Ann Med Res 2021;28(1):73-7

Annals of Medical Research
DOI: 10.5455/annalsmedres.2020.12.1201

Original Article

Importance of hair trace metal analysis after pectus bar implantation

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Abstract
Aim: This study aimed to determine if there was a significant increase in scalp hair levels of trace metals in children with implanted pectus bars and investigate previously unreported hair metal levels after minimally invasive repair of pectus excavatum (MIRPE).
Materials and Methods: Between November 2013 and December 2019, we prospectively collected scalp hair samples from patients before MIRPE and prior to pectus bar explantation (1 day before bar removal) to evaluate trace metal levels following the implantation of metal bars. Two study groups were involved: a group of consecutive patients who underwent pectus bar removal 2–5 years after MIRPE (study group, n = 97), and a group including the same patients (control group, n = 97) prior to MIRPE.
Results: The mean patient age was 13.3 ± 2.7 years (range, 11–19 years) preoperative and 16.4 ± 2.3 years (range 14–23 years) postoperative; 64% of the patients were male (n = 62). Statistically significant increases in all studied trace metal levels (chrome, iron, nickel, and molybdenum) were identified in the intergroup comparison of hair trace metal analysis.
Conclusion: The results of this prospective study show that hair is a good biological marker for the monitoring and study of trace metals released from pectus bars. This simple assessment may be useful for the screening of trace metal increase due to the pectus bar. When metal allergy is suspected during follow-up after MIRPE, the availability of preoperatively collected hair samples will be quite beneficial.

Keywords: Hair trace metals; metal allergy; stainless steel pectus bar

INTRODUCTION

Pectus excavatum is a common chest wall deformity which is mostly treated by insertion of a stainless steel bar. The metalware is recommended to remain in place for 2–5 years before elective bar removal (1). The examinations on explanted pectus bars revealed that there are surface metal changes and impaired chemical composition consistent with corrosion (2,3). The particles and ions are released due to dissemination of metallic wear debris from implanted metalware after corrosive events. Metallic debris can be detected locally in the surrounding tissues and systemically in the body fluids, organs, and scalp hair (4).

Hair sampling is non invasive, its collection does not require medical personnel, and the samples can be stored or transported at room temperature. In addition, the concentrations in hair reflect fairly long-term exposure (5,6) Thus, hair sampling appears as an advantageous method in human biomonitoring. There are articles on trace metal analysis in the blood and urine (7); however, there are no studies on whether the detection of metals in the hair could be useful in patients with pectus bars to reveal potential in-progress trace metal release. This study aimed to determine if there was a significant increase in scalp hair levels of trace metals in children with implanted pectus bars and investigate previously unreported hair metal levels after MIRPE.

MATERIALS and METHODS

In this prospective study, we collected data from 187 patients who underwent minimally invasive repair of pectus deformities between November 2013 and December 2019. We tested possible skin reaction by attaching the pectus bar that will be implanted, to the thoracic body surface of the patient for 72 h. We did not perform MIRPE in patients with a positive skin reaction (n=4). The inclusion criteria

Received: 22.12.2020 **Accepted:** 19.07.2021 **Available online:** 26.01.2021
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were diagnosis with pectus excavatum and having received the same pectus bar model, whereas the exclusion criteria included the use of multiple pectus bars in MIRPE (n = 14), diagnosis of pectus carinatum (n = 71), having undergone revision MIRPE surgery (n = 7), and loss of clinical follow-up (n = 2).

In our prospective study; scalp hair samples from patients before MIRPE and one day before bar removal, were collected in order to analyze trace metal levels after pectus bar implantation. We analyzed studied cases in two groups. Study group of patients who underwent pectus bar removal (n = 97), and control group of same patients (n = 97) before bar implantation. We analyzed trace elements including iron (Fe), chrome (Cr), nickel (Ni) and molybdenum (Mo) in extracted hair samples. The increase of studied trace metal levels were examined.

