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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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META-ANALYSIS

Melatonin intervention to prevent delirium in hospitalized patients: A meta-analysis

Wei You, Xiao-Yu Fan, Cheng Lei, Chen-Cong Nie, Yao Chen, Xue-Lian Wang

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Abstract

BACKGROUND

Evaluation of the effectiveness of melatonin is necessary to prevent the development of delirium in hospitalized patients. Melatonin (N-acetyl-5-methoxy-tryptamine) is a hormone produced by the pineal gland of the brain from the amino acid tryptophan. Synthetic melatonin supplements have been used for various medical conditions, especially sleep-related diseases, and have proved to be successful.

AIM

To determine the effect of melatonin on the prevention of delirium in hospitalized patients.

METHODS

A literature search of the CNKI, Wanfang Database, VIP Database, China Biomedical Literature Database, PubMed, Embase, Cochrane Library, Web of Science, and other databases was conducted. The CNKI, Wanfang Database, VIP Database (VIP), and China Biomedical Literature Database were searched for Chinese studies, and PubMed, Embase, Cochrane Library, Web of Science and other databases were searched for international studies. It will be established in June 2021 in a randomized controlled trial (RCT) whether melatonin treatment for 6 mo prevents delirium in hospitalized patients. Literature screening, quality review, and data extraction were carried out using the Cochrane Manual 5.1.0

systematic evaluation method, and Stata 15.0 software and Review Manager 5.3 were used for meta-analysis and processing.

RESULTS

A total of 18 new RCT articles and 18 experimental subjects were identified. The results of the meta-analysis showed that following the occurrence of delirium, melatonin reduced the incidence of delirium in patients (RR = 0.69, 95%CI: 0.60-0.80), which is of significance, but heterogeneity was significant I^2 = 62%. Subgroup analysis was performed to examine the source of heterogeneity, and it was found that different patient types were the source of heterogeneity; the research on subgroup analysis was of high quality and homogeneous. To determine the reliability and robustness of the research results, a sensitivity analysis was carried out. The results showed that after excluding individual studies one by one, the effect size was still within 95%CI, which strengthened the reliability of the original meta-analysis results. Melatonin has a significant preventive effect on delirium in hospitalized medical patients [RR = 0.60, 95%CI: 0.47-0.76), P < 0.001].

CONCLUSION

Melatonin can reduce the rate of delirium in medical patients, and the role of melatonin in reducing the incidence of delirium in surgical patients and critical care unit patients requires further study.

Key Words: Melatonin; Delirium; Prevention; Meta-analysis; Randomized controlled trial

Core Tip: Melatonin was shown to be effective in preventing delirium in hospitalized patients in this meta-analysis. Eighteen studies were reviewed involving 2137 patients and it was found that melatonin significantly reduced the incidence of delirium in hospitalized medical patients, but the effectiveness of melatonin in reducing the incidence of delirium in hospitalized surgical patients and intensive care unit patients requires further research.

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INTRODUCTION

Delirium, also known as the state of conscious confusion, is a disorder of consciousness (which is the clarity of perceiving the environment), changes in consciousness (including changes in thinking), cognitive disorders, mental illness, and sleep-wake movements. The delirium is a recognized Complications of medical diseases, especially elderly patients, which is related to the mortality rate, and increase in Hospital costs[1,2]. In the palliative care setting, it is reported that the prevalence of delirium on admission is 20%-42%, and as high as 88% in the last few hours or days of life. Delirium is an acute neurocognitive disorder, in which a person's awareness of the surrounding environment is reduced, and attention disorder is its core feature; other mental deficits and perceptual abnormalities may also occur [3]. The collective symptoms of delirium can affect patients due to these characteristics and accompanying changes in psychomotor dysfunction or attention deficit hyperactivity disorder. Delirium is a symptomatic disorder, and its clinical management is challenging, especially when psychomotor agitation is present. This is especially true in the case of advanced disease and hospice care, where the patient's physical and functional decline can lead to a high degree of vulnerability to delirium (such as infections and adverse drug reactions)[5-6]. When delirium appears, it is associated with a mortality rate of 10% to 75%, although death may be more related to both advanced age and delirium. It is estimated that drug-induced delirium accounts for 22% to 39% of all cases. A study involving elderly hospitalized patients found that in their study population, the most likely cause of delirium was drug use[7-10]. Antipsychotics and anti-anxiety agents are FDA-approved therapies for the treatment or prevention of delirium; however, data have revealed their lack of efficacy and the risk of serious side effects[11].

Melatonin (N-acetyl-5-methoxytryptamine) is a hormone produced by the pineal gland in the brain from the amino acid tryptophan. Synthetic melatonin supplements have been used for various medical conditions, especially sleep-related diseases, and have proved to be successful[12]. Delirium is charac-

terized by a disturbance in the circadian sleep-wake cycle, which leads to the hypothesis that the neurotransmitter melatonin and associated metabolic changes are involved in the pathogenesis of delirium. After admission, especially after admission to the intensive care unit (ICU), the metabolism of melatonin is disturbed, all of which are factors that cause delirium. These characteristics suggest an association between melatonin abnormalities and delirium. Although there is still a lack of evidence of causality[2], melatonin regulates the body's sleep-wake cycle, season, and circadian rhythm[13]. It is a sleep-improving substance. Oral melatonin has been widely used nationally and internationally. Although melatonin depletion is considered to be one of the mechanisms of delirium, there have been some studies on the effect of melatonin on the prevention of delirium; however, there are differences in the various research results. Therefore, this study analyzed randomized controlled trials (RCTs) of melatonin interventions to prevent delirium using a meta-analysis, aiming to quantitatively synthesize the results of multiple studies to provide more reliable quantitative results and to target patients in different situations. The best intervention measures to prevent delirium in hospitalized patients are recommended to provide evidence-based data and serve as a basis for the prevention and clinical treatment of delirium in hospitalized patients.

