Comparative Study of the Effect of Risperidone Versus Quetiapine on Relief of Agitation, Psychosis and Delirium developed in Moderate Traumatic Brain Injury Patients

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Abstract

Background: Traumatic brain injury (TBI) is considered an important worldwide public health epidemic, economic and social issue affecting all societies.

Objectives: To assess & determine the efficacy and safety of atypical antipsychotics (Risperidone & Quetiapine) in the management of agitated behaviors following moderate TBI.

Patients and methods: prospective randomized controlled study conducted among 60 adult patients with TBI admitted to the trauma ICU department of Minya University Hospital (MUH) during the study period which starts on July 15, 2022. 60 patients were randomly allocated into one of three groups**:** Risperidone group received (0.5 mg up to 2 mg once daily), Quetiapine group received (25 mg up to 100 mg once daily) and control group. All patients received conventional treatment.

Results: The current study reveals there was insignificant difference among the three groups as regard CT brain findings also, there is a significant difference among the three groups as regard the control of agitated behaviors following TBI. Regarding Richmond Agitation Sedation Scale (RASS score) at day risperidone group revealed significantly decreased from day 3rd to day 9th than quetiapine group ($p< 0.05$). Also, RASS at night, risperidone group show significantly decrease from day 2nd to day 9th ($p< 0.05$).

Conclusions: The current study established the superiority of Risperidone over Quetiapine in the management of agitated behaviors following TBI.

Keywords: Traumatic brain injury; Atypical antipsychotics; Agitated behaviors.

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Introduction

Traumatic brain injury (TBI) is considered a major global public health Problem, with both economic and social impacts affecting all societies. It is considered the leading cause of disability and mortality in the majority of nations. Patterns of injury have shifted in recent years, with an increase in the incidence of injuries, specifically contusions, among elderly patients (**Lombard and Zafonte, 2005; Saoût et al., 2011**).

Symptoms of severe TBI (sTBI) usually include consciousness disorders. Frequently, individuals who have recovered from a coma manifest aberrant behavior, including agitation. When severe TB cases regain consciousness during the subacute phase, they experience agitation and delirium (**Singh et al., 2014**).

Agitation and combative behavior are frequently observed symptoms among intensive care unit (ICU) patients who have suffered acute TBI. Agitation and hostility are commonly observed neurobehavioral consequences during the initial phases of recuperation following TBI (**Bogner et al., 2001; McNett et al., 2012**). Behavioral symptoms such as these impede rehabilitation efforts and disrupt patient care. These unintentionally aggressive actions have the potential to disrupt medical procedures (**Wood and Boucher, 2012; Williamson et al., 2016**).

70% of cases who are hospitalized with TBI experience agitation, which negatively impacts both the duration of their stay and their functional outcomes. By means of inadvertent removal of tubes and catheters, agitation may lengthen the duration of a patient's stay in the intensive care unit, and it may be associated with a variety of complications (**Bruns and Hauser,2003; McNett et al., 2012**).

Risperidone is considered atypical antipsychotic drug and used for management of symptoms and signs of dementia (BPSD) for long time, such as agitation, aggressiveness, and psychosis (**Bhat et al., 2023**). Also, oral risperidone was found to be effective and safe in management of mild agitation **(Simpson et al., 2024).** Quetiapine in low dose was found to be effective in preventing delirium in high-risk, surgical trauma ICU patients (**Abraham et al., 2021).**

Accordingly, these Neurobehavioral sequelae pose difficulties for critical care professionals in terms of clinical management. Nevertheless, the current body of research on post-traumatic delirium (PTD) is relatively scarce, despite the fact that it is probable to be more prevalent among ICU cases in general compared to the general population (**Khellaf et al., 2019; Taylor, 2017**).

Patients and methods

Study design: The current study is a prospective randomized controlled study that included 60 adult cases with isolated moderate TBI, recruited from trauma ICU department of Minya University Hospital (MUH), during the study period which starting from date July 15, 2022. patients were selected to be participants in the present work according the following inclusion criteria age between 18 and 60 years, moderate Head Trauma Patients (GCS 9-12), both sexes and no surgical interference requiring heavy sedation and muscle relaxation.

