Research Paper

The Effect of Iron Chelators on urine Beta Microglobulin(β2M) and Serum Sodium on Patients with Thalassemia Major

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ABSTRACT

Background and Objectives: Thalassemia is the most common genetic disease associated with the body’s recurrent blood transfusions and iron overload. Iron chelators can reduce the adverse effects of iron overload through various mechanisms. However, concerns have recently been raised about their negative impact on renal function. The current study, therefore, examined the effect of different iron chelators on renal function in patients with thalassemia major.

Subjects and Methods: This cross-sectional descriptive study included primary thalassemia patients (5 - 25 years) referring to Ahwaz Thalassemia Center for regular blood transfusion and regular treatment with iron chelators. They were divided into 3 groups (deferiprone 60-80 mg/kg/d, deferasirox 15-35 mg/kg/d and deferoxamine 11-48 mg/kg/d). Blood and 24-hour urine samples were collected to determine glomerular filtration rate (GFR) and biochemical factors.

Results: No significant difference was observed between the studied groups in terms of GFR, urine albumin, serum creatinine, serum cystatin C, serum and urine phosphorus, and urine sodium (p > 0.05), but serum sodium and urine β2microglobulin (β2M) were significantly different between the studied groups (p < 0.05). Serum sodium was significantly higher in the deferiprone group compared to the control (P=0.004). Urine β2M was significantly higher in the deferoxamine and deferasirox groups in comparison with the control group (P=0.041, P=0.013). Finally, serum sodium was significantly higher in the deferiprone and deferasirox groups than that in the deferoxamine group (P=0.001, P=0.021).

Conclusion: Urine beta-2 microglobulin increased in patients receiving deferoxamine and deferasirox compared to the control group, which might indicate primary kidney damage.

Keywords: Thalassemia major, Iron chelator, Cystatin C, Beta-microglobulin

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Extended Abstract

Introduction

Thalassemia is the most common genetic disease associated with the body’s recurrent blood transfusions and iron overload. Iron chelators are compounds designed to bind and remove excess iron from the body. By leveraging various mechanisms, they work to counteract the harmful impact of iron overload, which is often a consequence of recurrent blood transfusions in individuals with thalassemia. Iron chelators can reduce the adverse effects of iron overload through various mechanisms. However, concerns have recently been raised about their negative impact on renal function. Hence, the current study examined the effect of different iron chelators on renal function in patients with thalassemia major. Findings of this study could greatly inform medical decisions and treatment strategies, contributing to optimization of the care and well-being of individuals grappling with thalassemia and iron overload.

Methods

This cross-sectional descriptive study included primary thalassemia patients aged 5 to 25 years. These individuals received regular blood transfusions as well as consistent treatment with iron chelators. They were divided into three distinct groups based on the specific iron chelator they were using. The groups were as follows:

1. Deferiprone Group: Individuals in this group received a dosage of 60-80 mg/kg/day of deferiprone.
2. Deferasirox Group: Patients in this group underwent treatment with a dosage ranging from 15-35 mg/kg/day of deferasirox.
3. Deferoxamine Group: This group consisted of individuals who received treatments with dosages varying from 11-48 mg/kg/day of deferoxamine.

Data collection included both blood and 24-hour urine samples obtained from the individuals in these groups. These samples were then used to determine the glomerular filtration rate (GFR) as well as various biochemical factors. The GFR is a specific measure used to assess how well the kidneys are filtering waste from the blood, thus providing valuable insights into kidney function. The principal goal of this research was to understand and compare the impact of these different iron chelators, deferiprone, deferasirox, and deferoxamine, on the glomerular filtration rate and the relevant biochemical factors in primary thalassemia patients within the specified age range.

By studying the effects of these different iron chelators on kidney function and the relevant biochemical markers, the researchers aimed to provide valuable data that could contribute to informed decision-making in thalassemia patient care. Findings of this study have the potential to help optimize treatment strategies, minimize potential risks, and improve the overall health and well-being of individuals with thalassemia and its associated treatments.

Results

No significant differences were observed between the studied groups in terms of GFR, urine albumin, serum creatinine, serum cystatin C, serum and urine phosphorus, and urine sodium (p-value> 0.05). However, our analysis did reveal a few significant differences among the groups:

- Serum Sodium: The serum sodium levels were notably different among the groups. Specifically, the deferasirox group exhibited significantly higher serum sodium levels compared to the control group (p=0.004). Additionally, serum sodium was significantly higher in the deferiprone and deferasirox groups compared to the deferoxamine group (p=0.001, p=0.021).

