ELSEVIER

Surgery for Obesity and Related Diseases ▮ (2016) 00–00

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

Melatonin premedication improves quality of recovery following bariatric surgery – a double blind placebo controlled prospective study

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Received August 30, 2016; accepted November 1, 2016

Abstract

Background: Melatonin has hypnotic, sedative, analgesic, anti-inflammatory, and antioxidant properties, and is a widely used sleep agent.

Objectives: Our aim was to evaluate the effect of melatonin premedication on postoperative recovery in patients undergoing bariatric surgery.

Setting: University Hospital, Israel.

Methods: Patients undergoing bariatric surgery were randomized to receive either 5 mg melatonin (M group) or placebo (P group) once on the night before surgery and again 2 hours before surgery. Quality of recovery was assessed using the QoR-15, a 15 item questionnaire on quality of recovery after surgery and anesthesia, regarding emotional state, physical comfort, psychological support, pain, and physical independence. A maximal score of 140 suggested good recovery (1 question was omitted due to irrelevance). The patients answered the questionnaire in the preanesthesia clinic, on admission to the operating room, and on the first postoperative day.

Results: A total of 44 patients completed the study. There was no statistical difference between M and P groups in the mean QoR-15 scores obtained before the surgery. Mean postoperative QoR-15 score was higher in the M group compared with the P group (118.3 ± 12.9 versus 107.8 ± 18.7, respectively; $P < .01$). Scores were also higher in the M group regarding pain ($P < .05$) and quality of sleep ($P < .05$).

Conclusions: Use of melatonin premedication improved the quality of recovery 1 day after bariatric surgery as measured by the QoR-15, specifically the quality of sleep and pain levels. Melatonin may serve as a premedication, especially when other options, like benzodiazepines are not recommended. (Surg Obes Relat Dis 2016;▮:00–00.)

Keywords: Melatonin; Premedication; Bariatric; QoR-15; Quality of recovery

Melatonin (N-acetyl-5-methoxytryptamine), is an endogenous hormone secreted from the pineal gland in a circadian rhythm [1]. It is supplied as an over-the-counter medication in the United States and as a prescription drug in other countries as a sleep aid and for treatment of sleep disorders [2,3]. Melatonin has hypnotic, sedative, analgesic, anti-inflammatory and antioxidant properties.

Patients undergoing surgery may experience anxiety or pain, which might influence postoperative pain levels [4]. Changes in circadian hormone release, in autonomous nervous system tone and in body temperature could also

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http://dx.doi.org/10.1016/j.soard.2016.11.001

influence morbidity and patient comfort after surgery. Changes in these factors could affect the quality of sleep and recovery from surgery [5]. Due to the sedative, analgesic, and hypnotic properties of melatonin, it is an effective premedication for reducing stress and anxiety before anesthesia and surgery and may have a positive effect on postoperative sleep and recovery. The recommended premedication dose of melatonin in adults is 5 mg [6]. Melatonin has relatively few and minor side-effects, such as drowsiness, headache, gastrointestinal disturbances, rash, and insomnia [4].

Patients undergoing bariatric surgery often have weight-related as well as metabolic co-morbidities (i.e., diabetes, obstructive sleep apnea, cardiovascular disease, and osteoarthritis, to name a few) [7]. The preoperative use of benzodiazepines for anxiety relief is not always recommended for these patients, due to a high prevalence of obstructive sleep apnea, which has been implicated in perioperative morbidity and mortality [8].

Melatonin may serve as a safe and effective premedication for bariatric surgery, and due to its unique properties, may also improve sleep quality and recovery from surgery and anesthesia. The aim of this study was to assess the effect of melatonin premedication on postoperative quality of recovery in patients undergoing bariatric surgery. The primary outcome parameter of this study was the QoR-15 questionnaire score, a 15 item questionnaire on quality of recovery which has been shown to measure health status after surgery and anesthesia [9].

Methods

Trial design

The study was a prospective, randomized, placebo-controlled, double blind study (Fig. 1), approved by the institutional review board and registered at the National Institutes of Health web site (ClinicalTrials.gov ID: NCT02424071). After obtaining informed consent, 60 morbidly obese patients undergoing bariatric surgery in a single, university hospital, were enrolled to participate in the study. Inclusion criteria were Hebrew speaking patients over the age of 18, and exclusion criteria was unwillingness to participate.

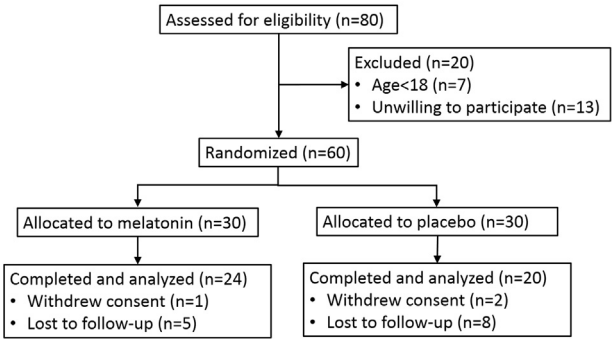

Fig. 1.

Eligible patients were randomized using a randomization table into one of 2 groups using sealed opaque envelopes containing either 2 melatonin capsules or 2 placebo capsules. Envelopes were drawn and opened at the time of study enrollment in the preanesthesia clinic by an anesthesiologist not otherwise engaged in the patient's care. The patients, the treating surgeons and anesthesiologists, and the nurse who presented the QoR-15 were all blinded to the treatment group. The melatonin group received 5 mg melatonin on the night before surgery and approximately 2 hours before surgery, and the placebo group received placebo capsules at the same time points. This premedication regimen was chosen based on previous studies reporting reduced pain scores or an opioid-sparing effect of melatonin [4].

Laparoscopic sleeve gastrectomy (LSG) and Roux-Y gastric bypass (LRYGB) were performed in a standardized fashion as previously described [10].

Data collection

Demographic and preoperative data were collected at the time of enrollment. The quality of recovery from anesthesia and surgery was assessed using a validated Hebrew version of the QoR-15 questionnaire [9]. The questionnaire is a shortened 15 questions version based on the QoR-40 [11]. Answers are scored in a Likert scale of 0 to 10. Questions in both questionnaires are divided into 5 topics: emotional state, physical comfort, psychological support, physical independence, and pain [12]. A recently published review showed the shortened, 15-question survey demonstrates results similar to the full version and is more patient friendly [9]. The item: "Been able to enjoy food" was omitted from the questionnaire due to fasting requirements and special diet imposed on patients before bariatric surgeries. The maximal score of the questionnaire was 140.

Patients were asked to answer the questionnaire 3 times: 1) in the preanesthesia clinic, 2) upon admission to the operating room (OR) approximately 1.5 hours after ingesting the second dose of premedication, and 3) on the first postoperative day (POD1). In addition, the following factors were compared: age, gender, basal metabolic index (BMI), American Society of Anesthesiologists (ASA) physical status score, and duration of surgery. Patients were also questioned about medication side effects.

Statistical analysis

Continuous variables are described as mean ± standard deviation and range and were compared by using Student's t test. Categorical variables are described using frequency distributions and are presented as frequency (%). Categorical variables were compared using the chi square, or