Exclusion Criteria were patients' first-degree relatives' refusal, with age less than 18 or more than 60, mild Head Trauma (GCS 12-15) or severe Head Trauma (GCS less than 7), pregnant women, allergy to study

drugs, contraindication to enteral feeding, pre-existing brain dysfunction, brain herniation and craniotomy.
Cases were classified into 3 equal groups:

- Group R: received Risperidone (0.5 mg up to 2 mg once daily) in orogastric or nasogastric tube plus the conventional treatment from day of admission till day of discharge.
- Group Q: received Quetiapine (25 mg up to 100 mg once daily) in orogastric or nasogastric tube plus the conventional therapy from day of admission till day of discharge.
- Group C: received conventional treatment only without any atypical antipsychotics.

Sampling technique: A consecutive sample of all adult patients with isolated moderate TBI that were recruited from trauma ICU department of Minya University Hospital (MUH) during the study period which starting from date July 15, 2022, and fulfilled the predetermined inclusion and exclusion criteria was included in the current study

Data collection

Every case who participated in the research underwent the subsequent analysis:

1- **Complete history including** Personal data. Past history of previous interventions. History of medical conditions (Diabetes, Hypertension and bronchial asthma). Date of hospital admission, Prior occurrence of any disease. Drug history, Hemodynamics (HR & NIBP) and Respiratory profile (RR & SpO2).

2- **Clinical examination was performed to all the study participants as the following:**

- Full outline of unresponsiveness (FOUR score), Richmond Agitation Sedation Scale (RASS score), and Glasgow Coma Scale (GCS). Temperature (T) in degrees Celsius, blood pressure (BP) in millimeter mercury and respiratory rate (RR) in cycles per minute. Our radiology consultant computed the Marshall CT classification, Rotterdam CT score, and computed tomography (CT) of the brain without contrast. Evaluation of the cardiovascular, nervous, and respiratory systems was done. A standard 12-lead electrocardiogram (ECG) was performed on every case who was enrolled.

3- **Investigations included:**

a. Laboratory investigations performed to all study participants [Total bilirubin (mg/dL), complete blood count (CBC), serum sodium in milliequivalent per liter (mEq/L), potassium in mEq/L, serum creatinine in milligram per deciliter (mg/dL), serum urea in mg/dL, random blood sugar in mg/dL, and aspartate aminotransferase in unit per liter "U/L"].

b. Radiological investigations were performed to all the study participants [CT of the Brain without contrast]. The study participants were classified according to Marshall CT classification (**Table.1**). The appropriate Rotterdam CT score was computed by our radiology consultant. (**Table.2**).

c. Typical sedative regimens comprised midazolam or propofol as part of usual therapy. Sedation interruption was performed twice daily in accordance with protocol at the facility. Opioids and analgesics were permitted as prescribed by the senior resident in attendance.

d. GCS and FOUR scores were

assessed every 12 hours for all groups (**Table.3**); CT brain scans were repeated as necessary. At regular intervals, vital signs such as MAP, pulse rate, respiratory rate, and temperature were assessed.

Table 1. Marshall CT classification

Scale	CT finding
Category I	No visible intracranial pathology
Category II	Midline shift of 0 to 5 mm Basal cisterns remain visible No high or mixed density lesions > 25 cm^3
Category III	Midline shift of 0 to 5 mm Basal cisterns compressed or completely effaced No high or mixed density lesions>25 cm^3
Category IV	Midline shift > 5 mm No high or mixed density lesions > 25 cm^3
Category V	Any lesion evacuated surgically
Category VI	High or mixed density lesions>25 cm^3 Not surgically evacuated

Table 2. Rotterdam computed tomography classification

Predictor	Score
Basal cisterns	
Normal	0
Compressed	1
Absent	2
Midline shift	
No shift or shift ≤ 5 mm	0
Shift > 5 mm	1
Epidural mass lesion	
Present	0
Absent	1
Intraventricular blood or subarachnoid hemorrhage	
Absent	0
Present	1
Sum score	+1

In the Rotterdam scoring system, 1 point is added as a sum score to make the Rotterdam grade numerically total 6 points, consistent with the motor score of the Glasgow Coma Scale and the Marshall classification.

