

Randomized Controlled Trial

Comparative effectiveness of quetiapine and haloperidol in delirium: A single blind randomized controlled study

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Abstract**AIM**

To evaluate the effectiveness of quetiapine and haloperidol in patients of delirium referred to psychiatry consultation liaison services.

METHODS

The study followed a single blind randomised controlled trial design. Thirty-two patients in the haloperidol group and 31 patients in the quetiapine group were assessed at the baseline and 6 consecutive days. Flexible dosing regimen (haloperidol: 0.25-1.25 mg; quetiapine 12.5-75 mg/d) was used. Delirium Rating Scale-Revised-98 (DRS-R-98) and mini mental status examination (MMSE) were the primary and secondary efficacy measures respectively.

RESULTS

Baseline DRS-R-98 severity score and MMSE scores did not differ between the 2 study groups. From baseline to day 6, there was significant reduction in the total DRS-R-98 scores, DRS-R-98 cognitive domain scores, DRS-R-98 non-cognitive domain scores and significant increase in the MMSE scores in both the groups. Both the groups did not differ on any of the assessments in terms of DRS-R-98 and MMSE scores. The effectiveness of both the medications was similar in adult and elderly (≥ 60 years) patients. At the end of the trial, 68.75% and 67.74% of subjects in the haloperidol and quetiapine group respectively had mean DRS-R-98 scores below 10. By 6th day, 12 (37.5%) patients in haloperidol group and 9 (29.03%) patients in the quetiapine group had

DRS-R98 score of "0" with no significant difference between the two groups ($P = 0.47$).

CONCLUSION

Quetiapine is as effective as haloperidol in the management of delirium.

Key words: Delirium; Quetiapine; Effectiveness; Atypical antipsychotics

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Core tip: This Comparative study showed that quetiapine when used in the doses of 12.5-75 mg/d is as effective as haloperidol in the doses of 0.25-1.25 mg in management of delirium. The effectiveness of both the medications was similar in adult and elderly (≥ 60 years) patients. By 6th day, 37.5% patients in haloperidol group and 29.03% patients in the quetiapine group had Delirium Rating Scale-Revised-98 score of "0" with no significant difference between the two groups. Accordingly, this study suggests that quetiapine is as effective as haloperidol in the management of delirium.

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INTRODUCTION

Delirium is considered to be a psychiatric emergency seen among medically compromised patients. Management of delirium involves addressing the underlying etiology, providing reorientation cues, ensuring safety of the patients along with improvement in the patient's functioning. Over the years haloperidol has been the main antipsychotic, which has been recommended for management of delirium. However, in view of the extrapyramidal side effects associated with haloperidol, over the last 15 years or so, many researchers have evaluated atypical antipsychotic in the management of delirium^[1].

Quetiapine is an atypical antipsychotic considered to have very low extrapyramidal side effect potential and good sedating effect. Due to these, over the years this has been evaluated in the management of delirium in few case reports^[2-5], retrospective studies^[6], open label trials^[7-13] and randomised controlled trials with some following open label design and others followed blinded assessments^[14-16]. These studies suggest that quetiapine is better than placebo^[15,16] in the management of delirium and as effective as amisulpride^[9] and haloperidol^[14]. Data also suggests that compared to placebo, quetiapine is associated with shorter time to first resolution of

delirium, shorter duration of delirium and had lower level of agitation among the intensive care unit patients^[15]. In further analysis of the data authors also showed that compared to placebo, quetiapine is associated with faster first resolution of symptoms of fluctuation, inattention and disorientation. However, it took longer time to first resolution of symptoms of agitation and hyperactivity^[17].

However, it is important to note that the data with regard to usefulness of quetiapine in management of delirium is limited with total number of patients treated with quetiapine in all the studies less than 200 patients, with none of the studies having more than 25 patients in the quetiapine arm. Hence, there is a need to expand this data. This led to the present single blind randomized, controlled trial, which assessed the effectiveness of quetiapine and haloperidol in patients of delirium, admitted in medical and surgical wards and referred to psychiatry consultation-liaison services.

