Correction to: Melatonin as an alternative sedation method during magnetic resonance imaging in preschool children with musculoskeletal problems

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Abstract

Magnetic resonance imaging (MRI) in preschool children is often challenging due to excessive motion artifacts. Sedation or general anesthesia (GA) are commonly used to prevent children from moving in the MRI scanner, with increased risk for cardiopulmonary complications and requirement for skilled personnel. Herein we investigated whether oral melatonin, a natural hormone implicated in circadian rhythm regulation, could be used as an alternative sedation method prior to the MRI in preschool children with musculoskeletal problems. Fifteen children with suspected juvenile idiopathic arthritis underwent a total of 16 MRI examinations following administration of 10 mg of oral melatonin; satisfactory images were obtained in all but one case, with no adverse events.

Conclusion: The use of melatonin before the musculoskeletal MRI in preschool children is an effective, safe and inexpensive alternative to standard sedation and general anesthesia in preventing motion artifacts.

What is known:

- Magnetic resonance imaging (MRI) is a well-recognized diagnostic method to visualize synovial inflammation and changes of cartilage and bone in juvenile idiopathic arthritis.
- MRI examination requires sedation or general anesthesia to ensure immobility in children who are uncooperative.

What is new:

- Additional to previous published studies we were able to show that melatonin for sedation for an MRI of joints, even without sleep deprivation, in the studied population may provide an alternative in children without behavioral problems, in order to avoid sedation/GA.

Keywords MRI · Sedation · Melatonin · Juvenile idiopathic arthritis

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Abbreviations

GA	general anesthesia
JIA	juvenile idiopathic arthritis
MRI	magnetic resonance imaging

Introduction

MRI is an important diagnostic tool in pediatric rheumatology, enabling early detection of synovial membrane inflammation and bone marrow edema, findings that precede joint erosions [2]. As excessive motion in the MRI scanner hinder the accurate diagnosis, the examinees are required to lay still, which is difficult for preschool children due to the claustrophobic environment, acoustic noise and the length of the exam. To avoid motion artifacts, sedation or general anesthesia are commonly used. These interventions in children have a well described risk and also incur substantial costs. Melatonin, a natural sleep cycle regulator that can induce sleep in children when administered orally, is discussed for over 10 years as an attractive alternative to conventional sedation due to its low cost and excellent safety profile. We wanted to examine whether the level of sedation with melatonin is adequate to perform a successful MRI scan of joints in order to avoid sedation/GA and thus reduce health costs and waiting lists.

Materials and methods

The study population was comprised of 15 children (median age = 4.5 years) with suspicion for juvenile idiopathic arthritis (JIA) and indication for joint MRI under sedation/GA. All children were prescribed prolonged-release melatonin product available in the Croatia and licensed for patients with primary insomnia aged 55 and over. A drug informed consent with parenteral information of off-label use was sought before administration. Melatonin was dispensed from pharmacy in a tablet. These tablets were crushed in order to enable the release profile like that of an immediate release preparation.

The study was done in the morning between 8 and 10 a.m.; parents were instructed to wake up the children an hour earlier than usual, and keep them awake until the MRI. Parents were asked about the amount of sleep prior to the examination and children slept 8–9 h during the night. An IV access for MRI contrast material was established in all the children upon arrival. Thirty minutes before the MRI 10 mg of melatonin added to a milk drink was administered to a child orally. We decided to administer the dose of 10 mg because it has

been shown in previous studies to be safe (without risk of respiratory compromise) and to have good sedative effect [5].

Mixing melatonin with milk was shown not to compromise the integrity of the drug and thus ensure delivery of the prescribed dose [9]. All children were placed in the darkened room in the close proximity to MRI room and they were accompanied by parents during preparation for MRI as well as during the scan. The average duration of imaging was 30 min. Awakening occurred spontaneously upon exiting the MRI machine in all the patients.

Results

We performed a total of 16 joint MRIs in 15 patients with suspected JIA. All children had non-steroidal anti-inflammatory agent in therapy. Adequate levels of sedation, allowing successful completion of the joint MRI, were achieved in 14/15 patients. Sedation level was assessed using University of Michigan sedation scale (MSS) [7]. Children were considered ready for scanning when they achieved level 3 (deeply sedated: deeply asleep and rousable to significant physical stimulation but settles soon afterwards) [10].

One patient had two MRI exams for different joints. The first one was successful, but the second one was ineffective (Table 1, Fig. 1). The quality of structural MRI scans was rated according to a five-point rating scale by an experienced radiologist as 1: no motion artifacts, excellent quality, 2: little motion artifacts, good quality, 3: moderate motion artifacts, acceptable quality, 4: excessive motion artifacts, poor quality, and 5: incomplete scan. Scans of score 1–3 were considered to be of sufficient quality for diagnostic purposes. In our sample, 15/16 had scans of good to excellent quality (score 1–2). One patient had ineffective MRI scan (score 4) [3].