The stainless steel pectus bar's main components are; Fe (62%), Cr (18%), Ni (15%), and Mo (3%); however, many other metals and semimetals (2%) are also contained in very small amounts (1.5% manganese, 0.5% silicium 0.2% cobalt, 0.2% copper, and 0.01% aluminum) (Medxpert® GmbH, Max-Immelmann-Allee 19, 79427 Eschbach, Germany). Cr, Fe, Ni, and Mo levels in the hair were analyzed before MIRPE and prior to metalware removal. Patient characteristics (age, sex, and bar size) were recorded prospectively. A stainless steel allergy test plate was placed preoperatively. The local institutional review board approved this study (no. 2013/11), and all patients and their legal guardians provided informed consent prior to participating.

We performed hair collection at <4 cm from the skin at the right side of the patient's head. Samples weighed at least 0.5 g following the recommendations of well-established studies (8). Following, obtained hair samples were reconditioned with an ultrasonic bath to remove any traces adhering to their surfaces that may disrupt the results. The samples were then placed in a heater for 12 h at 50°C. Dried samples were stored at room temperature until analysis. To enable the full analysis of the trace metal levels in the hair samples, the samples were diluted; afterwards, they were digested in acid (6 mL of 65% HNO3 and 3 mL of 30% H2O2) in a microwave oven (Milestone Ethos 900). The samples were then stored at 20°C until analysis. This analysis was performed using an inductively coupled plasma-mass spectrometry technique. Metal quantification was performed with a high-resolution and double-focus element mass spectrometer (Thermo X Series 2 Model Power 1350 Auxiliary flow, 0.5 mL/mm; Nebuliser flow, 0.75 mL/mm model) equipped with a Meinhard-type concentric nebulizer, a Scott double-step non-refrigerated nebulization chamber, and a Fassel-type torch with a 1-mm inner diameter injector tube. The equipment was located at Istanbul Yeditepe University.

Surgical technique

After performing via two lateral incisions, pectus bar is implanted under videothoracoscopy. The stainless steel pectus bar was first bent individually to the shape of the patient's chest using a pectus bar tabletop bender. Insertion of the bar involved entering the thoracic cavity on the right side of the anterior chest wall, passing underneath the sternum, and exiting the thorax on the left side in the MIRPE procedure. Substernal pectus bar is in contact with the pleura, and its lateral parts are fixated in the soft tissue using two metal stabilizers.

Statistical analysis

Statistical analysis of the results was performed by the SPSS statistics program (SPSS Inc., ver 22.0, IBM, Chicago, IL, USA). Mean ± standard deviation and range for continuous variables and categorical variables in percentages, were reported by descriptive statistics. The Mann-Whitney U test was used in the comparative statistical analyses of the studied two groups. P values smaller than 0.05 were reported as statistically significant.

RESULTS

The mean patient age was 13.3 ± 2.7 years (range, 11–19 years) preoperative versus 16.4 ± 2.3 years (range, 14–23 years) postoperative; 64% (n = 62) of the patients were male. Pectus bar removal was performed after a mean 35 ± 4.8 months (range, 23–47 months). The mean pectus bar size was 270 ± 55 mm (range, 180–360 mm).

The preoperative mean levels of trace metals in the hair were: Ni, 34.1 ± 114.9 ppm (range, 0.02–672); Cr, 6.93 ± 5.5 ppm (range, 0.04–31); Fe, 7.86 ± 6.5 ppm (range, 0.1–33), and Mo, 0.29 ± 0.5 ppm (range, 0.01–4.03). After the bar implementation, the mean levels of trace metals in hair were Ni, 36.86 ± 40.8 ppm (range, 6.54–340.7); Cr, 20.92 ± 19.5 ppm (range, 4.35–124.4); Fe, 23.2 ± 22.9 ppm (range, 3.08–186.9 ppm); and Mo, 1.4 ± 3.38 ppm (range, 0.001–31.25 ppm). Statistically significant increases in all studied trace metal levels were noted on the intergroup comparison (Table 1).