MATERIALS AND METHODS

This study was conducted in multispeciality tertiary care hospital. Institute Ethics Committee approved the study. The trial was submitted to Clinical trial registry of India. Proxy written informed consent was obtained from the primary caregivers of the patients who were staying with the patient during the hospitalization prior to randomization. The purpose of the study was explained to the caregivers. The caregivers were told about the currently available pharmacotherapy for management of delirium. The caregivers were explained about the commonly used pharmacological agents along with their efficacy and side effect profile. They were informed about the evidence available for quetiapine for management of delirium. The primary caregivers were informed that they could withdraw consent at any stage.

The study was an equivalence trial which followed a single blind randomised controlled trial design. Randomization was done based on the computer generated randomization table, which was done prior to starting of the study. Consecutive patients diagnosed with delirium by the consultation liaison psychiatry team were considered for this research.

Only those patients who fulfilled a diagnosis of delirium (based on the Diagnostic and Statistical Manual, 4th Revision)^[18] and were aged more than 18 years were included into the study. Patients with delirium associated with alcohol or benzodiazepine withdrawal, poisoning due to overdose and delirium associated with dementia (based on clinical history) were excluded. Patients who were unresponsive to any verbal or physical stimulus, those with history of aphasia, profound hearing or visual loss, those with prolonged QTc interval (> 500 ms) and past history of hypersensitivity to any of the drugs were also excluded. Patients who had developed neuroleptic malignant syndrome were also not considered for this study. Those with comorbid Parkinson's disease, psychotic or mood disorders and terminal illnesses were also excluded.

For this study, 101 patients were assessed initially. Twenty-seven patients were excluded because they did not fulfil the selection criteria for the study, *i.e.*, 4 patients had comorbid psychiatric illness, drug withdrawal state was present in 5 cases, prolonged QTc interval (> 500 ms) in electrocardiogram (ECG) was seen in 4 patients, 1 patient had Parkinson's disease, 3 patients had terminal illness, in 5 cases the delirium was associated with organophosphorous poisoning and 2 patients were younger than 18 years of age. According only 77 out of 104 patients were eligible for the study and their primary caregivers were approached for the study, out of which written informed consent was given by 70 caregivers. These patients were allocated to receive haloperidol ($n = 35$) or quetiapine ($n = 35$) based on predetermined random number generated prior to recruitment.

Four patients (2 in the quetiapine and 2 in the haloperidol group) were not available for assessment after the initial assessments of 1-2 d as they left the hospital against the medical advice (LAMA). One patient in quetiapine group, the primary treating team used Inj. Haloperidol for management on the second day and as a result the patient was excluded. Two patients (one from each group) could not be started on the assigned medication, due to deterioration in the clinical status [1 subjects went into coma and 1 was transferred to intensive care unit (ICU)] on the same day.

Accordingly out of 70 patients only 63 completed the trials with 32 in the haloperidol group and 31 in the quetiapine group.

The dose of medication was adjusted as per the clinical judgement. Flexible dosing regimen (haloperidol: 0.25-10 mg and quetiapine: 12.5-75 mg/d) was used. At our consultation-liaison psychiatry practice setup, haloperidol is usually administered in the dose of 0.25 mg two to three times a day and titrated as per the requirement and majority of the patients are managed with 0.75 to 2.5 mg of haloperidol per day. In case of agitation, a dose of 1.25 to 2.5 mg is given intravenously and same is repeated as per need. For quetiapine a regimen of 12.5 mg/d OD dose was started and depending on the need the dose was increased to 75 mg/d.

Based on the daily clinical assessment, dose titration was done; however, in case the patient was agitated, dose titration was done as per the requirement. In case the delirium improved, the dose used on the previous day was continued till the end of the trial.

One of the investigators (SG) was responsible for the randomization and dose adjustments and another investigator (SM) who was blinded for the medication being administered carried out the clinical assessments.

Besides use of haloperidol or quetiapine, patients were continued on medications for their medico-surgical ailments. However, any medication (like benzodiazepines, steroids, *etc.*) that could possibly contribute to delirium or those medications which were not essential were discontinued. The underlying etiologies for delirium were managed with appropriate measures. The primary

caregivers of all the patients were advised to provide optimal level of environmental stimulation, avoid sensory impairments of the patient and make the environment familiar to the patient by ensuring proper environmental cues that could facilitate orientation.

