Study groups:

I- Group 1 : 20 patients to whom Amantadine were given intraoperative at a dose of 100mg IV infusion over 3 hours, then amantadine was given at a dose of 100mg IV infusion over 3 hours every 12 hours for 7 days then was switched to tablet form at a dose of 300mg per day divided into 3 equal doses, the 1 st was given in the morning and the last before 5 o'clock PM.

II- Group 2: 20 patients to whom placebo were given instead of amantadine at the same form and intervals.

Randomization was done using a sealed envelop technique that contained 20 labels of (amantadine) and another 20 labels of (placebo).

- Careful anesthetic history obtained from relatives.
- Good assessment of patient Glasgow coma scale.
- Full physical examination of all systems was done.

On arrival in the operating room:

Patients will be monitored using: ECG, noninvasive blood pressure (NIBP) and pulse oximetery (SpO2). Also, bispectral index will be monitored and the average of base line readings will be recorded.

Rapid sequence inducion will be performed, using propofol 1-2mg/kg, rocuronium 0.6mg/kg and fentanyl 1-2mic/kg.

Amantadine was given to patients of the first group intraoperative at a dose of 100mg IV infusion over 3 hours, then amantadine was given at a dose of 100mg IV infusion over 3 hours every 12 hours for 7 days then was switched to tablet form at a dose of 300mg per day divided into 3 equal doses, the 1 st was given in the morning and the last before 5 o'clock PM. second group patients were given placebo instead at the same form and intervals.

Both groups were treated by our standard treatment protocol (mechanical ventilation with slightly hypocapnia, head position, sedation, temperature control, seizures control, euvolemia with mean blood pressure more than 70mm Hg, parentral and enteral feeding, antibiotics).

Measurements:

- Glasgow coma scale at time of arrival, immediate post operative, after 3 days and after 2 weeks.

• Bispectral index reading at time of arrival, immediate post operative, after 3 days and after 2 weeks.

Statistical analysis:

Data were coded and entered using the statistical package SPSS version 22. Data was summarized using mean, standard deviation, median, minimum and maximum. Comparisons between groups were done using the non–parametric Mann-Whitney test. Comparison between values measured at arrival and after 2 weeks were done using the non–parametric Wilcoxon signed rank test. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between variables was done using Spearman correlation coefficients. p-values less than 0.05 were considered as statistically significant.

Results

Demographic data analysis including sex, age, type of injury between both groups were performed and showed that there were no statistically significant differences between the study groups as regards patients data (p-value <0.05) (Table 2).

There were 14 male and 6 female patients in group1 and 15 male and 5 female in group 2.

There were 6 patients with acute subdural hematoma, 12 patients with extradural hematoma, 0 patient with gunshot to the head and 2 patient with intracerebral hematoma in group 1.

There were 4 patients with acute subdural hematoma, 12 patients with extradural hematoma, 1 patient with gunshot to the head and 3 patient with intracerebral hematoma in group 1.

The age of patients in both groups ranged from sixteen to sixty three years old. In group1 the mean age was 31.65± 12.84 years old versus 29.85 ± 12.51 years old in group 2 which is statistically insignificant p-value 0.655 (Table 3).

Analysis of the Glasgow coma scale in both groups at time of arrival, immediate postoperative, 5 days postoperative and 2 weeks postoperative:

- The Glasgow coma scale at time of arrival was 7.00±2.75 in group 1 and 7.9±2.67 in group 2 which was statistically insignificant p-value 0.311.
- The Glasgow coma immediate post operative was 7.55±3.07 in group 1 and 8.20±2.91 in group 2 which was statistically insignificant p-value 0.556.
- The Glasgow coma scale 5 days postoperative was 10.00±3.61 in group 1 and 9.9±3.6 in group 2 which was statistically insignificant p-value 0.944.
- The Glasgow coma scale 2 weeks postoperative was 11.74±4. 15 in group 1 and 10. 11 ±4.56 in group 2 which was statistically insignificant p-value 0.271.