MATERIALS AND METHODS

Document retrieval

The search was conducted using operating system principles (P: PIC, which stands for the research object; I: Search strategy, which stands for the search object); C: Comparison strategy, realization; O: Search research design, research design. The databases PubMed, Web of Science, Cochrane Library, Embase, and Chinese databases, including China Biomedical Literature Database, Wanfang Data Medical Journal Library, Weipu Database, CNKI, *etc*. were searched. The search period was from establishment of the database through June 2021. Chinese database search terms were: (Melatonin) and (OR delirium neurocognitive impairment) and (randomized controlled trial or randomized controlled or randomized) and English database search terms were "melatonin" and "Delirium" and 'randomized controlled trials' or 'randomized controlled trials' or 'randomized'.

Search strategy

The following search terms were used: ("Delirium" [Mesh]) OR (title) (acute subdelirium [title/abstract]) OR (delirium, sub [title/abstract]) OR (delirium, acute sub [title/abstract] OR (Sub-Delirium [title/abstract]) or (Mixed Origin Delirium [abstract]) OR (Mixed Origin Delirium [title/abstract]) OR (Mixed Origin Delirium [title/abstract]) AND (Melatonin [title/abstract]) AND (Randomized Controlled Trial [Publication Type] OR (Randomized [title/abstract] AND Control [title/abstract] AND Trial [title/abstract]). This study has been registered on the PROSPERO website (No. CRD42021264902).

Inclusion and exclusion criteria

Inclusion criteria were: (1) Research subjects: clinically hospitalized patients, including patients in surgery, internal medicine, and ICU, the criteria for diagnosing delirium were determined by the CAM = Delirium Confusion Assessment (CAM) criteria[14,15]; (2) Intervention measures: The selected study was an RCT, and there were no significant differences between the experimental group and the control group before the experiment; and (3) Outcome indicators: the main observation indicator was RR (Relative risk).

The exclusion criteria included: reviews, conference papers, systematic reviews, dissertations, animal experiments, repeat publications, unavailable full text or incomplete data extraction, low quality of the literature or obvious research flaws; already suffering from mental illness before admission, patients with abnormalities, severe sensory disturbances, history of depression or delirium, or long-term use of antipsychotic drugs.

Study selection and data extraction

Two researchers who had received systematic evidence-based training performed the literature assessment and data extraction. They independently read, screened, and retrieved relevant content based on the inclusion and exclusion criteria. Excel entry was used to extract data, the first author Wei You completed the literature screening, and data extraction was completed by author Xiaoyu Fan. After completion, cross-checking was carried out. If there was disagreement, this was resolved by discussion or joint negotiation with the third author Cheng Lei. The relevant data extracted from the included studies were the title, first author, publication time, research country (region), sample size, intervention time, evaluation indicators, and other information.

Quality assessment and publication bias

Two researchers who had undergone rigorous evidence-based training assessed the quality of the literature. The quality of the included studies was assessed using the bias risk assessment approach

provided by the Cochrane Handbook 5.1.0, and discrepancies were addressed through discussion or by third-party researchers. The evaluated items included: (1) The generation of a random allocation plan; (2) Whether to carry out the allocation plan**;** (3) Whether to blind the subjects and researchers; (4) Whether to blind the evaluators; (5) Incomplete results; (6) Selectively reported research results; and (7) Other sources of bias. The evaluation result of "yes" indicated that the risk of bias was low; the result of "no" indicated that the risk of bias in the study was higher; "unclear" indicated that the study did not mention or did not have sufficient information to evaluate whether bias was present. Publication bias was tested using Egger's Funnel plots.

Statistical analysis

Review Manager 5.3 and Stata 15.0 software were used to conduct a meta-analysis on the extracted data. Subgroup analysis was conducted to analyze the heterogeneity of the included study results, and the corresponding effect model was selected based on the results: if $P \geq 0.1$ and $I^2 < 50\%$, this indicated that the statistical heterogeneity between the studies was acceptable. A fixed-effects model was chosen for data merging; if $P < 0.1$ and $I^2 \geq 50\%$, this indicated that the clinical heterogeneity between studies was large, and the source of heterogeneity was assessed or a random-effects model was chosen for data merging. Two categories of delirium incidence and relative risk (RR) were selected for analysis, and the 95%CI was calculated. When necessary, a sub-analysis of potential heterogeneity factors was performed, as well as an analysis to test the data.