Primary efficacy measure

Delirium Rating Scale-Revised-98 (DRS-R-98)^[19] was used as the primary outcome measure. The DRS-R98 is a 16-item scale with 13 severity and 3 diagnostic items that rate the preceding 24-h period. Each item is rated 0 (absent/normal) to 2/3 (severe impairment). Higher severity scores (0-39) indicating more severe delirium. The scale has high interrater reliability, sensitivity and specificity for detecting delirium in mixed neuropsychiatric and other hospital populations^[19]. Both, the severity scale (13 items) and the total scale (16 items) have been validated for repeated measures.

Secondary efficacy measure

Additionally the patients were assessed on Mini mental status examination (MMSE)^[20] and this was used as a secondary outcome measure for the study. It is a 30 point scale widely used in delirium and dementia research.

Assessments

Patients were initially evaluated at the baseline and 6 subsequent consecutive 6 d, at a particular time of the day (6-8 PM) on DRS-R-98 and MMSE.

Additionally, at the baseline, patients were assessed on Amended Delirium Motor Checklist^[21,22], Short IQCODE^[23] and etiology checklist.

Amended Delirium Motor Checklist (Amended DMC)^[21,22] comprises of 13 items (5 hyperactive features and 8 Hypoactive features) of activity patterns that can be rated by both physicians and nurses. Each item is evaluated in absolute manner, *i.e.*, there is some evidence of the particular behaviour in last 24 h or not. Based on the number of criteria met for hyperactive and hypoactive checklists, the patients are categorized into hyperactive, hypoactive, mixed or no subtypes.

Short IQCODE^[23] was used to evaluate the cognitive functions in the last 6 mo. It is a 16-item instrument that allows for the assessment of cognitive status for a defined period prior to the interview point, *e.g.*, six months previously. It is rated based on an interview with a key relative. Each item is rated on a 5 point scale with a score of 3 indicating no change (higher scores denote worsening while lower denote improved cognition). The scale is scored by adding all items and then dividing the total score by 16 to get a mean score per item. The suggested cutoff for suspected dementia is a score > 3.31-3.38.

The etiology checklist was designed for this study and included 47 commonly associated factors which are known to be associated with delirium. Each item was rated as present or absent. For the laboratory parameters, if any of the values was out of the laboratory

range of the hospital it was considered as present.

Statistical analysis

SPSS-14 was used to analyse the data. Mean and standard deviation were calculated for the continuous variables and frequency and percentages were calculated for the ordinal or nominal variable. Comparisons between the groups were done by using students *t* test/ χ^2 test. If the DRS-R-98 data had non-normal distribution, then these were compared by using non-parametric tests. For the same, instead of paired *t* test, Mann-Whitney *U* test and Wilcoxon sign rank test were used. Repeat measure ANOVA was used to evaluate the effectiveness of medications on the primary and secondary outcome measure.

RESULTS

The mean age of the participants was 46.42 (SD: 18.26) and slightly less than one-third of the study sample was ≥ 60 years. The mean duration of education in years for the participants was 9.60 (SD: 4.22). Majority of the patients were male, from urban locality and had hospital emergent delirium. The average duration of delirium was 2.61 (SD: 2.08) d prior to enrollment into the trial. The mean IQCODE score was 3.07 (SD: 0.29) with only 3 patients scoring above 3.31, however, clinically these patients were never diagnosed with dementia. In terms of motor subtype, majority of the patients had hyperactive delirium and the mean number of etiologies associated with delirium was 6.82 (SD: 3.60). The mean baseline DRS-R-98 total score for the study sample was 31.52 (SD: 3.34). There was no statistically significant difference between the groups on any of the above variables (Table 1). Two patients with short IQCODE score were in the quetiapine group and 1 patient was in the haloperidol group.

The average dose of haloperidol was 0.67 mg (SD: 0.35; range 0.25-1.25) and that of quetiapine was 31.83 mg (SD: 4.10; range 12.5 -75).

For the haloperidol group the average baseline DRS-R98 severity score and MMSE scores were 24.81 (SD: 2.19) and 7.50 (SD: 3.83) respectively and those for quetiapine group were 25.48 (SD: 3.60) and 6.83 (SD: 4.45) respectively with no significant difference between the two groups. As shown in Table 1 there was no significant difference in the DRS-R98 scores and MMSE scores from day 1 to day 6 between the two groups.