Analysis of the bispectral index readings in both groups at time of arrival, immediate postoperative, 5 days postoperative and 2 weeks postoperative:

- The bispectral index at time of arrival was 55.05 ± 12.48 in group 1 and 56.25 ± 11.72 in group 2 which was statistically insignificant p-value 0.892.
- The bispectral index just post operative was 57.00 ± 13.53 in group 1 and 57.00± 11.43 in group 2 which was statistically insignificant p-value 0.787.
- The bispectral index 5 days postoperative was 67.89± 13.90 in group 1 and 66.00 ± 16.42 in group 2 which was statistically insignificant p-value 0.768.
- The bispectral index 2 weeks postoperative was 74.26± 16.84 in group 1 and 67.32± 18.80 in group 2 which was statistically insignificant p-value 0.261.

Analysis of improvement of Glasgow coma scale in both groups since arrival till 2 weeks postoperative:

- In amantadine group, the GCS was 7.00±2.75 at time of arrival and became 11.74±4.15 two weeks postoperative which is a statistically significant improvement (p-value <0.001).
- In placebo group, the GCS was 7.90 ±2.67 at time of arrival and became 10.11 ±4.56 two weeks postoperative which is a statistically significant improvement (p-value 0.006).

Analysis of improvement of BIS readings in both groups since arrival till2 weeks postoperative:

- In amantadine group, the BIS readings were 55.05± 12.48 at time of arrival and became 74.26 ± 16.84 two weeks postoperative which is a statistically significant improvement (p-value <0.001).
- In placebo group, the GCS was 56.25 ± 11.72 at time of arrival and became 67.32 ± 1 8.80 two weeks postoperative which is a statistically significant improvement (p-value 0.002).

Analysis of the rate of improvement (the relation between the change in GCS and BIS at time of arrival and two weeks postoperative) between the two groups:

- Glasgow coma scale rate of improvement in group1 was 4.53±2.61 and in group 2 was 2.11±2.81 which is statistically significant p-value 0.014.
- But Bispectral index improvement in group 1 was 18.11±10.65 and in group 2 was 10.58±11.69 which is statistically insignificant p-value 0.062.

Table (1): Patients' sex and type of trauma data.

	Amantadine group		Placebo group		p-value
	Count	%	Count	%	
ex:					
F	6	30.0	5	25.0	0.723
M	14	70.0	15	75.0	
Type of injury:					
Acute subdural hematoma	6	30.0	4	20.0	0.810
Extradural hematoma	12	60.0	12	60.0	
Gunshot to head	0	.0	1	5.0	
Intracerebral hematoma	2	10.0	3	15.0	

Table (2): Patients' age data.

	Amantadine group					Placebo group					p-value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age	31.65	12.84	29.00	16.00	60.00	29.85	12.51	26.00	17.00	63.00	0.655

Table (3): Analysis of the Glasgow coma scale in both groups at time of arrival, immediate postoperative, 5 days postoperative and 2 weeks postoperative.

	Amantadine group					Placebo group					p-value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
GCS at time of arrival	7.00	2.75	7.50	3.00	12.00	7.90	2.67	8.00	4.00	12.00	0.311
GCS directly postoperative	7.55	3.07	8.00	3.00	13.00	8.20	2.91	8.00	4.00	13.00	0.556
GCS 5days postoperative	10.00	3.61	11.00	3.00	15.00	9.90	3.60	10.00	4.00	15.00	0.944
GCS 2 weeks postoperative	11.74	4.15	14.00	3.00	15.00	10.11	4.56	11.00	3.00	15.00	0.271

Table (4): Analysis of bispectral index readings in both groups at time of arrival, immediate postoperative, 5 days postoperative and 2 weeks postoperative.

	Amantadine group					Placebo group					p-value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
BIS at time of arrival	55.05	12.48	56.50	34.00	78.00	56.25	11.72	53.00	38.00	78.00	0.892
BIS directly postoperative	57.00	13.53	58.50	32.00	80.00	57.00	11.43	55.00	40.00	76.00	0.787
BIS 5 days postoperative	67.89	13.90	69.00	44.00	92.00	66.00	16.42	66.00	39.00	87.00	0.768
BIS 2 weeks postoperative	74.26	16.84	81.00	39.00	93.00	67.32	18.80	68.00	36.00	91.00	0.261

Table (5): Analysis of improvement of Glasgow coma scale in both groups since arrival till 2 weeks postoperative.