RESULTS

Characteristics of the included studies

The flowchart of the research selection process is shown in Figure 1. The literature search retrieved 217 related documents from the Chinese and English databases. The document management software deleted 173 duplicate documents, read the titles and abstracts, and eliminated a total of 63 articles including reviews, systematic reviews, reviews, and animal experiments. Further research included reading the full text, deleting contents with inconsistent research data or inconsistent intervention measures/control measures (90 documents), excluding non-RCT literature (1), and one study with inconsistent outcome indicators was excluded. A total of 18 articles were finally re-analyzed, and the functions of the re-study are shown in Table 1. The basic characteristics of the literature in 18 articles were reviewed[16-33] and published in 2010-2021. The languages of the included literature are English and Chinese, and the study included 16 English articles and 2 Chinese articles. A total of 521 studies were involved. All included studies were divided into the control group and experimental group. The intervention in the experimental group was melatonin, and the intervention in the control group was a placebo (Table 1).

The experimental group was given melatonin to prevent delirium, and the control group was given placebo to prevent delirium.

Learning quality assessment

This study included 18 RCTs, 18 of which were of high quality, 6 of which scored 6 points, 7 of which described the method of random allocation sequence in full, and 18 assessed subjects using a blind approach. All trials provided complete data and no other potential risk of bias. The risk of bias in selective reporting was low. As shown in Figure 2, the standard was "+" and the standard "-" was not met. Figure 3 shows a statistical chart of the proportion of each item in the literature quality evaluation. See Figure 2 and Figure 3 for details.

Meta-analysis results

The overall effect of melatonin in all selected samples showed that it prevented delirium in hospitalized patients. Overall homogeneity ($I^2 = 62\%$, $P < 0.0003$) indicated multiple studies, and there was heterogeneity between the data; therefore, the random-effects model was used for analysis, but subgroup analysis was needed to determine the heterogeneity between multiple sets of data in this meta-analysis, as shown in Table 2 and Figure 4 (Forest map).

Heterogeneity test

The 18 documents in this study were tested for heterogeneity, and it was found that $I^2 = 62\% > 50\%$, and the Q test showed $P = 0.0003 < 0.1$, suggesting that the documents selected in this study were heterogeneous. Further investigation using Rabe diagrams and star diagrams indicated that there was a strong possibility of heterogeneity in the literature with regard to different patient types (Figures 5 and 6). Therefore, heterogeneity testing was required.

Sensitivity analysis

Sensitivity analysis is a method of testing the stability of results obtained under certain assumptions by

Table 1 Characteristics and details of the included studies.

Ref.	Sample size (example)		Intervention		Age		Diagnostic criteria
	T	C	T	C	T	C	
Sultan *et al*[16], 2010	53	49	Melatonin	Placebo	70.4 ± 7.1	72.3 ± 6.4	CAM
de Jonghe *et al*[17], 2014	186	192	Melatonin	Placebo	84.1 ± 8.0	83.4 ± 7.5	CAM
Wang *et al*[18], 2018	30	30	Melatonin	Placebo	70.7 ± 4.3	69.9 ± 4.5	CAM
Prabhat *et al*[19], 2019	50	50	Melatonin	Placebo	69.30 ± 4.05	70.64 ± 3.76	CAM
Ford *et al*[20], 2018	98	104	Melatonin	Placebo	69 ± 8.3	67.6 ± 8.0	CAM
Chen *et al*[21], 2020	45	45	Melatonin	Placebo	71.36 ± 7.12	73.56 ± 6.65	CAM
Javaherforoosh Zadeh *et al*[22], 2019	30	30	Melatonin	Placebo	60.26 ± 9.50	62.9 ± 8.08	CAM
Oh *et al*[23], 2020	33	38	Melatonin	Placebo	71.3 ± 5.1	71.6 ± 5.2	CAM
Al-Aama *et al*[24], 2010	61	61	Melatonin	Placebo	84.3 ± 5.9	84.6 ± 6.2	CAM
Hatta *et al*[25], 2014	33	34	Melatonin	Placebo	78.2 ± 6.6	78.3 ± 6.8	CAM
Agar *et al*[26], 2016	14	16	Melatonin	Placebo	76.3 ± 5.6	76.0 ± 5.3	CAM
Jaiswal *et al*[27], 2018	36	33	Melatonin	Placebo	75.3 ± 5.3	75.6 ± 5.7	CAM
Lawlor *et al*[28], 2020	30	30	Melatonin	Placebo	67 ± 5.9	67 ± 6.0	CAM
Mengel *et al*[29], 2021	164	164	Melatonin	Placebo	74 ± 1.3	73 ± 1.5	CAM
Vijayakumar *et al*[30], 2015	26	30	Melatonin	Placebo	36.9 ± 10.3	38 ± 14.4	CAM
Nishikimi *et al*[31], 2017	45	43	Melatonin	Placebo	68.0 ± 5.1	68.0 ± 5.3	CAM
Abbasi *et al*[32], 2018	67	70	Melatonin	Placebo	52.5 ± 18.4	49.9 ± 19	CAM
Jaiswa *et al*[33], 2019	59	58	Melatonin	Placebo	58.1 ± 14.1	56.1 ± 15.8	CAM

T: Experimental group; C: Control group; CAM: Delirium confusion assessment method standard determination.

Table 2 Meta-analysis of the prevention of delirium by melatonin in the studied hospitalized patients

	Independent sample	Homogeneity test			Two-tailed test		Effect size and 95% confidence interval
		χ^2	*P*	I^2	*Z*	*P*	
Random effects model	2137	44.49	$P < 0.0003$	62%	5.06	$P < 0.00001$	0.69 (0.60, 0.80)

changing some important factors that affect the combined results, such as inclusion criteria, literature evaluation, loss to follow-up, and different effect sizes, and then re-analyzing the data. The results before and after changing the conditions were compared, to judge the stability of the meta-analysis conclusions. A sensitivity analysis of the 18 articles found that different types of hospitalized patients had a greater impact on the heterogeneity, and it was necessary to further determine the source of heterogeneity (Figure 7).