Table 3. Four score

Four Score	
Eye response	
Eyelids open or opened, tracking, or blinking to command	4
Eyelids open but not tracking	3
Eyelids closed but open to loud voice	2
Eyelids closed but open to pain	1
Eyelids remain closed with pain	0

Motor response	
Thumbs up, fist, or peace sign	4
Localizing to pain	3
Flexion response to pain	2
Extension response to pain	1
No response to pain or generalized myoclonus status	0
Brainstem reflexes	
Pupillary and corneal reflexes present	4
One pupil wide and fixed	3
Pupillary or corneal reflexes absent	2
Pupillary and corneal reflexes absent	1
Absent pupillary, corneal and cough reflex	0
Respiration	
Not intubated, regular breathing pattern	4
Not intubated, Cheyne- stokes breathing pattern	3
Not intubated, irregular breathing pattern	2
Intubated, breathes above ventilator rate	1
Intubated, breathes at ventilator rate or apnea	0

Ethical considerations: Official authorization was acquired from the ICU of Minya University Hospital (MUH). As well as Institutional Research Board (IRB) approval for the study was obtained from the faculty of medicine's ethical committee. Written informed consent was obtained from first-degree relatives of the cases. The study procedures and the service rendered were both devoid of any adverse effects on the participants. The study protocol was approved by the Scientific Research Ethical Committee of Faculty of Medicine, Minya University under IRB approval number 368:2022

Statistical analysis

Utilizing MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium) and SPSS 22.0 for windows (SPSS Inc., Chicago, IL, USA), all data were gathered, organized, and subjected to statistical analysis. In order to assess the normality of the data, the Shapiro Walk test was applied. In order to represent qualitative data, frequencies and relative percentages were utilized.

As indicated, the chi-square test (j2) and Fisher exact were utilized to compute the difference between qualitative variables. Mean ± standard deviation (SD) was utilized to represent quantitative data for parametric data, while median and range were employed for non-parametric data. For parametric and non-parametric variables, the difference between two categories of quantitative variables was computed using the Independent T test and the Mann Whitney test, respectively.

When comparing more than two dependent groups of normally distributed variables, a one-way ANOVA test was utilized. In contrast, the Kruskal-Wallis test was applied to variables that did not follow a normal distribution. All significant statistical comparisons utilized two-tailed tests. The significance level of a P-value is 0.05, the significance level of a highly significant difference is 0.001, and the significance level of a difference is 0.05.

Results

In relation to demographic data of the studied groups, **(Table.4)** illustrates that the mean age of the 3 studied groups were 34.6 ± 12.84, 39.8 ± 11.73 and 39.2 ± 13.05 for group R, Q and C respectively. The study participants of groups R and Q were distributed equally between male and female by 50 for both of then the while 70% of group C were male Also, there is insignificant difference among three groups as regard age and sex.

Table 4. Demographic data of the three studied groups.

Variables	Group R (N=20)	Group Q (N=20)	Group C (N=20)	P
Age (years) Mean ± SD	34.6 ± 12.84	39.8 ± 11.73	39.2 ± 13.05	.364
Sex				
Female	10 (50%)	10 (50%)	6 (30%)	.338
Male	10 (50%)	10 (50%)	14 (70%)	

In relation to CT brain findings among the studied groups, **(Table.5)** illustrates that intra-parenchymal hemorrhage was present in the three groups by 20%,15% and 15 % respectively while the epidural hemorrhage was present in the study groups by 15% ,0% and 5% respectively. The extradural hemorrhage was present in the 3 groups by 20%,35% and 30 % respectively. Also, there is insignificant difference among the three groups as regard CT brain findings.

Table 5. CT brain findings between the three studied groups.

Variables	Group R (N=20)	Group Q (N=20)	Group C (N=20)	P
Intraparenchymal hemorrhage	4 (20%)	3 (15%)	3 (15%)	.750
Epidural hemorrhage	3 (15%)	0	1 (5%)	
Extradural hemorrhage	4 (20%)	7 (35%)	6 (30%)	
Subarachnoid hemorrhage	5 (25%)	4 (20%)	5 (25%)	
Subdural hemorrhage	4 (20%)	6 (30%)	5 (25%)	

In relation to MAP measurements among the three groups, **(Table.6)** illustrate that MAP from 2nd to 9th day was a significant difference among the three studied groups regarding MAP from 2nd to 9th day. Thus, MAP measurements were significantly lower among group R compared to group Q.

