Spine Deformity

www.spine-deformity.org

Spine Deformity 6 (2018) 48−53

Metal Ion Release During Growth-Friendly Instrumentation for Early-Onset Scoliosis: A Preliminary Study

Caglar Yilgor, MD[a], Ayaz Efendiyev, MD[b], Filiz Akbiyik, MD[c], Gokhan Demirkiran, MD[b], Alpaslan Senkoylu, MD[d], Ahmet Alanay, MD[a], Muharrem Yazici, MD[b,*]

[a]*Orthopedics and Traumatology, Acibadem Mehmet Ali Aydınlar University, İçerenköy Mh. No:32 Kerem Aydınlar Kampüsü, Kayışdağı Cd., 34752 Ataşehir, Turkey*

[b]*Orthopedics and Traumatology, Hacettepe University, 06100 Sihhiye, Ankara, Turkey*

[c]*Medical Biochemistry, Hacettepe University, 06100 Sihhiye, Ankara, Turkey*

[d]*Orthopedics and Traumatology, Gazi University, Emniyet Mahallesi, 06560 Yenimahalle, Ankara, Turkey*

Received 30 October 2016; revised 1 May 2017; accepted 18 June 2017

Abstract

Background: Metal ions released from spinal instruments can cause localized debris and distribute systemically to settle on distant organs. Children with early-onset deformities live with metallic implants for a substantial amount of time. No research focused on metal distribution in growth-friendly instrumentations. The aim of this study was to compare age-matched growing rod (GR) and magnetically controlled growing rod (MCGR) groups to noninstrumented controls.

Methods: The study was designed as a multicenter, prospective, cross-sectional case series. GR and MCGR applications of three institutions were included. A total of 52 children were enrolled. Blood samples were collected between December 2014 and February 2015. Biochemical serum analyses were performed to trace and quantify titanium, vanadium, aluminum, and boron. The GR group included 15 children. Mean age was 10.7 (range 6-15). MCGR group included 22 children. Mean age was 8.5 (range 2-13). Fifteen age-matched nonoperated children formed the control group. The mean age was 10.4 (range 5-15). One-way analysis of variance, Kruskal-Wallis, and Mann-Whitney *U* tests were used for comparisons.

Results: The mean serum titanium level in control, GR, and MCGR groups were 2.8 ± 1.4, 7.3 ± 4.3, and 10.2 ± 6.8 μg/L, respectively. GR and MCGR group titanium levels were higher than controls' ($p = .008$ and $p < .001$). The mean serum vanadium level in control, GR, and MCGR groups were 0.2 ± 0.0, 0.2 ± 0.0, and 0.5 ± 0.5 μg/L, respectively. MCGR group vanadium level was higher than control ($p < .001$) and GR groups ($p = .004$). Mean serum levels in control, GR, and MCGR groups were, respectively, 5.4 ± 4.1, 8.1 ± 7.4, and 7.8 ± 5.1 μg/L for aluminum and 86.7 ± 2.7, 86.9 ± 2.5, and 85.0 ± 6.6 μg/L for boron. The distribution of aluminum and boron were similar across groups ($p = .675$ and $p = .396$).

Conclusions: Both GR and MCGR applications significantly release titanium and possibly aluminum. MCGR further releases vanadium. MCGR possibly releases more titanium than traditional GR. Time-dependent alterations of serum ion levels, structural properties of the MCGR device, and exposure caused by magnetic distraction processes warrant investigation.

Keywords: Metal ion release; Early onset scoliosis; Growth-friendly instrumentation; Growing rods; Magnetically controlled growing rods; Titanium; Vanadium

Introduction

The treatment of early-onset spinal deformities is a challenge as curve correction in growing spines will not always result in healthy children because of the age and growth-dependent relationship between the spinal column and the thoracic wall. Growing rods (GR) act as temporary internal braces that allow and stimulate growth of the spine, lungs, and the thoracic cage while controlling the deformity [1]. Thus, among surgical alternatives, GR is a state-of-the-art procedure when an early-onset deformity cannot be

IRB approval: This study was reviewed and approved by Hacettepe University Clinical Researches Ethics Board.

Author disclosures: CY (none); AE (none); FA (none); GD (none); AS (none); AA (personal fees from DePuy Synthes, personal fees from Stryker Spine, grants from DePuy Synthes, outside the submitted work); MY (personal fees from DePuy Synthes, outside the submitted work).

*Corresponding author. Department of Orthopedics and Traumatology, Faculty of Medicine, Hacettepe University, 06100 Sihhiye, Ankara, Turkey. Tel.: 00 90 505 6191351; fax: 00 90 312 3100161.

E-mail address: mimyazici@gmail.com (M. Yazici).

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http://dx.doi.org/10.1016/j.jspd.2017.06.005

managed nonsurgically. The more recently available magnetically controlled growing rods (MCGR) have evolved the concept of GR applications by introducing noninvasive lengthening feasibility [2].