Subgroup analysis

Subgroup analysis is also a commonly used method to identify heterogeneity in a meta-analysis. It investigates the source of heterogeneity from the perspectives of clinical and methodological heterogeneity, and it can incorporate the issue of effect size by referring to homogeneity research. According to the characteristics that may cause heterogeneity, the different types of experimental patients were analyzed in subgroups. In terms of the grouping of patients, the patients were divided into three subgroups: inpatient surgical patients, inpatient medical patients, and inpatient ICU patients. This is shown in the Forest diagram. Both the surgical group and the internal medicine group demonstrated statistical significance ($P < 0.05$), but not the ICU group ($P > 0.05$). Sensitivity analysis was performed on the analysis results. Two effect models (fixed and random) were used. After each study was eliminated one by one, the meta-analysis was performed again. The results found that the surgical group had high heterogeneity, indicating that the source of heterogeneity was not the research literature. Considering that many factors cause delirium, it is not possible to blindly adopt the random effect model to merge the effect size; following exclusion of the article by Stuti[27] in the internal medicine group, the

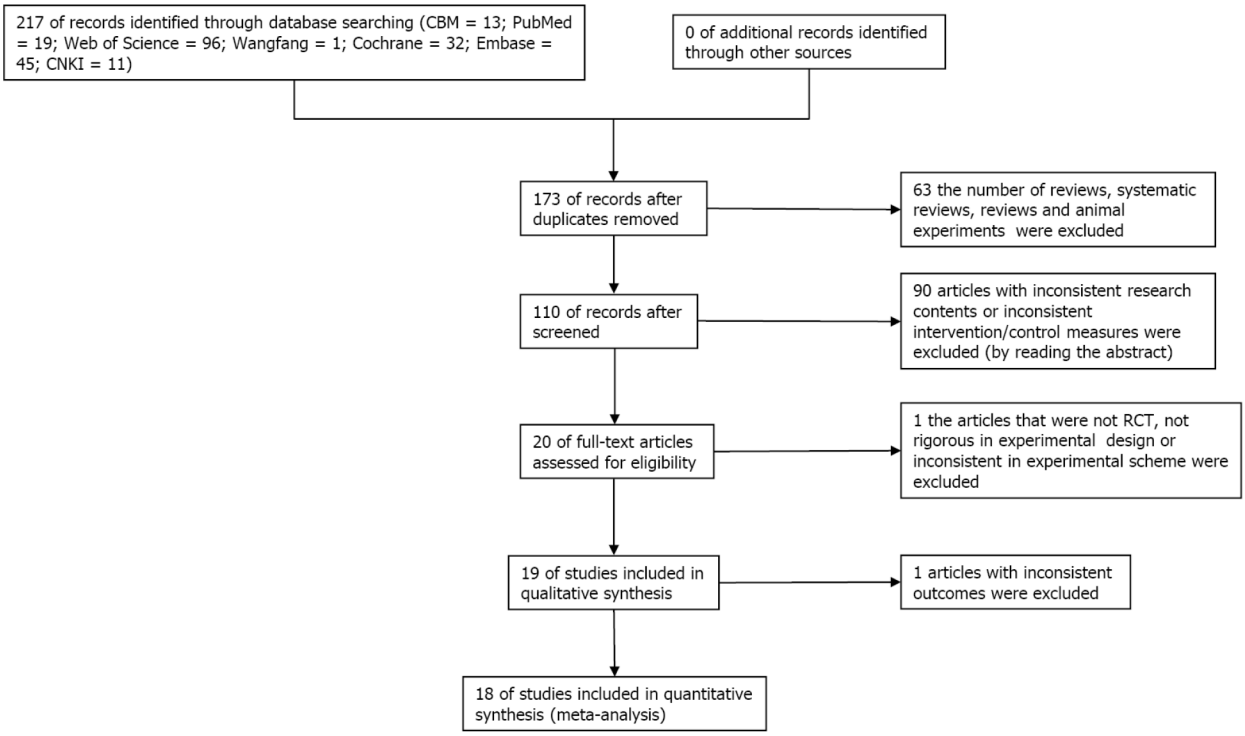

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Figure 1 Flow diagram of study selection (up to June 2021). CBM: Chinese Biological Medical database; CNKI: China National Knowledge Infrastructure; VIP: China Science and Technology Journal database; WF: Wanfang database and foreign language databases including PubMed, Embase, Cochrane Library, Web of Science, *etc.*

