

The Effect of Melatonin Supplement on High Arterial Blood Pressure: An Overview from Clinicaltrials.gov

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Background: Melatonin is a hormone produced by the pineal gland primarily at night. It has been suggested that melatonin may possess various cardiovascular benefits, including the potential to lower blood pressure. For this reason, we sought to identify and provide evidence of the effectiveness of melatonin on high arterial blood pressure in clinical trials.

Methods: Using the search term “melatonin and hypertension”, a search of the ClinicalTrials.gov database was performed on October 10th, 2023. I defined the exclusion and inclusion criteria to isolate appropriate clinical trials. Inclusion criteria for the search included hypertension that utilized melatonin as a treatment supplement; all non-related trials were omitted from the search. The data extractions, including study title, study type, study status, and intervention and outcome details, were compiled.

Results: Of the 13 clinical trials identified, only three focused on examining the effects of melatonin. The study titles, enrollment numbers, conditions, statuses, interventions, and outcome measures have been explained in depth. Information gathered from these clinical trials will assist us in identifying the possible risks and benefits of melatonin with respect to high arterial blood pressure.

Conclusion: Melatonin has been shown to be an effective treatment for lowering blood pressure. More research is required to fully establish the potential benefits and risks and highlight the mechanisms through which melatonin may influence blood pressure regulation.

Keywords: melatonin, blood, clinical trials, arterial, supplement

Introduction

Blood pressure is the force exerted by the blood against the walls of the arteries as the heart pumps it throughout the circulatory system. It is typically measured in millimeters of mercury (mmHg) and expressed as two values: systolic pressure over diastolic pressure. High blood pressure, also known as hypertension, is a significant global health concern contributing to an increased risk of cardiovascular diseases, stroke, and other adverse health outcomes. Hypertension affects an estimated almost one-third of the adult population worldwide, making it a critical public health issue.¹ As a result, interest has been growing in identifying novel therapeutic strategies and dietary supplements that may help regulate blood pressure and mitigate the risks associated with hypertension.^{2,3} One such dietary supplement that has gained attention in recent years for its potential impact on arterial blood pressure is melatonin.^{3,4}

Melatonin is a hormone produced by the pineal gland primarily at night, and it plays a vital role in regulating the circadian rhythm and sleep-wake cycle.^{5,6} Beyond its role in sleep regulation, melatonin has been suggested to possess various cardiovascular benefits, including the potential to lower blood pressure.⁴ This has led to a surge in research investigating the relationship between melatonin supplementation and arterial blood pressure.^{4,7} Many studies have shown that melatonin's impact on blood pressure regulation can be multifaceted. It is believed to influence blood pressure through its interaction with various physiological pathways, including the renin-angiotensin-aldosterone system (RAAS), nitric oxide (NO) production, and sympathetic nervous system (SNS) activity.⁸ Several studies showed that melatonin administration can reduce blood pressure by modulating the activity of these pathways. For example, melatonin has been found to inhibit the release of renin and aldosterone, which are key

regulators of blood pressure.⁷ Additionally, melatonin's antioxidant properties may help protect vascular endothelial cells from oxidative stress, further contributing to its potential antihypertensive effects.⁸ In this study, we used results from ClinicalTrials.gov to examine the effectiveness of melatonin on high arterial blood pressure.

Methods

Search Strategy

On October 10th, 2023, a thorough investigation was performed on ClinicalTrials.gov to identify all relevant studies regarding the effect of melatonin as a supplementary intervention for hypertension and associated indications. The term “melatonin and hypertension” was entered into the search engine website to generate pertinent results. The utilization of such a specific search query aimed to generate a focused and refined set of results, contributing to the comprehensive understanding of the current landscape of research on melatonin's role as an intervention for hypertension and related conditions.

Reviewing Search Results

The procedure for identifying appropriate clinical trials relied on specific criteria detailed in the area of interest of the research. The inclusion criterion for clinical trials investigating hypertension was that such trials were required specifically to demonstrate the effect of melatonin as a treatment. Clinical trials that did not demonstrate the effect of melatonin as a treatment were excluded from the review.

Data Extraction

Several data, including study title, type, intervention details, status, and outcome, were collected from the website.

Results

Analysis of the Number of Clinical Trials Relevant to the Review

An inclusive search of the ClinicalTrials.gov website on October 10th, 2023, indicated 13 registered trials specific to hypertension. These identified clinical trials were carefully documented and focused on the potential of melatonin as a supplementary treatment for hypertension.