	Amantadine group					Placebo group				
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum
GCS at time of arrival	7.00	2.75	7.50	3.00	12.00	7.90	2.67	8.00	4.00	12.00
GCS 2 weeks postoperative	11.74	4.15	14.00	3.00	15.00	10.11	4.56	11.00	3.00	15.00
p-value			<0.001					0.006		

Table (6): Analysis of improvement of BIS readings in both groups since arrival till 2 weeks postoperative.

	Amantadine group					Placebo group				
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum
BIS at time of arrival	55.05	12.48	56.50	34.00	78.00	56.25	11.72	53.00	38.00	78.00
BIS 2 weeks postoperative	74.26	16.84	81.00	39.00	93.00	67.32	18.80	68.00	36.00	91.00
p-value	<0.001					0.002				

Table (7): Analysis of the rate of improvement (the relation between the change in GCS and BIS at time of arrival and two weeks postoperative) between the two groups.

	Amantadine group					Placebo group					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	*p*-value
GCS improvement (2W post–at arrival)	4.53	2.61	4.00	.00	9.00	2.11	2.81	2.00	–4.00-	7.00	0.014
BIS improvement (2W post–at arrival)	18. 11	10.56	18.00	.00	38.00	10.58	11.69	10.00	–15.00-	32.00	0.62

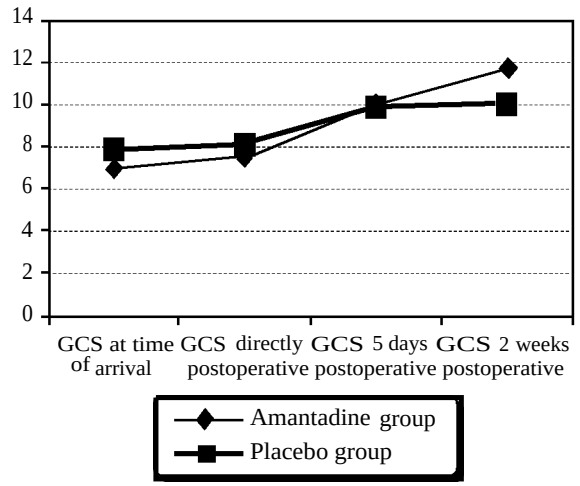

Fig. (1): Rate of improvement (the relation between the change in GCS at time of arrival and two weeks postoperative) between the two groups.

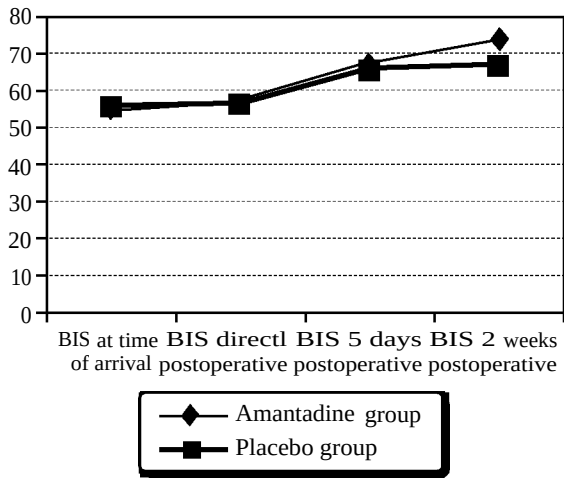

Fig. (2): Rate of improvement (the relation between the change BIS readings at time of arrival and two weeks postoperative) between the two groups.

Discussion

Despite the prevalence and cost of TBI-related disabilities there is a paucity of literature reviewing modern approaches to pharmacotherapy. There is, however, growing evidence that medications may speed recovery by enhancing some neurological functions without impacting others.

Pharmacotherapy is increasingly being used in both the sub acute (less than 1 month post-TBI) and chronic (more than 1 month post-TBI) phases.