Effectiveness of haloperidol and quetiapine

In terms of both DRS-R-98 and MMSE, there was significant improvement in both the study groups from day 1 through day 6 (Table 2). Additionally, repeat measure ANOVA was used to evaluate the effectiveness for both the groups. As there was significant difference in the Mauchly's test of Sphericity, Green-House Geissier within subject effect was considered while interpreting the "F"

and "P" values in the repeat measure ANOVA. Accordingly, ANOVA with repeated measures with a Greenhouse-Geisser correction, showed significant reduction in the mean scores for DRS-R-98 for haloperidol group (*F* value = 134.25, corrected DF = 82.44; *P* < 0.0005) and also in the quetiapine group (*F* value = 118.78, corrected DF = 91.23; *P* < 0.0005). Repeat measure ANOVA for MMSE scores with a Greenhouse-Geisser correction for haloperidol group (*F* value = 73.86, corrected DF = 74.84; *P* < 0.0005) and quetiapine group (*F* value = 69.62, corrected DF = 77.83; *P* < 0.0005) were also significant.

For both the groups, there was significant difference between the DRS-R-98 scores for each day except for lack of significant difference between day 5 and 6, indicating that with each subsequent day, there was significant improvement from baseline to day 5. As with DRS-R-98, in both the groups, there was significant difference between the MMSE scores for each day except for lack of significant difference between day 5 and 6 in the haloperidol group and 4 and 5, day 4 and 6 and day 5 and 6, indicating that with each subsequent day, there was significant improvement in MMSE from baseline to day 5 in haloperidol group and baseline to day 4 in the quetiapine group.

No significant difference was seen between the two groups, in terms of percentage of patients whose DRS-R-98 score dropped down below 10 (Table 1). Overall by using a cutoff of DRS-R98 severity score of < 10, haloperidol was found to be efficacious in 68.75% and quetiapine was found to be efficacious in 67.74% of cases, with no significant difference between the two groups. As is evident from Table 1, with each passing day there was increase in proportion of patients achieving the DRS-R-98 score of < 10, from baseline to day-5.

At the end of the trial, 12 (37.5%) patients in haloperidol group and 9 (29.03%) patients in the quetiapine group had DRS-R98 score of "0" with no significant difference between the two groups (χ^2 value: 0.508; *P* = 0.47).

Further analysis was done for each day to evaluate the effect of both the medications on the cognitive and non-cognitive domains of DRSR-98 and no significant difference emerged between both the groups for assessment on any given day. In terms of efficacy measure when the repeat measure ANOVA was used, scores on the non-cognitive domain in the haloperidol group showed significant reduction for each day except for lack of significant difference between day 4-5, day 4-6 and day 5 and 6. Similarly in the quetiapine group, there was significant difference between the scores for each day except for lack of significant difference between day 3-4, day 3-5, day 3-6, day 4-5, day 4-6 and day 5 and 6. In terms of cognitive symptoms there was significant difference between the scores for each day in the haloperidol and quetiapine groups except for lack of significant improvement between day 5 and 6 in the quetiapine group.

Data was also analysed separately for young and

Table 1 Sociodemographic, clinical profile, delirium subtype, Delirium Rating Scale-Revised-98 and mini mental status examination ratings for both the study groups