Only three of the thirteen registered trials focused on the impact of melatonin, thus aligning with our inclusion criteria and research objectives – Table 1. The three clinical trials are reported as completed, have results, and are interventional and observational. Table 1 details the study titles, conditions, statuses, enrollment sizes, interventions, and outcome measures. The data gathered from these three clinical trials will assist our understanding of the potential risks and benefits of melatonin in relation to hypertension.

There were 93 participants in the included clinical trials and all of the studies were in Phase II of the clinical trials.

Discussion

In recent years, clinical trials investigating the effects of melatonin supplements on human blood pressure have yielded mixed results.^{3,12} Some studies have reported a modest reduction in blood pressure with melatonin supplementation, particularly in individuals with hypertension or at risk of developing hypertension.¹² However, the magnitude of the blood pressure-lowering effect varies among studies, and not all have demonstrated a significant impact.¹³ Factors such as dosage, duration of supplementation use, and the baseline blood pressure of participants may contribute to the variability in study outcomes.^{13,14} Regarding safety and contraindications, melatonin is generally considered safe when used for short-term purposes, such as adjusting sleep patterns. However, the long-term safety of melatonin supplements, especially in high doses, is still a subject of ongoing research.¹⁵ Individuals with specific medical conditions or those taking medication should consult with healthcare professionals before starting melatonin supplementation due to potential interactions and side effects.

Table I Data from <https://clinicaltrials.gov>, Updated on October 10th, 2023

#	Title	Status	Conditions	Interventions and Dosing	Primary Outcome Measures	Secondary Outcome Measures	Study Phase	Number of Participants	Year
1	"Melatonin Supplements for Improving Sleep in Individuals with Hypertension" ⁹	Completed	Sleep disorders and hypertension	Melatonin vs placebo	Sleep quality, sleep efficiency measured by polysomnography (total sleep time as a percentage of 8 hours of sleep), measured following 3 weeks of melatonin/placebo supplementation.	Change in systolic blood pressure (SBP) measured by monitoring of ambulatory blood pressure (ABP) over 24 hours. Measurement taken following 3 weeks of supplementation and compared with baseline.	Phase II	16	2010
2	"Melatonin and Nighttime Blood Pressure in African Americans – 24 mg Study" ¹⁰	Completed	Hypertension	Melatonin vs placebo	Mean nighttime SBP. Recording SBP using an ABP monitor. The period between self-reported sleep onset through to end of self-reported sleep was recorded. The mean values of many measurements were reported at the end of a 4-week period. The mean nighttime diastolic blood pressure (DBP) was recorded using an ABP monitor. The period between the onset of self-reported sleep through to the end of self-reported sleep was recorded. The mean values of many measurements were reported at the end of a 4-week period.	Mean nighttime Mean Arterial Pressure (MAP) was measured. This measures the average blood pressure in the subject's arteries during one complete heartbeat (cardiac cycle) at nighttime. The mean nighttime heart rate (HR), SBP and DBP over 24 hours were measured. The mean values of all measurements were reported at the end of a 4-week period.	Phase II	40	2014
3	"Melatonin and Nighttime Blood Pressure in African Americans – 8 mg Study" ¹¹	Completed	Hypertension	Melatonin vs placebo	Mean nighttime SBP. The nighttime SBP was recorded using an ABP monitor. Measurements were recorded from the onset through to the end of self-reported sleep. The mean values of many measurements were reported at the end of a 4-week period. Mean nighttime DBP. This was recorded using an ABP monitor. Measurements were recorded from the onset of self-reported sleep through to the end of self-reported sleep. The mean values of many measurements were reported at the end of a 4-week period.	Nighttime MAP, mean nighttime HR, SBP, DBP were measured. The heart rate was calculated using ABP monitoring. Nocturnal BP was measured. Nocturnal BP is dipping represents the mean nocturnal to mean daytime systolic BP and diastolic BP ratios, equivalent to the percentage drop in nighttime SBP in comparison to SBP during the day. The percentage of participants displaying melatonin-related side effects after a 4-week treatment period.	Phase II	37	2014

Conclusion

Melatonin's potential as a dietary supplement for regulating arterial blood pressure is a subject of ongoing research and debate. While some evidence suggests a favorable impact, more extensive and rigorous studies are needed to establish its effectiveness and safety as an antihypertensive agent. As our understanding of melatonin's mechanisms and its relationship with blood pressure continues to evolve, it holds promise as a complementary approach to managing hypertension, but cautious optimism should guide both research and clinical practice.

Disclosure

The author declares that the study was carried out without any affiliations or financial ties that could potentially raise concerns of a conflict of interest.

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