Pharmacological treatments of patients with disorders of consciousness aim to improve arousal levels and recovery of consciousness.

Amantadine was used as an antiviral and antiparkinsonian agent **[13,14]**.

Multiple case reports support the use of amantadine as an effective drug for improving conscious level and vigilance.

A case report by Zafonte et al., **[15]** evaluated the impact of amantadine on cognition in a male 35 y who had been assaulted to the head with a blunt object. The patient presented with a GCS score of 3. The patient showed improvement at a dose of 400mg/day. The patient was rehabilitated to become independent in his activities of daily living.

Also, Wu and Garmel **[16]** reported a female 82y with improved ability to function after use of amantadine for TBI. She remained unresponsive after a motor car accident with a GCS of 6 for 3 days before the use of amantadine. After 6 doses

of amantadine 150mg bid, she could withdraw from pain, open her eyes spontaneously, and respond to her name. By day 7, she was alert and oriented.

Sawyer et al., [17] study is a meta analysis in which the previous two case reports were included. 3 retrospective studies, and 2 randomized, double blind, controlled trials of amantadine therapy for early arousal in TBI were identified and reviewed. improvements in arousal and cognition, have been observed in patients with TBI when amantadine has been initiated 3 days to 5 months after injury. At doses of 200-400mg/day.

However, multiple limitations were observed as the studies show variability in designs some study designs were retrospective where biases in patient selection and treatment allocation could not be prevented, heterogeneity in patient populations, Causes of TBI were often heterogeneous, and time from injury was also often variable and sometimes not stated. In addition, amantadine dosing and treatment duration were variable, time following injury, and use of numerous different outcome measures (the glassgow coma scale, the Disability Rating Scale (which has a score of 29 points assessing patient's arousability, awareness, responsivity, cognitive ability for self care, dependence on others and psychosocial adaptability), Coma Recovery Scale-Revised (CRS-R) scores (which consists of 23 items that comprise 6 subscales addressing auditory, visual, motor, communication and arousal functions), EEG and biochemical markers), Clinical observations were likely performed by non blinded staff and may not have been performed by the same staff for all patients.

We conducted our study design in a different way than most of the previous studies that, amantadine was used in patients undergoing surgery only, was started very early in the operative theatre and bispectral index was used with Glasgow coma scale as parameters for assessing conscious level.

In our current study, both groups, amantadine group and placebo show improvement in conscious level guided by comparing the results of Glasgow coma scale at time of arrival and 2 weeks post operative.

In amantadine group, the GCS was 7.00 ±2.75 at time of arrival and became 11.74 ±4. 15 two weeks postoperative which is a statistically significant improvement (p-value <0.001).

In placebo group, the GCS was 7.90 ±2.67 at time of arrival and became 10. 11 ±4.56 two weeks postoperative which is a statistically significant improvement (p-value 0.006).

These results are consistent with Giacino et al., [18] in which, 184 patients in a vegetative or minimally conscious state (a condition of severely altered consciousness in which minimal but definite behavioral evidence of self or environmental awarenees), 4 to 1 6 weeks after traumatic brain injury and receiving inpatient rehabilitation were randomly assigned to receive amantadine or placebo for 4 weeks and were followed for 2 weeks after the treatment was discontinued. The rate of functional recovery on the Disability Rating Scale (DRS; range, 0 to 29, with higher scores indicating greater disability), was compared over the 4 weeks of treatment (primary outcome) and during the 2-weeks. Both groups show significant improvement in conscious level guided by disability rating scale.

But in Saniova study [19], it was different, 74 patients with severe head injury (GCS <8) were divided into two group, in 1 st group amantadine was started 3 days post trauma in 41 patients at a dose of 200mg bid, the level of consciousness has improved in 39, the average initial GCS in this group was 4.74±2.26 and the average outcome GCS of the surviving patients was 9.76±3.95.

Patients after regaining consciousness were transferred to other departments. Mean hospitalization time of the patients was 8.36 days. Only two patients died in this group (6.06%).

