

## Why we recommend asthmatic patients not to take Asphalia:

We have not had any specific reports from asthmatic Asphalia users of any adverse symptoms. However, several peer reviewed studies report that their symptoms increase when exogenous melatonin is administered. For example, the US study below:

**Sutherland ER, Ellison MC, Kraft M, Martin RJ (2003)**

Elevated serum melatonin is associated with the nocturnal worsening of asthma.

J Allergy Clin Immunol. 2003 Sep;112(3):513-7.

Department of Pediatrics, National Jewish Medical and Research Center, 1400 Jackson Street, Denver, CO 80206, USA.

**BACKGROUND:** Increased airway inflammation at night contributes to the nocturnal worsening of asthma. In vitro studies have shown exogenous melatonin to be pro-inflammatory in asthma, but it is unknown whether endogenous melatonin levels are a controller of airway inflammation in nocturnal asthma. **OBJECTIVE:** Our aim was to determine 24-hour patterns of serum melatonin and their relationship to overnight decline in physiology in subjects with nocturnal asthma, non-nocturnal asthma, and in healthy controls. **METHODS:** Observational study of pulmonary physiology and melatonin levels in patients with nocturnal asthma (n = 7), non-nocturnal asthma (n = 13), and healthy controls (n = 11). Subjects maintained a constant sleep-wake regimen for 7 days. On day 8, serum melatonin was measured every 2 hours by radioimmunoassay and analyzed by cosinor modeling. The correlation between serum melatonin levels and overnight change in spirometry was evaluated by Spearman's rank correlation analysis. **RESULTS:** In subjects with nocturnal asthma, peak melatonin levels were significantly elevated compared with healthy controls (67.6 +/- 5.0 pg/mL versus 53.5 +/- 4.0 pg/mL, P =.03). Melatonin acrophase was delayed in nocturnal asthma (02:54 versus 01:58 in healthy controls, P =.003, and 02:15 in non-nocturnal asthma, P =.01). In subjects with nocturnal asthma, increasing melatonin levels were significantly and inversely correlated with overnight change in FEV(1) (r = -.79, P =.04), a relationship that was not observed in non-nocturnal asthma or healthy controls. **CONCLUSIONS:** Nocturnal asthma is associated with elevation and phase delay of peak serum melatonin levels. Elevated melatonin levels might contribute to the pathogenesis of nocturnal asthma.

### *Comment*

*These results only relate to patients suffering from nocturnal asthma, and the study itself is small, with only 7 nocturnal asthmatic candidates. There were no effects seen with non-nocturnal asthmatics. Nevertheless even though a larger study is needed to confirm the results, caution is evidently needed. By contrast a later Brazilian study concluded the opposite, and that melatonin actually improved the quality of sleep in asthmatic patients:*

**Francineide L. Campos, Francisco P. da Silva-Júnior, Veralice M. S. de Bruin and Pedro F. C. de Bruin**

## **Melatonin Improves Sleep in Asthma**

### **A Randomized, Double-blind, Placebo-controlled Study**

*American Journal of Respiratory and Critical Care Medicine* Vol 170. pp. 947-951, (2004)  
© 2004 [American Thoracic Society](#)

Department of Pharmacy and Department of Medicine, Universidade Federal do Ceará, Fortaleza, Brazil

Disturbed sleep is common in asthma. Melatonin has sleep-inducing activity and reportedly affects smooth muscle tone and inflammation. The aim of this study was to evaluate the effect of melatonin on sleep in patients with mild and moderate asthma. This was a randomized, double-blind, placebo-controlled study. Twenty-two consecutive women with asthma were randomized to receive melatonin 3 mg (n = 12) or placebo (n = 10) for 4 weeks. Sleep quality and daytime somnolence were assessed by the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale, respectively. Pulmonary function was assessed by spirometry. Use of relief medication, asthma symptoms, and morning and evening peak expiratory flow rate were recorded daily. Melatonin treatment significantly improved subjective sleep quality, as compared with placebo ( $p = 0.04$ ). No significant difference in asthma symptoms, use of relief medication and daily peak expiratory flow rate was found between groups. We conclude that melatonin can improve sleep in patients with asthma. Further studies looking into long-term effects of melatonin on airway inflammation and bronchial hyperresponsiveness are needed before melatonin can be recommended in patients with asthma.

#### *Comment:*

*This Brazilian study is a little larger than the previous one, but the results do not have high significance, ( $p=0,04$  is only just significant,  $p=0.05$  being the minimum) and so the authors are justifiably cautious before recommending melatonin as an adjuvant for asthma patients.*