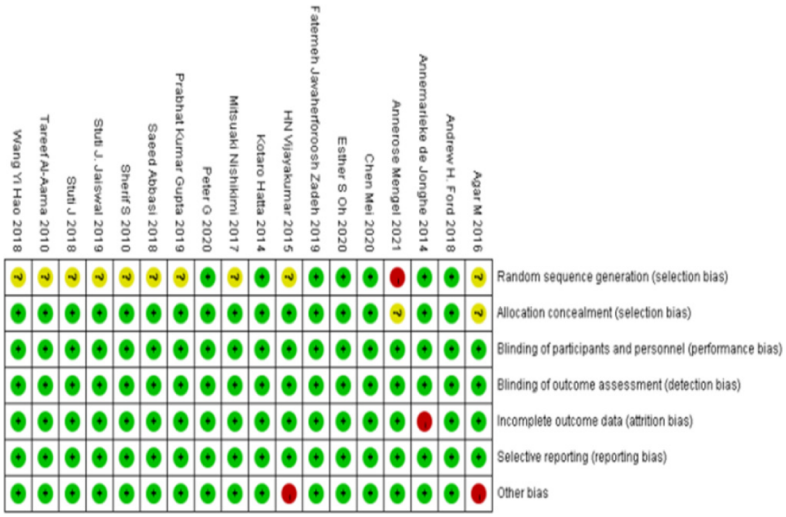

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Figure 2 Methodological quality of the included studies. Category: "+" up to standard, "-" not up to standard.

combined effect size of the meta-analysis changed markedly, indicating that the source of heterogeneity in the internal medicine group was due to Stuti J, suggesting that the results of this study were robust. Individual studies were excluded one by one following subgroup analysis, and the sensitivity analysis approach of analyzing the difference between the combined effect size and the total effect size of the remaining studies, also known as impact analysis, was used. Among hospitalized patients in internal medicine, the effect sizes after excluding studies one by one were all within the 95%CI value of the total effect size. Therefore, they had little effect on the total combined effect size and were acceptable. The original meta-analysis results were strengthened to make them more convincing.

In the groups of patient (surgery, internal medicine, ICU), their I^2 were 75%, 45%, and 36%, respectively, indicating that there was no obvious heterogeneity in internal medicine patients in the subgroups; but if the three subgroups were combined, I^2 was 61% indicating that there was hetero-

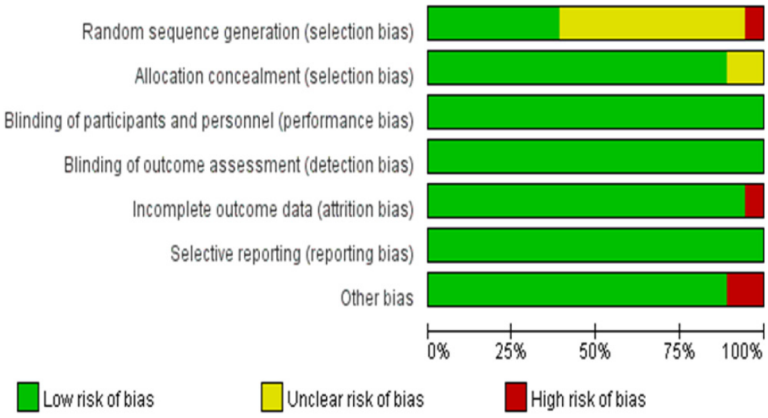

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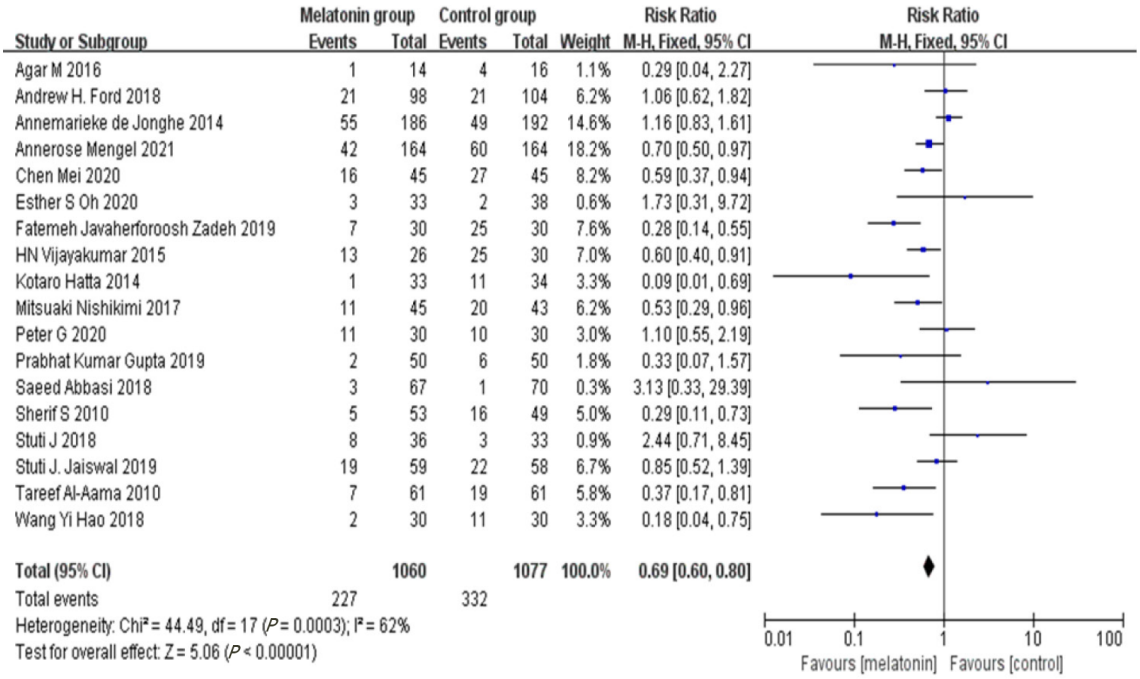
Figure 3 Distribution of the methodological quality of the included studies.