Table 1. Hair Trace Metal Analysis in MIRPE Patients

Metal	Study Group (n = 97) *Mean ± SD (range)	Control Group (n = 97) *Mean ± SD (range)	P^m
Ni	36.86 ± 40.8 (6.54-340.7)	34.1 ± 114.9 (0.02-332)	0.001
Cr	20.92 ± 19.5 (4.35-124.4)	6.93 ± 5.5 (0.04-31)	0.001
Fe	23.2 ± 22.9 (3.08- 186.9)	7.86 ± 6.5 (0.1- 33)	0.001
Mo	1.4 ± 3.38 (0.001-31.25)	0.29 ± 0.5 (0.01.- 4.03)	0.001

Cr, Chrome; Fe, Iron; MIRPE, Minimally Invasive Repair of Pectus Excavatum; Mo, Molybdenum; Ni, Nickel; SD, Standard Deviation; *ppm in µg/g; mMann-Whitney U test

We suspected trace metal allergy due to increased trace metals in 6 patients (6%) who had skin lesions, systemic allergic symptoms, nagging recurrent pain, and consistent bilateral pleural effusion. The temporary presence of pleural effusions in the early postoperative period, which may be explained by the empty space created by elevation of the sternum or atelectasis, can be considered physiological (9). Since the symptoms in these patients occurred after a mean 40 days (range, 24–60 days), we did not assume that the symptoms were natural. All of these patients' complaints passed after treatment with antibiotics and prednisolone, which supported our probable diagnosis of metal allergy. There was no pathology in the blood or pleural fluid analysis or urinary test or signs of infection. Unfortunately, we could not analyze trace metals in the hair, blood, or urine of these patients at the time, because there was a strictly maintained schedule of material admission for trace metal analysis between our hospital and university due to limited technical capabilities.

DISCUSSION

There are many studies in the field of arthroplasty on the release of metal ions due to metalware corrosion. Stainless steel pectus bars, which are used in most minimally invasive pectus repairs, have lower corrosion resistance and susceptibility to wear than those used in arthroplasty; thus, there is a higher risk of potentially dangerous metal ions being released (10). Various studies have stated that metal level concentrations above 10–50% in the circulatory system accumulate in the scalp hair and they return to normal levels after 2-4 years (11-13). Hair is composed of proteins (65–95%, mainly keratin), water (15–35%), lipids (1–9%), and minerals (up to 1%) (14). Hair is a slow-growing tissue that does not show rapid fluctuations of metal levels; however, it is more useful for assessing the patient's exposure history and the tissue metal charge than the amount being transported at a given time (15). There are multiple studies on trace metal release analysis in the blood and urine after MIRPE; therefore, we used our limited technical resources to analyze trace metals in hair samples. Furthermore, the Environmental Protection Agency and the International Atomic Energy Agency recommend the use of scalp hair for monitoring the levels of most trace elements since they are found in hair in greater amounts than anywhere else in the body (16,17).

Several studies have commented on the usability of hair as a biomarker of trace element exposure in pediatric group (18). Hair has remarkable potential as a biomarker because it reflects the historical exposition of a variety of substances, including metals (19). Hair collection avoids invasive methods and does not cause patient discomfort. It reflects long-term potential intoxication of metal ions since it is not dependent on occasional situations. Hair analysis is a cheaper method compared to blood and urine because medical personnel for sample obtaining and cold storage for transportation are unnecessary. Hair samples can be stored in room temperature for a long time without chemical degradation (15). On the other hand, both blood and urine collections require specialized materials for sample transportation and conservation and require cold storage at all times. Moreover, urinalyses are unfavorable for the patient since 24-hour urine samples are needed, which adds uncertainty about proper sample collection due to possible inconvenience. Furthermore, we observed that various studies used preoperative patient samples as a control group to perform more accurate trace metal analysis because trace metal ion concentrations are quite variable among hair, blood, and urine (15,20). Therefore, comparing trace metal analysis results with reported reference ranges of studied metals does not provide the physician with qualified results. Thus, in our prospective study, we collected hair samples preoperatively.