In placebo group, there were 33 patients with average income GCS 4.70±2. 14, mean hospitalisation time was 9.36 days. The average outcome GCS was 5.73±3.57 and 17 patients died (51.51%).

But B. Saniova [19] was a retrograde pilot study of patients only with severe head injury which may explain the great difference in results.

In our current study, upon comparing the two groups (amantadine and placebo) regarding conscious level guided by Glasgow coma scale readings preoperative, immediately postoperative, 5 days postoperative and 2 weeks postoperative, there was no statistically significance.

But when comparing the rate of improvement (the relation between the change in GCS at time of arrival and two weeks postoperative) between the two groups.

Glssgow coma scale rate of improvement in group 1 was 4.53±2.61 and in group 2 was 2. 11 ± 2.81 which is statistically significant p-value 0.014.

This may be explained that amantadine group started with patients with lower Glasgow coma scale on arrival than placebo group, but statistically insignificant and ended up with statistically insignificant higher readings after 2 weeks.

The net result was a statistically significant change in improvement of conscious level guided by Glasgow coma scale between the two groups.

This improvement is consistent with Giacino et al., study, **[18]**. which was a multicenter, randomized, controlled trial. During the 4-weeks treatment period, recovery was significantly faster in the amantadine group than in the placebo group, as measured by the DRS score (p=0.007), indicating a benefit with respect to the primary outcome measure. In a prespecified subgroup analysis, the treatment effect was similar for patients in a vegetative state and those in a minimally conscious state. The rate of improvement in the amantadine group slowed during the 2 weeks after treatment (weeks 5 and 6) and was significantly slower than the rate in the placebo group (p=0.02). The overall improvement in DRS scores between baseline and week 6 (2 weeks after treatment was discontinued) was similar in the two groups.

Also, our results are consistent with Hughes et al., **[20]** study, in which 123 patients with severe head injury (GCS less than 8) were divided into two groups, in 1 st group 28 patients were given amantadine at a dose of 100 to 200mg twice daily. 95 patients were a control group.

46% of patients in amantadine group showed emergence from coma while only 38% of patients in placebo group showed emergence.

These low results may be explained that, patients with severe head injury were the only candidates of the study.

Also, our results are consistent with Meythaler et al., **[21]**, a cross over study, in which 35 patients four days to six weeks post trauma with GCS ≤ 10 at 1 st 24 hours after injury, were divided into two groups, in 1 st group 15 patients were given amantadine at dose of 200mg/day for 6 weeks followed by placebo for another 6 weeks without washout. 20 patients in second group were given placebo for 6 weeks followed by amantadine for another 6 weeks.

Disability rating scale was observed, it was found that patients improved more while being on amantadine.

Only one study Schneider et al., **[22]** suggests that no significant difference in rates of improvement for patients receiving placebo versus amantadine, the study was a cross over study carried on patients with closed head injury in rehabilitation unit, only 10 patients were candidates for the study, patients were divided into two groups, patients were given amantadine or placebo for 2 weeks followed by 2 weeks wash out then the alternative was given (placebo or amantadine), amantadine was given in doses of 50 to 150mg twice daily.

This different results could be explained that, the sample size was small (10 patients only), the wash out period, doses of amantadine was relatively small.

In our current study bispectral index was used as a parameter to assess conscious level beside the clinical assessment (Glasgow coma scale).

As far as we know No other study made use of bispectral index but some made use of the same principle (electrical monitoring of the brain) in form of EEG monitoring such as Steube et al., **[23]**, in this study A connection was not always seen between the clinical therapeutic outcomes and the EEG changes. Thus, clinical improvements were seen without a corresponding EEG correlate and, on the other hand, patients with prompt normalization of the EEG curve did not always show the expected clinical improvement. Patients who showed normal basic EEG activity at the start of treatment derived particular benefit from amantadine therapy. These patients showed very good or good therapeutic outcomes in 84% of cases.

Others used biochemical observations such as Saniova et al., **[19]**.

In our current study, upon comparing the two groups (amantadine and placebo) regarding conscious level guided by Bispectral index readings preoperative, immediately postoperative, 5 days postoperative and 2 weeks postoperative, there was no statistically significance.