The "growth" of these growth-friendly applications should obviously come to an end as the child reaches toward skeletal maturity. This point is generally referred to as "graduation." To date, a consensus on how to graduate the patients has not been reached. Implant removal, maintaining the implants as is, and reinstrumentation with definitive spinal fusion are implemented based on surgeons' preferences. No matter how they graduate, these children live with some kind of metallic implants for a significant amount of time [3], which may go well beyond a couple of decades.

Metal ion release has been addressed in adolescent idiopathic scoliosis (AIS) literature. Localized metal debris has been well documented in the paraspinal soft tissues surrounding instruments [4]. Systemic distribution via blood and lymphatic vessels and distant organ settlement of particulate debris have also been demonstrated [5]. When compared to instrumented spinal fusion for AIS, GR applications comprise fewer implants but they are more frequently manipulated. Therefore, although the dose and mode may vary, logically thinking, children with early-onset deformities treated with growing rods should also be subjected to metallic exposure. Yet, no research has focused on metal-ion release and distribution in growth-friendly instrumentation for early-onset scoliosis (EOS).

The mechanism and time-dependent serum-level alterations of metal ion release is an ongoing discussion. Moreover, the local and systemic long-term clinical effects of increased metal ion levels are yet to be determined. Nonetheless, it is reasonable to think that the suggested various potential deleterious effects would increase as the duration and amount of exposure increases. Therefore, metal-ion release and distribution in growth-friendly instrumentation merits investigation.

The aim of this study was to compare the serum metal ion levels of age-matched GR and MCGR patients to noninstrumented controls. This cross-sectional analysis further aims to form the fundamental knowledge on this topic to set a basis for relevant future studies.

Materials and Methods

The GR and MCGR applications of three institutions were included in this study. The blood samples were collected in the three months between December 2014 and February 2015 consecutively for this cross-sectional study. A total of 52 children were included.

The GR group included 15 children, with a mean age of 10.7 years (range 6-15). The index surgical operations were performed between March 2005 and September 2013. The average time between the index surgery and the time the blood was driven was 54 months (range 16-129). Two children had a single rod, and 13 had double-rod constructs. A total of 126 screws and 5 hooks were used at the anchor points, with an average of 8.73 implants per construct (range 4-16). A transverse connector was used only on one patient. Screws, hooks, blockers, cross connectors, and rods were made of a titanium alloy that contains 5.5% to 6.75% aluminum, 3.5% to 4% vanadium, <0.3% iron, <0.2% oxygen, <0.08% carbon, <0.05% nitrogen, and <0.015% hydrogen (Pediatric Xia; Stryker, Kalamazoo, MI).

The MCGR group included 22 children, with a mean age of 8.5 years (range 2-13). The index surgical operations were performed between August 2010 and December 2014. The average time between the index surgery and the time the blood was driven was 23 months (range 1-58). Five children had a single rod, and 17 had double-rod constructs. A total of 186 screws and 6 hooks were used at the anchor points with an average of 8.72 implants per construct (range 8-15). A transverse connector was used on 3 patients. Same screws, hooks, blockers, and cross connectors were used as in the GR group. The rods used also have a similar metallic composition. MCGR rods are made of Ti-6Al-4V ASTM F136 titanium alloy that contains 5.5% to 6.5% aluminum, 3.5% to 4.5% vanadium, <0.25% iron, <0.13% oxygen, <0.08% carbon, <0.05% nitrogen, and <0.012% hydrogen. MCGR further contains boron in its central housing portion (MAGEC; NuVasive, San Diego, CA).

Fifteen age-matched nonoperated children who are conservatively followed in our clinic formed the control group. These children suffered from spinal disorders of similar etiologies, yet their curves were milder in that they were not candidates for surgical intervention. Mean age was 10.4 years (range 5-15).

In all three institutes, lengthening procedures for GR were done with a six-month interval and for MCGR with two- to three-month intervals. Blood samples were collected in the GR group in the preoperative hospitalization period before a lengthening procedure. Similarly, samples were obtained in the MCGR group in the clinic before lengthening.

All venous blood samples (10 mL) were collected in Trace Element Vacutainer tubes (Becton, Dickinson, UK). The serum was extracted after coagulation and centrifugation (4,000 rpm for 10 minutes, at room temperature) and stored at −80°C until analysis. The specimens from all three institutions were then transferred to an accredited laboratory (AnkaLab, Ankara, Turkey) that has internal and external quality control programs.

Serum titanium, vanadium, aluminum, boron, and iron levels were measured by the inductively coupled plasma mass spectrometry technique in an Agilent 7500 series ICP-MS (Agilent Technologies, Santa Clara, CA). The normal reference values and ranges in this laboratory were as follows: total serum iron: 37-145 μg/dL, titanium: <7.7 μg/L, vanadium: <0.05 μg/L, aluminum: 1-14 μg/L, and boron <100 μg/L.