PURPOSE: To test the hypothesis that there are the melatonin dose response effect on pain threshold after taking into account the interindividual and intraindividual variability. We tested the pressure pain tolerance, the heat pain tolerance, and the sedative effect.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy subjects</td>
<td>Intervention groups: 1) sublingual melatonin 0.05 mg/kg, 2) sublingual melatonin 0.15 mg/kg, 3) sublingual melatonin 0.25 mg/kg, 4) placebo</td>
<td>Phase II</td>
</tr>
</tbody>
</table>

Estimated Enrollment: 60 patients

Study Type: Intervention
Study Start Date: 2011-05-01
Completion Date: 2011-11-01
Study Design: Randomized, in parallel, double-blind, controlled with placebo
Treatment duration: Two hours (One session)
SUBLINGUAL MELOTONIN

Sublingual melatonin 0.05mg/kg  Dose 0.05
Sublingual melatonin 0.15mg/kg  Dose 0.15
Sublingual melatonin 0.25mg/kg  Dose 0.25
Placebo  Placebo

Study allocation:
Randomization in fixed block size of 12, stratified by gender

ENDPOINT CLASSIFICATION:
Dose response-effect

INTERVENTION MODEL:
Parallel Assignment

MASKING:
Before the recruitment phase, the sealed envelopes containing the allocated treatment were prepared and numbered sequentially. The envelopes were only allowed to be opened after the subject signed the consent form; envelopes were opened by the nurse who administered the medications. Throughout the study period, randomization was performed by two investigators who were not involved in subject evaluation. Other individuals who were involved in patient care were unaware of the treatment group to which the patients belonged.

Primary purpose:
Dose-response effect of melatonin in pain threshold

ELIGIBILITY
Healthy
Ages Eligible for Study:
19 to 49 years
Genders Eligible for Study:
Female and male
Accepts Healthy Volunteers
Yes

STUDY ELIGIBILITY CRITERIA

Inclusion criteria
- Healthy subjects
- Age: 19 to 60 years

Exclusion criteria
Current acute or chronic pain;
Use of analgesics in the past week;
Rheumatologic disease;
Clinically significant or unstable medical psychiatric disorder;
History of alcohol
Substance abuse in the past 6 months;
Neuropsychiatric comorbidity;
Use of central nervous system medications.

INVESTIGATORS

Principal Investigator: Wolnei Caumo MD, PhD.

Locations:
Department: Laboratory of Pain & Neuromodulation
THE PRIMARY OUTCOMES:

- Pain pressure threshold (PPT)
- Pain tolerance to PPT

THE SECONDARY OUTCOMES:

- Sedation level on VAS and BIS (bi-spectral index)