Table 6. Mean arterial blood pressure measurements between the three studied groups.

Variables	Group R (N=20)	Group Q (N=20)	Group C (N=20)	P
1st day Mean ± SD	108.33 ± 5.77	106.8 ± 4.77	107.67 ± 5.42	.675
2nd day	102.3 ± 7.5	106.7 ± 4.71	107.7 ± 5.42	**.016**

Mean ± SD				
3rd day Mean ± SD	97.67 ± 6.68	105.5 ± 4.75	107.2 ± 5.95	**<0.001**
4th day Mean ± SD	98.13 ± 4.71	100.88 ± 2.69	105.26 ± 5.13	**<0.001**
5th day Mean ± SD	95.64 ± 4.59	100 ± 2.43	104.74 ± 4.88	**<0.001**
6th day Mean ± SD	94.44 ± 5.0	99.74 ± 2.53	102.04 ± 4.73	**<0.001**
7th day Mean ± SD	92.78 ± 4.91	99.1 ± 2.62	102.29 ± 5.12	**<0.001**
8th day Mean ± SD	93.3 ± 4.1	99.1 ± 3.17	100.5 ± 2.67	**.001**
9th day Mean ± SD	90.1 ± 3.33	99.3 ± 2.79	97.5 ± 3.45	**.005**
10th day Mean ± SD	93.3 ± 3.51	99.64 ± 2.88	97.3 ± 3.86	.556

Concerning Heart Rate measurements between the three studied groups, (**Table.7**) illustrates that there is a significant difference in HR among the three groups analyzed between the third and tenth day. Thus, HR measurements were significantly increased among group R than group Q.

Table 7. Heart Rate measurements between the three studied groups.

Variables	**Group R** (N=20)	**Group Q** (N=20)	**Group C** (N=20)	**P**
1st day Mean ± SD	105.7 ± 2.96	105.1 ± 3.24	105.2 ± 2.61	.743
2nd day Mean ± SD	106.35 ± 3.69	104.1 ± 3.73	104.4 ± 2.94	.078
3rd day Mean ± SD	107.4 ± 3.56	102.8 ± 3.88	103.9 ± 2.87	**<0.001**
4th day Mean ± SD	108.6 ± 4.1	101.8 ± 4.07	103.11 ± 2.56	**<0.001**
5th day Mean ± SD	108.27 ± 4.46	101.13 ± 4.66	102.26 ± 2.96	**<0.001**
6th day Mean ± SD	108.55 ± 4.39	100.69 ± 5.3	101.35 ± 3.99	**<0.001**
7th day Mean ± SD	107.75 ± 5.42	99.1 ± 5.15	100.5 ± 4.27	**.001**
8th day Mean ± SD	106.29 ± 3.77	97.43 ± 4.58	98.23 ± 4.55	**.001**
9th day Mean ± SD	107.4 ± 2.19	98.1 ± 5.1	96.25 ± 3.73	**<0.001**
10th day Mean ± SD	105.1 ± 3.25	100.3 ± 4.73	97.67 ± 1.16	**.026**

About RR measurements between the three studied groups, (**Table.8**) displays that between day two and day five, there is a substantial variance in RR among the three groups that were examined. Thus, RR measurements were significantly lower among group R compared to group Q.