DOI: 10.12998/wjcc.v10.i12.3773

Figure 4 Meta-analysis forest diagram of melatonin in the prevention of delirium in hospitalized patients in this study. CI: Confidence interval.

geneity, the intervention effect of melatonin in preventing delirium in different hospitalized patients was inconsistent, and the different types of hospitalized patients were the source of the heterogeneity. Melatonin had a stronger effect in reducing the incidence of delirium in hospitalized medical patients, according to subgroup analysis (P < 0.01) as shown in Figure 8. Therefore, Stuti's[27] article was eliminated. Following removal of this study, the heterogeneity test was performed again. The results showed that the remaining 6 documents did not demonstrate heterogeneity (I^2 = 45% < 50%, P = 0.1). After elimination of this study, the fixed-effects model was used to combine the effect size.

Bias test

To determine whether there was publication bias in this study, a funnel chart was developed. The funnel chart for this study is shown in Figure 9. The funnel chart results of hospitalized patients in internal medicine showed a symmetrical distribution, suggesting that the publication bias of the included literature was small.

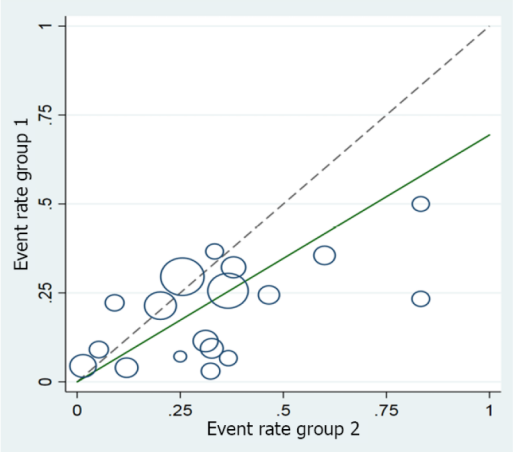


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Figure 5 Diagram of melatonin in the prevention of delirium in hospitalized patients in this study. It can see that the small circles and the middle circles are distributed on both sides of the oblique line in the figure, indicating that the heterogeneity is small, the large circles are not aligned, and the heterogeneity is strong.

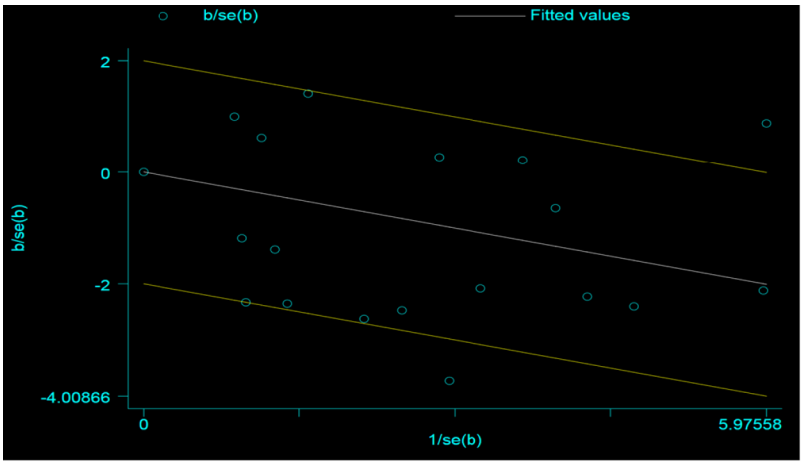

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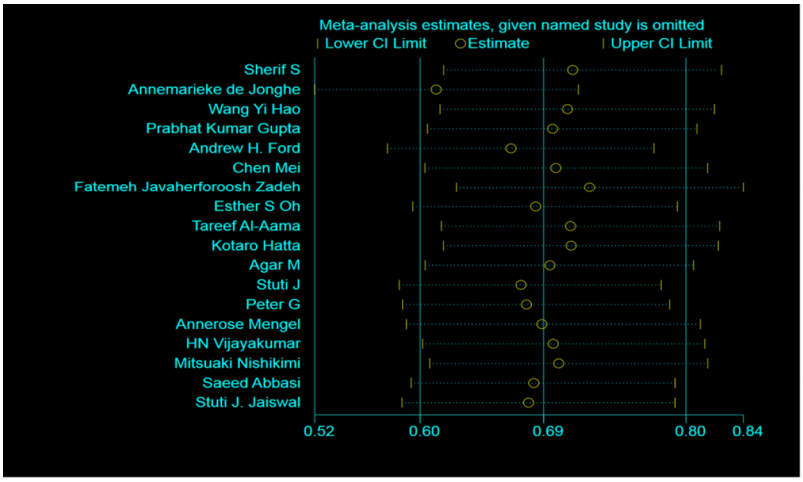
Figure 6 Galbraith diagram of melatonin in the prevention of delirium in hospitalized patients in this study (star chart).

DISCUSSION

Delirium is characterized by dramatic changes in cognition, which are accompanied by changes in consciousness and in mental state, and these changes will fluctuate over time[34]. The incidence of delirium on admission is 11%-33%. The number of elderly patients in the emergency department, internal medicine, and surgery wards of general hospitals has increased by 6%[35-37].