These results are also consistent with our results of Glasgow coma scale.

But, when comparing the rate of improvement (the relation between the change in BIS at time of arrival and two weeks postoperative) between the two groups.

Bispectral index improvement in group 1 was 18.11 ± 10.65 and in group 2 was 10.58 ± 11.69 which is statistically insignificant p-value 0.062.

The improvement in group 1 was slightly higher than group 2 but still statistically insignificant, which is different from the results obtained when comparing the improvement in Glasgow coma scale.

This may be explained that, despite the strong correlation between BIS and GCS, most of the studies show high degree of scatter of BIS values for any given GCS score, indicating the lack of determination between BIS and GCS [24].

Some studies such as Gill et al., [25] stated that BIS monitoring did not reliably correlate with GCS in emergency department patients as they noted a moderate correlation. The problem with this moderate correlation was the wide variability of BIS values corresponding to GCS.

Conclusion:

We found from this study that the rate of improvement of patients given amantadine was significantly higher than those given placebo.

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قيمة أستخدام عقار الأمانتادين على تحسين درجة الوعى فى مرضى إصابات الرأس المنعزلة استرشاداً بمقياس جلاسجو لدرجة الوعى ومقياس ثنائى الطيف

أستخدام عقار الأمانتادين فى علاج العدوى الفيروسية وكدواء فعال لعلاج الشلل الرعاش مؤخراً ، أشارت الأبحاث الطبية إلى فعالية الأمانتادين فى تحسين درجة الوعى واليقظة مؤدياً فى بعض الأحيان الى تحسين كبير وملموس. الأمانتادين عقار فعال فى علاج اضطرابات الوعى ومقارنة ببقية الأدوية فهو قليل الأعراض الجانبية.

الآلية التى يعمل بها العقار غير واضحة وإن كان الأمانتادين يبدوا وكأنه يعمل كمضاد لـ (إن ميثيل، دى أسبارتات) وكمحفز غير مباشر للدوبامين.

لقد قمنا بهذه الدراسة لإكتشاف تأثير الأمانتادين على تحسين درجة الوعى فى حالات الإصابة المنعزلة للرأس والتى تحتاج الى تدخل جراحى.

بعد موافقة اللجنة الأخلاقية وبعد أخذ إقرار بالموفقة على الإجراء من الآقارب بعد شرح وافى له فقد تمتقسيم ٤٠ مريض أعمارهم بين ١٦و ٦٥عاماً مصابين بإصابات منعزلة للرأس متوسطة أو حادة وتحتاج تدخل جراحى الى مجموعتين عشوائياً.

تم أعطاء الأمانتادين لمرضى المجموعة الاولى أثناء إجراء العملية بجرعة ١٠٠ مجم بالتقطير الوريدى على مدار٣ ساعات ثم أعطى الأمانتادين بجرعة ١٠٠مجم بالتقطيرالوريدى على مدار٣ ساعات كل ١٢ ساعة ولمدة ٧ أيام ثم تم تحويلة الى أقراص بجرعة ٣٠٠ مجم مقسمة على مدار اليوم إلى ٣ جرعات متساوية، الاولى تعطى فى الصباح والأخيرة فى الخامسة مساءاً.

البلاسيبو (دواء بلا مادة فعالة) أعطى للمجموعة الثانية بنفس الشكل والمدد الزمنية. قمنا بمقارنة مقياس جلاسجو للغيبوبة وقراءات معامل ثنائى الطيف عند وصول المريض مباشرةً بعد إجراء الجراحة وبعدها بثلاث أيام وأسبوعين.

وقد وجدنا أن التحسن فى معامل جلاسجو للغيبوبة فى المجموعة الاولى كان ٤.٥٣±٢.٦١ وكان فى المجموعة الثانية ٢.١١±٢.٨١ وهو ما له دلالة إحصائية.

نستنتج من هذه الدراسة أن معدل التحسين فى المرضى المعالجين بالأمانتادين كان آعلى بشكل دال عنه فى المرضى الذين لم يتناولوا العقار.