Table 8. RR measurements between the three studied groups

Variables	Group R (N=20)	Group Q (N=20)	Group C (N=20)	P
1st day Mean ± SD	20.7 ± 1.08	20.7 ± 1.13	20.65 ± 1.27	.988
2nd day Mean ± SD	18.35 ± 1.35	20.65 ± 1.39	20.15 ± 1.18	**<0.001**
3rd day Mean ± SD	18.4 ± 1.39	20.7 ± 1.17	19.95 ± 0.887	**<0.001**
4th day Mean ± SD	19.18 ± 1.38	20.8 ± 1.01	20.68 ± 1.16	**<0.001**
5th day Mean ± SD	19.53 ± 0.834	20.41 ± 1.18	20.47 ± 1.26	**.038**
6th day Mean ± SD	19.82 ± 0.982	20.54 ± 1.05	20.18 ± 1.07	.253
7th day Mean ± SD	19.67 ± 0.866	20.36 ± 1.21	20.75 ± 1.07	.065
8th day Mean ± SD	19.38 ± 0.518	20.71 ± 1.11	20.54 ± 1.39	.051
9th day Mean ± SD	19.83 ± 0.408	20.1 ± 0.707	20.88 ± 1.13	.078
10th day Mean ± SD	21.03 ± 0.465	19.17 ± 0.386	21.3 ± 0.577	.139

F: One-way ANOVA test.

In relation to SO2 readings between the three studied groups, (**Table.9**) mentions that there is insignificantly different among the three groups as regard SO_2 different management.

Table 9. SO_2 readings between the three studied groups

Variables	Group R (N=20)	Group Q (N=20)	Group C (N=20)	P
1st day Mean ± SD	95.55 ± 2.04	95.6 ± 1.7	95.54 ± 1.91	.995
2nd day Mean ± SD	96.1 ± 2.18	96.15 ± 1.57	95.35 ± 1.66	.343
3rd day Mean ± SD	95.55 ± 1.57	94.9 ± 1.86	95.75 ± 1.59	.254
4th day Mean ± SD	96.1 ± 1.88	95.2 ± 1.74	95.21 ± 1.69	.270
5th day Mean ± SD	95.31 ± 1.61	96.19 ± 1.8	96.01 ± 1.6	.346
6th day Mean ± SD	94.78 ± 1.3	95.69 ± 2.1	95.82 ± 1.63	.331
7th day	96.17 ± 1.47	95.82 ± 1.4	96.1 ± 1.98	.906

Mean ± SD				
8th day Mean ± SD	96.4 ± 2.41	98.86 ± 0.378	97.92 ± 2.47	.159
9th day Mean ± SD	99.1 ± 0.214	98.8 ± 0.447	97.75 ± 3.15	.632

F: One-way ANOVA test.

Regarding GCS measurements between the three studied groups, (**Table.10**) documented that there is a significant difference among the three groups as regard GCS 7th day. Thus, GCS in the 7th day was significantly lower among group R compared to group Q.

Table 10. GCS measurements between the three studied groups.

Variables	**Group R** (N=20)	**Group Q** (N=20)	**Group C** (N=20)	**P**
1st day Mean ± SD	9.9 ± 0.788	9.95 ± 0.826	9.9 ± 0.718	.973
2nd day Mean ± SD	10.25 ± 0.967	10.35 ± 0.988	10.4 ± 0.933	.931
3rd day Mean ± SD	11.1 ± 1.37	11.0 ± 1.03	11.0 ± 1.08	.952
4th day Mean ± SD	11.61 ± 1.29	11.15 ± 0.813	11.32 ± 0.582	.315
5th day Mean ± SD	12.15 ± 1.1	12.25 ± 0.447	12.0 ± 0.667	.605
6th day Mean ± SD	12.22 ± 1.3	12.42 ± 0.669	12.53 ± 0.801	.715
7th day Mean ± SD	12.0 ± 1.27	12.64 ± 0.505	13.0 ± 0.516	**.019**
8th day Mean ± SD	13.17 ± 1.17	13.18 ± 0.408	13.46 ± 0.776	.675
9th day Mean ± SD	14.33 ± 0.577	13.6 ± 0.548	13.63 ± 0.518	.152

About RAAS at day between the three studied groups, (**Table.11**) shows that RAAS at was significantly decreased in group R in comparison to group Q than group C from 3rd day to 9th day.