In palliative care, the clinical management strategy for delirium episodes is to identify and treat correctable precipitating factors if they are consistent with the patient's desired treatment objectives; when the desired care goals are completely focused on comfort or delirium, the clinical management method is to identify and treat correctable precipitating factors. When episodes are difficult to treat, the therapeutic intervention must focus on symptomatic management of painful symptoms, such as perceptual disturbance or agitation. Antipsychotic drugs have been advocated for the first-line pharmacological treatment of painful delirium symptoms[38,39]. However, there is evidence that antipsychotic drugs have no preventive effect on delirium in hospitalized adults, and their therapeutic effects are limited[12,40,41]; in a recent trial of palliative care patients, antipsychotic drugs were less effective than placebo. Exacerbation of mild to moderate delirium can occur[42]. The proposed overall management approach is shifting to larger preventive measures, especially non-pharmacological interventions, and minimizing the use of antipsychotic drugs[43]. Multi-component non-pharmacological interventions, including maintenance of sleep hygiene, have significant effects in preventing delirium in the elderly[44,45], but in studies of palliative care populations, similar interventions plus suppressive therapy have not been effective in preventing delirium. Sleep-wake cycle disorder is not the core diagnostic criterion for the diagnosis of delirium, but it is reported that the prevalence of delirium in cancer patients is between



DOI: 10.12998/wjcc.v10.i12.3773

Figure 7 Sensitivity analysis of melatonin in the prevention of delirium in hospitalized patients.

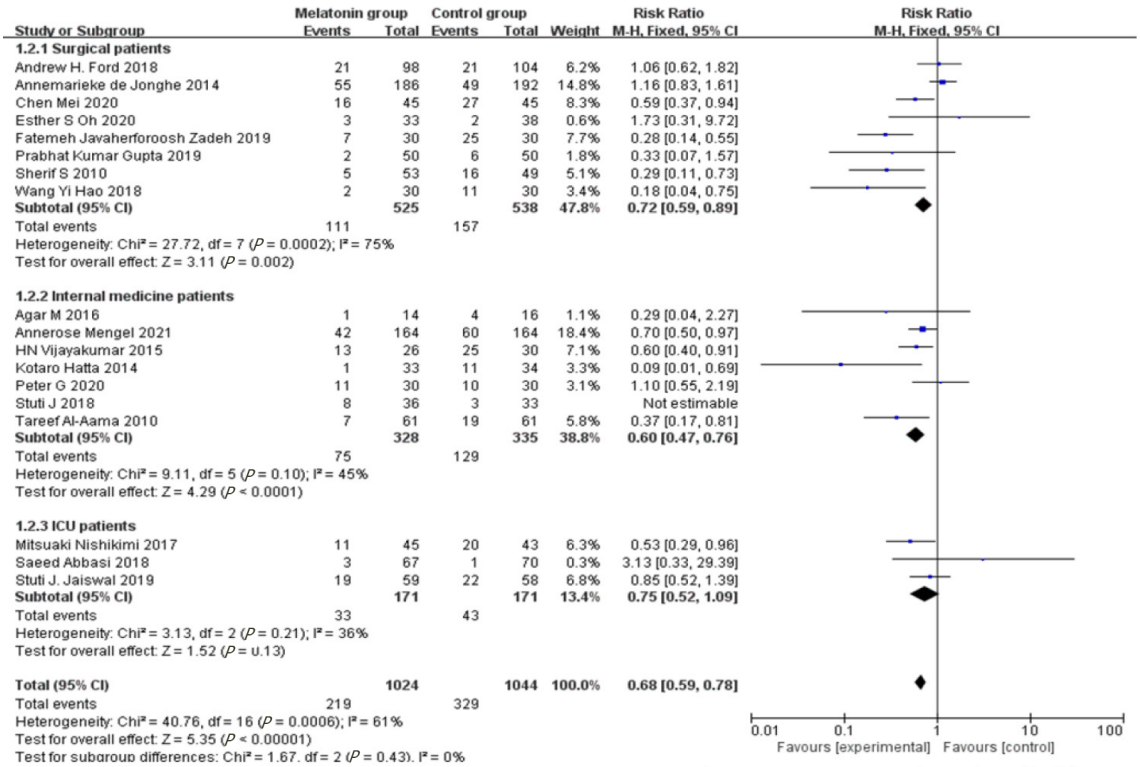


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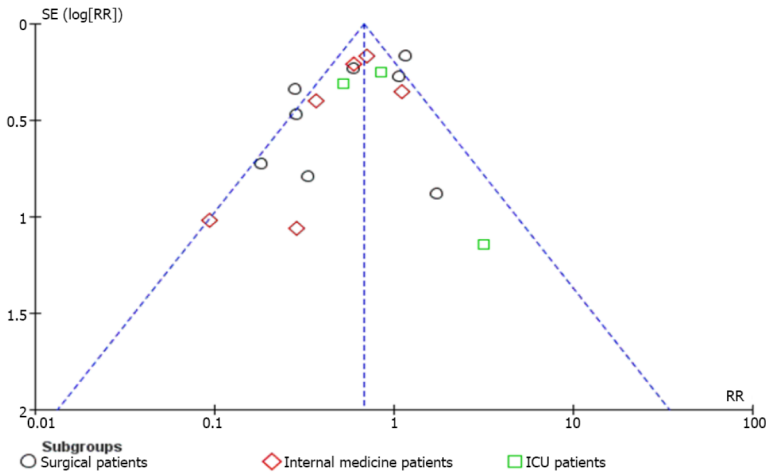
Figure 8 Forest diagram of subgroup analysis according to the type of inpatients (surgery, internal medicine, and intensive care unit).