There are potential mechanisms underlying metal ion release after pectus bar implantation. Metallic debris is generated by mechanical fretting and electrochemical corrosion (21). Although pectus bars are not articulating implants, they broadly bear a chest wall stress force of approximately 32 pounds (14 kg) (22,23). We hypothesize that motion forces produced by the constant diaphragmatic and chest wall movements cause pectus implant wear or corrosion. These motion forces are mostly distributed at the metal-on-metal (bar and metal stabilizer) interface, followed by metal-on-bone (bar and sternum–costal surface) and metal-on-soft tissue (metal stabilizer–bar and musculus serratus anterior) interfaces (7). The visual of corrosion on the distal surfaces of several explanted bars would support this hypothesis (Figure 1). Additionally, bending of the bars also leads to changes in the surface and little fractures, resulting in metal release (20). Another explanation could be the diffuse release of metal ions from the surface of the pectus bar, especially in areas that contact the visceral pleura, may trigger foreign body responses produced by macrophages (24). The precise underlying mechanism of trace metal release in patients who undergo MIRPE remains to be elucidated. Several studies revealed significant trace metal release by analyzing blood and urine samples of patients who underwent MIRPE (7,20). Here we analyzed hair samples and observed that substernal metal bars can lead to a significant release of trace metal ions; all studied trace metal levels were significantly elevated in the study group.

Figure 1. Visual of macroscopic surface defects of explanted pectus bars

After MIRPE, the trace metal ion release from the pectus implants could cause bilateral effusions, stinging recurrent lateral pain, and systemic or local allergic symptoms that mostly respond to steroids and antibiotics (20), whereas no studies reported diarrhea, nausea, abdominal pain, or vomiting, the common symptoms of metal poisoning. Immunological reactions involving hypersensitivity and aseptic loosening are probably caused by the response of macrophages due to metal ion release. A large spectrum of immunomodulatory effects caused by the release of trace metal ions, are due to the interaction of T- and B-lymphocytes which are phagocytosed by macrophages (25). The stainless steel bar should be removed before designated time in severe cases, when the patient fails to respond to treatment (26-28). Fortunately, we were not obliged to explant any pectus bars; none of our cases became severe. We speculate that trace metal release might cause the observed nonspecific and allergic symptoms in MIRPE patients. Several studies have shown that a significant release of trace metal ions is correlated with MIRPE and insertion of a stainless steel bar causes allergic symptoms and local tissue reactions without clear signs of infection in approximately 6–8% of cases (29,30). In our study, we observed possible symptoms of metal allergy in 6% of patients (n = 6). Ultimately, our data also suggest that trace metal allergy is a possible conflict in MIRPE patients.

LIMITATIONS

A comparative analysis with literature could not be performed based on a lack of data in the literature. Hair samples usually include environmental impurities, sweat, cosmetics, sebum, or surface material and can be easily contaminated from the exterior because of its high surface to volume ratio. External contamination from air, water, dust, or hygiene products and cosmetics may cause the presence of other metals and trace elements. The effect of physical growth and various dietary habits on trace metal levels in the studied hair samples are unknown in our study group. Due to lack of metal allergy skin test or lymphocyte transformation test, metal allergy was diagnosed through clinical symptoms without presence of laboratory data. Lastly, multivariate analysis could not be performed due to limited number of sample size.

CONCLUSION

The results of this prospective study showed that hair is a good biological marker for the monitoring and study of trace metals released from pectus bars. A hair sample is easy to obtain and preserve and is cost-free, unlike blood and urine samples. This simple assessment may be useful for the screening of trace metal increase due to the pectus bar. When trace metal allergy is suspected during follow-up after MIRPE, preoperatively collected hair samples will be quite beneficial.

Conflict of interest : The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: Istanbul Mehmet Akif Ersoy Thoracic and Cardiavascular Surgery Training and Research Hospital Clinic Ethic Commitee approved this study (no. 2013/11).

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