Variables	Haloperidol <i>n</i> = 32 mean (SD)	Quetiapine <i>n</i> = 31 mean (SD)	χ^2/t -test
Age (yr)	44.40 ± 16.76 (range 18-76)	48.51 ± 19.75 (range 18-85)	0.89 (<i>P</i> = 0.37)
Age ≥ 60 yr	7 (32%)	12 (38.7%)	2.11 (0.146)
Education (No. of years)	9.81 ± 4.46 (range 0-15)	9.38 ± 4.03 (range 0-17)	0.396 (<i>P</i> = 0.693)
Male	28 (87.5%)	21 (67.74%)	3.55 (<i>P</i> = 0.06)
Locality- Urban	21 (65.6%)	24 (77.4%)	1.073 (<i>P</i> = 0.300)
Type of onset - hospital emergent	23 (71.87%)	25 (80.64%)	0.668 (<i>P</i> = 0.414)
Duration of delirium prior to assessment (d)	2.38 ± 1.81	2.83 ± 2.32	0.85 (<i>P</i> = 0.398)
Total IQCODE	3.01 ± 0.053	3.13 ± 0.40	1.57 (0.12)
Delirium subtype as per amended DMSS			
Hyperactive	28 (87.5%)	27 (87.09%)	
Hypoactive			5.36 (<i>P</i> = 0.76)
Mixed	3 (9.37%)	2 (6.45%)	
	1 (3.12%)	2 (6.45%)	
Mean dose (mg/d)	0.67 ± 0.35 (range 0.25-1.25)	26.63 ± 15.61 (range 12.5-75)	
Mean number of etiologies	7.06 ± 3.31	6.58 ± 3.92	0.52 (<i>P</i> = 0.60)
DRS-R-98 total score at baseline	31.21 ± 2.40	31.83 ± 4.10	0.73 (<i>P</i> = 0.46)
DRS-R-98 scores (severity items only)			
Day 0	24.81 ± 2.19	25.48 ± 3.60	0.89 (<i>P</i> = 0.37)
Day 1	20.46 ± 3.93	19.54 ± 6.40	0.68 (<i>P</i> = 0.49)
Day 2	15.43 ± 6.19	13.54 ± 7.67	1.07 (<i>P</i> = 0.28)
Day 3	11.46 ± 6.58	9.51 ± 7.29	1.11 (<i>P</i> = 0.26)
Day 4	8.65 ± 6.73	7.83 ± 7.42	0.45 (<i>P</i> = 0.64)
Day 5	6.46 ± 6.06	6.48 ± 6.84	473 (<i>P</i> = 0.749) ¹
Day 6	5.43 ± 5.84	5.58 ± 5.84	466.5 (<i>P</i> = 0.679) ¹
DRS-R-98 < 10 on day 0	0	0	-
DRS-R-98 < 10 on day 1	0	3 (9.67%)	FE = 0.11
DRS-R-98 < 10 on day 2	5 (15.62%)	8 (25.80%)	0.99 (<i>P</i> = 0.31)
DRS-R-98 < 10 on day 3	14 (43.75%)	16 (51.61%)	0.39 (<i>P</i> = 0.53)
DRS-R-98 < 10 on day 4	21 (65.62%)	20 (64.51%)	0.009 (<i>P</i> = 0.92)
DRS-R-98 < 10 on day 5	23 (71.85%)	22 (70.96%)	0.006 (<i>P</i> = 0.93)
DRS-R-98 < 10 on day 6	22 (68.75%)	21 (67.74%)	0.007 (<i>P</i> = 0.93)
MMSE scores			
Day 0	7.50 ± 3.83	6.83 ± 4.45	0.63 (<i>P</i> = 0.53)
Day 1	11.31 ± 5.91	11.80 ± 6.02	0.328 (<i>P</i> = 0.74)
Day 2	15.50 ± 5.16	16.00 ± 6.37	0.343 (<i>P</i> = 0.73)
Day 3	18.28 ± 0.73	18.38 ± 6.26	0.070 (<i>P</i> = 0.94)
Day 4	20.34 ± 5.72	20.67 ± 6.41	0.218 (<i>P</i> = 0.828)
Day 5	21.93 ± 5.01	21.58 ± 5.74	0.263 (<i>P</i> = 0.794)
Day 6	23.00 ± 4.75	22.54 ± 5.34	0.354 (<i>P</i> = 0.724)

¹Mann-Whitney *U* value. DRS-R98: Delirium Rating Scale-Revised-98; MMSE: Mini mental status examination; FE: Fisher Exact test.

elderly patients (≥ 60 years). No significant difference was noted in the DRS-R-98 and MMSE scores on any of the assessments between the haloperidol and quetiapine groups among the elderly (≥ 60 years) and the young adults.

DISCUSSION

In 2 decades or so some data has emerged for the efficacy of atypical antipsychotic medications in management of delirium. Present study was also a step in the same direction. Most of the earlier studies which have evaluated efficacy of quetiapine have done so in sample sizes less than 25 in quetiapine arm. Most of the previous studies have been open label studies^[7-14], with only few studies following randomization and blinding^[15,16].

Like our previous study^[24], the present study too followed a single blind randomised controlled trial design, included patients with delirium with different etiologies in

a sample which predominantly comprised of young adult subjects (< 60 years) admitted to medico-surgical wards. Outcome was assessed by using DRS-R-98 and MMSE, which are considered to be useful for serial evaluation of delirium. However, unlike the previous study^[24], in the present study, besides analysing the data for the whole group, separate analysis was done for adult and elderly groups. Further, the DRS-R-98 data was evaluated separately for cognitive and non-cognitive symptoms. Motor subtypes were assessed by using validated scales, and besides ruling out dementia on the basis of clinical history cognitive functions in the last 6 mo were assessed by using short-IQCODE.