75% and 100%[46,47]. Although the pathophysiology of delirium is complex and not fully understood, melatonin disorders and related sleep-wake cycle disturbances are thought to be contributing factors to delirium. This is consistent with the initiation and maintenance of sleep; it plays an important role in the regulation and synchronization of the sleep-wake cycle and circadian rhythm[48]. According to reports, melatonin circadian rhythm disorders are found in postoperative patients and critically ill patients, especially in sepsis patients[49-51]. Melatonin disorders have therefore been confirmed in the majority of clinical patients with the highest risk of delirium, and this is the main hypothetical basis for the exogenous use of melatonin to prevent delirium. Postoperative delirium is closely related to postoperative cognitive dysfunction. In addition, postoperative delirium is considered to be a predictor of postoperative cognitive decline[52].

Although there is increasing attention on the effects of melatonin and melatonin receptor agonists in promoting sleep and preventing delirium in critically ill patients and other high-risk populations[53], the heterogeneity of melatonin supplementation to prevent delirium has ruled out broad concluding



DOI: 10.12998/wjcc.v10.i12.3773

Figure 9 Funnel chart of subgroup analysis according to the type of hospitalized patients (surgery, internal medicine, and intensive care unit).

recommendations[54].

A total of 18 studies and 2137 patients were included in this systematic review and meta-analysis. The results of the study suggest that melatonin has a more significant effect in preventing delirium in hospitalized patients ($P < 0.01$), but no outstanding advantages have been observed in surgery and ICU patients, especially in surgical patients, although the effect was significant ($P < 0.01$). However, the heterogeneity in each study was strong. Melatonin cannot yet be considered effective in preventing delirium in surgical (post-surgery) patients; in ICU patients, the effectiveness of melatonin in preventing delirium in patients was not significant ($P > 0.01$), and there are currently few RCT-based studies on the effect of melatonin in the prevention of delirium in ICU patients. Multi-center, large-sample randomized controlled experimental data are still required to support these findings. Melatonin can be used to prevent delirium in hospitalized patients. However, it is unknown whether it is worthy of clinical recommendation, and the results of this study should be treated with caution.

This systematic study only retrieved publically available Chinese and English publications, and there are limitations in the retrieval of other languages and grey literature, which may cause certain publication bias. However, many predisposing factors of delirium were taken into account (for example, higher age, cognitive impairment, and dementia) and predisposing factors (for example, infections, drugs, and electrolyte disorders). Future studies should consider different subgroups of medical, surgical, and trauma patients, and patients with a higher incidence of delirium, such as the elderly, to evaluate which subgroup benefits most from exogenous melatonin supplementation. Larger RCTs should assess the possible differential melatonin effects in different patient subtypes to determine which subgroups of patients can benefit from melatonin to prevent delirium and which dose and duration of melatonin management are the most effective.

CONCLUSION

Melatonin may reduce the incidence of delirium in medical patients, but did not significantly reduce the occurrence of delirium in surgical and ICU patients.

ARTICLE HIGHLIGHTS

Research background

From an evidence-based perspective, this study examined the influence of melatonin on the prevention of delirium in hospitalized patients. The results suggest that in patients with delusional behavior and dermatology ward (ICU) patients, the effect of melatonin on delirium was confirmed. Thus, melatonin may be a treatment option for delirium with careful design for different types of respondents, and more standardized options.

Research motivation

Recently, research on the effect of melatonin on the occurrence of delirium in hospitalized patients has

attracted more and more attention. However, it is unknown whether melatonin can play a role in different types of hospitalized patients. The use of melatonin to prevent delirium has aroused increasing interest in doctors. However, whether melatonin can play a role in different types of hospitalized patients needs further research.

Research objectives

We conducted a meta-analysis, mainly for one purpose. It was based on high-quality studies with a large enough sample size to calculate a reliable estimate of the incidence of melatonin in preventing delirium in hospitalized patients, and to evaluate the role of melatonin in reducing the incidence of delirium in different types of patients.

Research methods

Various databases were searched and relevant studies on the incidence of delirium treated with melatonin in hospitalized patients were retrieved. In our meta-analysis, fixed-effects and random-effects models were used to estimate the incidence of delirium in hospitalized patients. Publication and sensitivity bias analysis was used to test the robustness of the data.

Research results

A total of 18 studies involving 2137 patients were eligible for this review. Melatonin was shown to be more effective in reducing the incidence of delirium in hospitalized medical patients, and the findings were statistically significant ($P < 0.01$).

Research conclusions

Melatonin can reduce the incidence of delirium in medical patients, but its impact on reducing the incidence of delirium in patients with behavioral disorders and ICU patients is unclear.

Research perspectives

Our meta-analysis showed that melatonin can reduce the incidence of delirium in hospitalized medical patients. Unfortunately, limited research has shown that the benefit is not seen in surgical patients or ICU patients. Further study to determine the role of melatonin in reducing the incidence of delirium in surgical and ICU patients is required.

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FOOTNOTES

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