Table 11. RAAS at day between the three studied groups

Variables	**Group R** (N=20)	**Group Q** (N=20)	**Group C** (N=20)	**P**
1st day Mean ± SD	4	4	4	1
2nd day Mean ± SD	3.85 ± 0.489	4	4	.162
3rd day Mean ± SD	3.45 ± 0.945	3.9 ± 0.308	4	**.008**
4th day Mean ± SD	2.75 ± 1	3.4 ± 0.821	3.85 ± 0.366	**<0.001**

5th day Mean ± SD	2.5 ± 1.35	3.31 ± 1.01	3.74 ± 0.653	**.004**
6th day Mean ± SD	2.7 ± 1.06	3.58 ± 0.669	3.82 ± 0.529	**.002**
7th day Mean ± SD	2.25 ± 0.886	3.09 ± 0.944	3.63 ± 0.719	**.002**
8th day Mean ± SD	1.88 ± 0.835	2.5 ± 1.07	3.46 ± 0.877	**.002**
9th day Mean ± SD	1.6 ± 0.548	2.4 ± 0.548	3.25 ± 0.463	**<0.001**

In relation to RAAS at night between the three studied groups,(**Table.12**) shows that RAAS at night was significantly decreased in group R in comparison to group Q than group C from 2nd day to 9th day.

Table 12. RAAS at night between the three studied groups

Variables	**Group R** (N=20)	**Group Q** (N=20)	**Group C** (N=20)	**P**
1st day Mean ± SD	3.95 ± 0.224	4	4	.374
2nd day Mean ± SD	3.7 ± 0.571	3.95 ± 0.224	4	**.021**
3rd day Mean ± SD	2.85 ± 1.18	3.7 ± 0.571	3.95 ± 0.224	**<0.001**
4th day Mean ± SD	2.63 ± 1.15	3.35 ± 0.875	3.75 ± 0.550	**.001**
5th day Mean ± SD	2.29 ± 1.49	3.25 ± 1.13	3.63 ± 0.761	**.005**
6th day Mean ± SD	2.4 ± 1.17	3.33 ± 0.778	3.53 ± 0.874	**.014**
7th day Mean ± SD	2.33 ± 0.866	2.91 ± 1.04	3.38 ± 0.885	**.037**
8th day Mean ± SD	1.5 ± 0.756	2.67 ± 0.516	3.15 ± 1.07	**.002**
9th day Mean ± SD	1.0 ± 0.707	1.8 ± 0.447	2.75 ± 0.886	**.003**

F: One-way ANOVA test.

Concerning ICU stay duration between the studied groups. (**Table.13**) shows that ICU stay was significantly decreased in group R in comparison to group Q and C. Moreover, all patients used catheters and used paracetamol & ketorolac as analgesia.

Table 13. ICU stay duration between the studied groups.

Variables	**Group R** (N=20)	**Group Q** (N=20)	**Group C** (N=20)	**P**
ICU stay (days) Mean ± SD	5.65 ± 2.21	6.7 ± 1.29	7.75 ± 1.86	**.010**

Discussion

TBI is the leading cause of long-term or persistent disability associated with trauma on a global scale and an imminent threat to public health. The CDC documented 61,000 fatalities attributable to TBI in 2019. Serious, moderate, or benign TBI may be classified according to the annual incidence rate of 50 million cases. Mild to moderate TBI constitutes approximately 90% of all TBIs (**Khellaf, 2019**).

TBI can result in mild, moderate, or severe neurological damage, which manifests both promptly following the impact (primary injury) and persists in the post-traumatic period (secondary injury). TBI can significantly disrupt daily functioning by impairing the capacity to work, sleep, operate a motor vehicle, read, communicate, and engage in a multitude of activities that were previously assumed as normal (**Taylor, 2017**).

A highly complex disease of the central nervous system (CNS) may be triggered by TBI, beginning with the primary pathology of the traumatic event that triggered the injury and progressing to an inflammatory and CNS tissue response. Long considered an almost inevitable complication of moderate to severe TBI, delirium has only recently been identified as an organ dysfunction syndrome amenable to potentially mitigating interventions. In critically morbid populations, delirium is independently associated with longer hospital stays, increased mortality, and poorer cognitive outcomes (**Dewan et al., 2018**).

Delirium is observed in around 50% of cases over the age of 50 who are referred to surgical ICUs for TBI. This proportion rises to 75% among patients aged 50 and above (**Roberson et al., 2021**).