The demographic profile (age and gender distribution) of the participants included in the present study is characteristics of patients with delirium seen in psychiatry consultation liaison services at our centre^[25,26] and those included in a previous antipsychotic trial from this centre^[24]. The dose of quetiapine in the present

Table 2 Efficacy of haloperidol and quetiapine

	Haloperidol group	Quetiapine group
	Paired “t” test/ Wilcoxon sign rank test	Paired “t” test/ Wilcoxon sign rank test
DRS-R98 severity scores		
Day 0 and day 1	7.10 ($P < 0.001$)	5.12 ($P < 0.001$)
Day 0 and day 2	9.48 ($P < 0.001$)	8.60 ($P < 0.001$)
Day 0 and day 3	11.69 ($P < 0.001$)	11.68 ($P < 0.001$)
Day 0 and day 4	14.08 ($P < 0.001$)	12.90 ($P < 0.001$)
Day 0 and day 5	17.63 ($P < 0.001$)	4.86 ($P < 0.001$) ¹
Day 0 and day 6	4.94 ($P < 0.001$) ¹	4.86 ($P < 0.001$) ¹
Day 3 and day 6	4.70 ($P < 0.001$) ¹	3.98 ($P < 0.001$) ¹
MMSE		
Day 0 and day 1	3.83 ($P = 0.001$)	4.81 ($P < 0.001$)
Day 0 and day 2	8.53 ($P < 0.001$)	7.40 ($P < 0.001$)
Day 0 and day 3	9.00 ($P < 0.001$)	8.66 ($P < 0.001$)
Day 0 and day 4	10.07 ($P < 0.001$)	9.45 ($P < 0.001$)
Day 0 and day 5	11.68 ($P < 0.001$)	10.55 ($P < 0.001$)
Day 0 and day 6	12.38 ($P < 0.001$)	12.23 ($P < 0.001$)
Day 3 and day 6	6.50 ($P < 0.001$)	5.66 ($P < 0.001$)

¹Wilcoxon Sign Rank test. DRS-R98: Delirium Rating Scale-Revised-98.

study is lower than the mean dose used in most of the previous studies (42.2 to 93.7 mg/d)^[6,8,11,14,16], evaluating quetiapine in delirium. This can be understood from the Pharmacogenomic evidence, which suggests that compared to people from West, patients from countries like India require lower doses of psychotropics^[27].

The present study suggests that quetiapine in low dose is as beneficial as haloperidol in management of delirium. This finding supports the available literature which suggests that quetiapine is efficacious in management of delirium^[7-16]. Present study also provides credence to the available evidence that quetiapine is as efficacious as haloperidol in management of delirium^[14]. This research also suggests that quetiapine is equally efficacious in adults and elderly population. Usefulness in elderly provides support to the previous studies^[11]. Accordingly it can be said that quetiapine can be considered as another option in the management of delirium.

There are few limitations of the present study. The sample size for the study was small and due to the same the possibility of a type I error cannot be ruled out. No power calculation was done for estimation of sample size for the study. We did not include a placebo control arm and the side effects of both the study medications were not evaluated. As the rater was aware that all the patients were receiving active treatment and hence this could have affected the ratings. The study was limited to referred patients. Due to very few patients in the hypoactive group and those with short IQCODE score above the cut-offs, efficacy could not be compared in different motoric subtypes and those with possible dementia and without dementia. The treating psychiatrist was not blinded to the medication and this would have some bearing on the dose used. Hence, these limitations

must be considered while interpreting the results of this study. This study suggests that quetiapine is as effective as haloperidol in the management of delirium in adult and elderly patients.

COMMENTS

Background

There is limited data on use of quetiapine in management of delirium.

Research frontiers

Very few studies have evaluated the effectiveness of atypical antipsychotics in delirium.

Innovations and breakthroughs

Few studies have evaluated the usefulness of quetiapine in management of delirium.

Applications

Quetiapine can be considered as an alternative to haloperidol in management of delirium.

Peer-review

This is an interesting randomized controlled trial comparing haloperidol and quetiapine in delirium not related to substance withdrawal. The study has been adequately performed and is well presented.

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