As in other studies no adverse effects from the single administration of melatonin were encountered [5]. We didn't observe any respiratory compromise or allergic reactions in the period immediately after the administration of melatonin, and soon after the scanning. In the follow-up period of one year,

Table 1 Patient medical reports

Age (yr) [mean (range)]	4,5 (3–6)
Weight (kg) [mean (range)]	19,4 (15–24)
I.V. cannula inserted	15
Time from administration to scan (min) [range]	30–45
Scan length (min)	30
Achieved deep sedation (Michigan Sedation Scale (MSS) 3)	15
Failed to reach deep sedation (MSS 0–1)	1

parents did not report any safety issues (previously explained and written in an informed consent) which regard to melatonin administration.

Discussion

Sedation/GA is not always successful in preventing the motion artifacts, which can lead to repeated examinations, negative psychologic impact on the child and the family, prolonged hospital stay and significant increase in cost [1]. In prospective study on 1062 children who underwent MRI or CT, Malviya et al. reported excessive motion in 12% of scans of sedated children and 0.7% of those completed with general anaesthesia [6]. To avoid the use of sedation and general anesthesia with pediatric MRI, alternative methods such as use of pacifiers, swaddling, sleep deprivation, explaining the procedure of the MRI investigation using photos or a video, using a small model of the MRI scanner to familiarize the child with the layout of the unit and mock scanner training protocol, melatonin or hypnosis have been explored [3, 4]. Melatonin, owing to its role in circadian rhythm regulation, is a sedative, anxiolytic and hypnotic agent with excellent safety profile, therefore suitable for premedication before general anesthesia, or as an alternative sedation method prior to diagnostic (i.e. audiography, MRI and EEG) or therapeutic interventions (i.e dental procedures) [8]. A previous prospective study in an unselected group of 40 children found that melatonin was an effective pre-MRI sedation method in 55% of 40 children with developmental or behavioral problems, with further increase to 76% when used after sleep deprivation [5]. The higher rate of success of melatonin administration in our study could be explained by the lack of other comorbidities that might influence the compliance. Furthermore, in order to alleviate anxiety and reduce movement during the examination all patients and parents/guardians were

familiarized with the examination prior to the scan explaining the procedure of the MRI investigation using photos and by the presence of an adult family member or guardian with the child prior to and during the scan. All children included in our study had an intravenous cannula inserted in order to give them gadolinium DTPA contrast. In order to avoid additional disturbance of children this procedure was done at least one hour before MRI examination. This time delay in our experience was sufficient in order to alleviate the distress in our patients so we advocate this approach in children. Sleep deprivation can reduce the need for sedation in young children and infants undergoing MRI examination [4]. Since musculoskeletal MRI examination in our study was performed in children as outpatient examination, we used no sleep deprivation in order to avoid the possible differences among children related to the compliance and cooperation of parents/guardians.

In summary, our study provides additional evidence for the effectiveness and safety of melatonin as a sedation method before the musculoskeletal MRI. Unlike in the previous studies, our patients all had newly established IV access, and this painful intervention did not interfere with the sedative effect of melatonin. A potential shortcoming of our study is the small sample size and use of MRI to image the joints, which are easier to immobilize than the other body parts. Although a direct comparison between melatonin and standard sedation/GA in a larger cohort of patient is needed to draw the final conclusion, the use of melatonin in our group of patients with musculoskeletal problems did have good sedative effect and we could get satisfactory MRI images suitable for interpretation. Thereby we managed to reduce health costs and prevent possible adverse events if using standard sedation/GA techniques. In conclusion, our rate of success may be due to the combination of the dose of melatonin, our training protocol, and lack of behavioral problems and comorbidities in the studied population.

Fig. 1 One of our patients who achieved good level of sedation and afterwards had excellent quality of pre- and post-contrast enhanced knee MRI scans (a, b), and our patient with ineffective sedation and thus poor quality knee MRI scan (c)

Authors' contributions Dr. Pasini conceptualized and drafted the initial manuscript, approved the final manuscript.

Dr. Marjanović helped with the radiologic procedures and findings and making the diagnosis, writing the initial manuscript and critically revised the manuscript.

Dr. Roić helped with the radiologic procedures and findings and making the diagnosis, writing the initial manuscript and critically revised the manuscript.

Dr. Dukarić helped with the radiologic procedures and findings and making the diagnosis, writing the initial manuscript.

Dr. Tripalo Batoš helped with the radiologic findings and making the diagnosis, writing the initial manuscript.

Dr. Bahtijarević was involved in the making the diagnosis, follow-up of the patient and writing the initial manuscript.

Dr. Gagro conceptualized initial manuscript, critically revised the manuscript, approved the final manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Compliance with Ethical Standards

An informed consent with parenteral information of off-label use was obtained.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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