Acute alterations in mental status that manifest as disorientation, inattention, and fluctuating levels of arousal constitute delirium. Although post-traumatic agitation and delirium are common during the rehabilitation phase, they can manifest at any stage of the hospital stay following a traumatic brain injury (TBI). Typically, they manifest within the first twenty-four hours after admission. Upon admission, delirium affects as many as 70% of cases transferred to inpatient neurorehabilitation for TBI (**Maneewong et al., 2017**).

sTBI patients are frequently observed exhibiting agitation in the hospital environment. As many as 90% of patients who have suffered a sTBI experience in-hospital agitation. This substantial variation can be accounted for by variations in diagnostic criteria and the under recognition or over recognition of these behaviors. It is noteworthy that these behaviors manifest as episodes of altered consciousness that occur when individuals regain consciousness following a posttraumatic stupor. The mechanisms that underlie posttraumatic agitation remain inadequately comprehended (**Ely et al., 2004**).

Multiple hypotheses stated that this behavior is probably the result of modifications in cerebral metabolism, dysregulation of neural transmission, or neural network remodeling. After neurologic insults, dysregulation of dopaminergic neurotransmission, for instance, frequently correlates with behavioral alterations (**Stéfan, and Mathé, 2016**).

Antipsychotics are frequently prescribed for the management of agitation following traumatic brain injury, notwithstanding the scarcity of evidence supporting their effectiveness. Formal monitoring of

agitation in PTD is necessary to ensure that antipsychotics are utilized to treat more severe manifestations of agitation and to assess treatment response. Understanding why prescribers use antipsychotics for agitation that is mild or below clinical thresholds requires further investigation (**Pouwels et al., 2019**).

Antipsychotics, for instance, are associated with a decreased risk of developing delirium in general intensive care unit (ICU) patients, whereas dexmedetomidine and remifentanil are linked to a reduced incidence and severity of delirium in other patients. Nevertheless, a dearth of high-quality research exists regarding acute treatment strategies for PTD (**McNett et al., 2012; McKay et al., 2021**).

The current study is prospective randomized controlled that was carried out on 60 adult cases with isolated moderate TBI, recruited from trauma ICU department of Minya University Hospital (MUH) during the study period starting from date July 15, 2022, to assess & evaluate the efficacy and safety of atypical antipsychotics (Risperidone & Quetiapine) in the management of agitated behaviors following TBI.

Cases were classified into 3 equal groups:Group R were given Risperidone (0.5 mg up to 2 mg once daily) in orogastric or nasogastric tube plus the conventional treatment from day of admission till day of discharge; Group Q received Quetiapine (25 mg up to 100 mg once daily) in orogastric or nasogastric tube plus the conventional treatment from day of admission till day of discharge.; Group C received conventional treatment only without any atypical antipsychotics.

In relation to Demographic data of the studied groups, the present investigation demonstrates that the average age of the 3 groups were34.6 ± 12.84, 39.8 ± 11.73 and 39.2 ± 13.05 for group R, Q and C respectively. The study participants of groups R and Q were distributed equally between male and female by 50 for both of then the while 70% of group C were male.

Also, there is insignificant difference among the three groups as regard age and sex. This result is in line with **Deb et al.(2020)** who mentioned that the placebo and risperidone categories contained cases with average ages of 43 and 39, respectively. Over 60% of both groups were male while this result is mismatched with Wang**, Winans and Zhao (2021)** who estimated that the age distribution of the 530 cases (29.1% female) was as follows: average age 44.8 years (SD 19.6 years), with a range of 18 to 94 years.

In relation to CT brain findings between the studied groups, the present research illustrates that intraparenchymal hemorrhage was present in the three groups by 20%, 15% and 15 % respectively while the epidural hemorrhage was present in the study groups by 15%, 0% and 5% respectively. The extradural hemorrhage was present in the 3 groups by 20%, 35% and 30 % respectively. Also, there is insignificant difference among the three groups regarding CT brain findings. In this context, **Roberson et al. (2021)** mentioned that Cranial fractures, extra-axial (epidural, subarachnoid, and subdural) or intra-axial (intraparenchymal or intraventricular) hemorrhages, contusions of the brain cortex, and microhemorrhages in multiple white matter structures indicative of diffuse axonal injury are among the CT findings observed upon presentation.

