PHARMACOKINETICS OF ORAL MELATONIN IN HIGH-RISK CRITICALLY ILL: STANDARD FORMULATION VS INCAPSULATION IN SOLID LIPID NANOPARTICLES (SLN).

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Introduction

Melatonin could be useful in critically ill thanks to its antioxidant, immunomodulating, and hypnagogue effects. When administered orally, its bioavailability is limited by a marked first pass hepatic metabolism. Incorporation in SLN, targeted to lymph after enteral administration may create a sustained release delivery system. This could maintain a prolonged blood concentration, and allow cellular internalization independent from MT1/MT2 membrane receptors.

Methods

In high-risk critically ill (SAPS II>32, mechanical ventilation >48 hours), repeated blood sampling were performed to assess melatonin levels from 2nd ICU day at 8 pm (endogenous levels) to 4th ICU day. Melatonin 3 mg (standard or incorporated in SLN) was administered via naso-gastric (NGT) or naso-jejunal (NJT) tube on 3rd ICU day at 8 pm.

Results

12 patients were enrolled. Age 68±11 years. SAPS II 49±11. Lenght of ICU stay 13 [10-16] days. Diagnosis: acute lung injury (5), septic shock (2), necrotizing fasciitis, abruption of aortic aneurism, pleural empyema, acute myocardial infarction, diabetes insipidus. 3 patients had NJT, while 9 NGT. Metoclopramide was used in 4 patients.

Both standard and SLN-melatonin formulations reached pharmacological blood levels 5 minutes after administration ($p<0.01$). A significant difference between groups rose from 30 minutes to 3 hours with SLN levels up to four time higher than standard formulation ($p<0.05$). Pharmacological blood levels lasted up to 10 hours with both formulations, with a trend in favour of SLN-melatonin ($p<0.08$).

Conclusions

SLN-melatonin seems to have a more favourable pharmacokinetic profile in order to determine meaningful clinical effects.