Also, **Asmar et al.(2020)** estimated that Subdural hematoma, epidural

hematoma and subarachnoid hemorrhage were present in both study groups (50.0%, 54.3%, 20.7%, 25.9, %39.7 and 44.0%) respectively.

In relation to Mean arterial blood pressure measurements between the studied groups, this investigation demonstrates that there is a statistically significant difference in MAP from the second to the ninth day among the three groups examined. Thus, MAP measurements were significantly lower among group R compared to group Q. Concerning Heart Rate measurements between the three groups, From the third to the tenth day, the current study demonstrates that there is a significant difference between the three categories in terms of HR. Thus, HR measurements were significantly increased among group R compared to group Q.

This result is mismatched with **Asmar et al.(2020)** who mentioned that regarding Vital parameters were ED SBP, mean ± SD, mm Hg 132.0 ± 18.0 and 132.0 ± 13.3 while ED SBP < 90, n (%), mm Hg were 10 (8.6) and 18 (7.8) 0.84 and ED HR, mean ± SD, were bpm 83.1 ± 11.7 84.8 ± 13.2 0.26 respectively for both groups with and without Quetiapine drugs. Also, they mentioned that there was insignificant difference between both groups as regard blood pressure and heart rate p>0.001.

About RR measurements between the studied groups, the present work displays that between day two and day five, there is a significant difference in RR between the three groups that were examined. Thus, RR measurements were significantly decreased among group R in comparison to group Q. In relation to SaO2 readings among the three studied groups, table 9 mentions that there is insignificant difference among the three groups as regard SaO_2 different management.

In this context **Moosavi et al.(2015)** estimated that There was no statistically significant difference between two groups regarding clinical global impression score (CGI-s) scores from the beginning to the end of this study (p<0.001), but the efficacy of both drugs in reducing CGI-s was significant. The positive and negative syndrome scale (PANSS) subscores (General/Positive/Negative) exhibited no statistically significant variation at the outset.

At the conclusion of week four, there was no statistically significant difference between the Risperidone and Quetiapine groups in terms of reducing positive (p=0.892) and negative (p=0.286) symptoms; however, there were significant differences between the two groups in terms of general symptoms (P=0.001). This indicates that during the acute phase of psychosis, Resperidone was more efficacious than Quetiapine at reducing general symptom scores of PANSS. Moreover, the disparity in overall scores between the two groups exhibited statistical significance (P=0.04).

Regarding GCS measurements between the studied groups, a significant difference exists among the three groups examined on the seventh day of GCS, according to the findings of the present study. Thus, GCS in the 7^{th} day was significantly lower among group R compared to group Q. this result in contradiction with **Moosavi et al.(2015** who mentioned that There was no significant difference observed among the groups in terms of declining positive and negative subscores on the PANSS. In terms of reducing the PANSS general psychopathology subscores and total score, risperidone outperformed quetiapine (p < 0.05). No significant difference in decreasing

CGI scores was observed between the two groups.

Concerning ICU stay duration between the studied groups. According to the findings of the present investigation, group R had a significantly shorter ICU stay than groups Q and C. Moreover, all patients used catheters and used paracetamol & ketolac as analgesia. This result is in contradiction with **Asmar et al.(2020)** who estimated that There was no significant variation observed in the length of stay in the intensive care unit (4.1 days versus 4.7 days; p = 0.75) or in the percentage of patients discharged to skilled nursing facilities (34.5% versus 31.9%; p = 0.63). ICP monitoring was performed on 40% of quetiapine-treated patients, according to subsequent analysis. Progressively decreasing ICP (β = −0.022 mm Hg/mg of quetiapine; p = 0.01) and increasing CPP (β = 0.031 mm Hg/mg quetiapine; p = 0.01) were observed in conjunction with increasing concentrations of quetiapine (p = 0.01).

Conclusion

The current research showed that both atypical antipsychotics Risperidone and Quetiapine were safe and effective in the management of agitated behaviors following TBI, However Risperidone was superior to Quetiapine in the management of agitated behaviors following TBI and also Risperidone was associated with better improvement in Richmond Agitation Sedation Scale and shorter ICU stay compared to Quetiapine.

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