- Urine β2-microglobulin (β2M): The levels of urine β2Microglobulin were significantly higher in the deferoxamine and deferasirox groups compared to the control group (p=0.041, p=0.013). These findings suggest that while several biochemical factors and GFR did not show any substantial differences among the studied groups, there were significant variations in serum sodium levels and urine β2Microglobulin levels. This indicates that different iron chelators may have distinct impacts on these specific markers. Understanding these distinctions can be crucial for healthcare professionals managing thalassemia patients, as it sheds light on the potential various effects of different iron chelators on these particular biochemical factors. Findings of this study can contribute to tailored and more precise treatment approaches for individuals with thalassemia. More specifically, they provide valuable insights into the potential effect of different iron chelators on specific biochemical markers, contributing to a deeper understanding of the nuanced effects of these treatments on kidney function and the related factors in thalassemia patients.

Conclusion

The observation that urine beta-2 microglobulin (β2M) levels increased in patients receiving deferoxamine and deferasirox compared to the control group suggests a potential indication of primary kidney damage. Understanding Urine Beta-2 Microglobulin (β2M): Beta-2 microglobulin is a protein found on the surface of many cells, including those in the kidneys. When kidneys are functioning normally, only trace amounts of this protein are found in the urine. However, increased levels of β2M in urine can be a sign of kidney damage because it indicates that the kidneys may not be effectively filtering and retaining this protein as they should. In the context of this study, the elevated levels of urine β2Microglobulin in patients receiving deferoxamine and deferasirox compared to the control group suggest the possibility of primary kidney damage. This increase may indicate that these specific iron
chelators, deferoxamine and deferasirox, could potentially contribute to or be associated with kidney damage in thalassemia patients. These findings have important clinical implications. Specifically, they warrant close monitoring and assessment of kidney function in individuals with thalassemia who receive these specific iron chelators. Monitoring urine β2Microglobulin levels can offer insight into the potential impact of these treatments on kidney health and guide healthcare professionals in adjusting treatment plans and implementing appropriate interventions to safeguard kidney function. This observation may prompt further research and exploration into the precise effects of these iron chelators on kidney function and β2M levels. Understanding the mechanisms behind the increase in urine β2Microglobulin levels can potentially lead to the development of strategies to mitigate any potential kidney damage associated with these treatments while optimizing their benefits in managing iron overload in thalassemia patients. In summary, the increase in urine β2Microglobulin levels in patients receiving deferoxamine and deferasirox compared to the control group suggests a potential indicator of primary kidney damage. This underscores the importance of ongoing vigilance and assessment of kidney health in individuals with thalassemia undergoing treatment with iron chelators.

Ethical Considerations

Compliance with ethical guidelines

This research was approved by the Postgraduate Education Council of Ahwaz University of Medical Sciences in 2021, respecting the rights of the authors and authors to use printed and electronic texts and resources and the approval of the research project in the Ethics Committee of Ahwaz University of Medical Sciences with code IR.AJUMS.HGOLESTAN.REC.1399.153. This study was conducted by sara mousavi larijani to obtain a doctorate degree in internal medicine.

Funding

This study was supported by Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Authors contributions

All authors contributed equally in preparing all parts of the research.

Conflicts of interest

The authors declared no conflict of interest.

Acknowledgements

The authors would like to thank vice chancellor for research and technology of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran for any support during the performing this study and Management and staff of Ahvaz Thalassemia Center for helping in this study.
مقاله پژوهشی
بررسی تأثیر شلاتورهای آهن بر بتا میکروگلوبولین ادرار و سدیم سرم بیماران مبتلا به تالاسمی ماژور

**تاریخ دریافت: ۹ مرداد ۱۴۰۲**
**تاریخ پذیرش: ۲۸ اکتبر ۱۴۰۲**
**تاریخ انتشار: ۲۸ هفتم دی ۱۴۰۲**

نویسنده مسئول:
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**مجله علمی پزشکی جنگدی شاپور**

کلمات کلیدی:
تالاسمی ماژور، شلاتور آهن، سیستاتین C، بتا میکروگلوبولین
یزدی، جنگی شapiaور

مهندسی پزشکی ایران، جنگی شapiaور

همانطور که در جدول ۴ نشان داده شد است، مقایسه روزی گروه‌های مورد مطالعه با گروه فردگرافامون با گروه کنترل و گروه دفراسیروکس با گروه کنترل نشان داد که عدد سدیم سرم در گروه دفراسیروکس و گروه کنترل تفاوت نامناسب داشته باشد (p<0.05). مقایسه حمام‌های شلیک‌وری در مورد آنها نشان داد که عدد سدیم سرم در گروه دفراسیروکس و گروه کنترل تفاوت اقلیدسی گروه دفراسیروکس نشان داد (p<0.05).

جدول ۱. مقایسه نوزادان گروه‌های مورد مطالعه

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Chelator Frequency (%)</th>
<th>Control frequency (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sex</td>
<td>Male</td>
<td>45 (100)</td>
<td>15 (100)</td>
<td>0.283</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>26 (57.8)</td>
<td>11 (73.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>19 (42.2)</td>
<td>4 (26.7)</td>
<td></td>
</tr>
</tbody>
</table>

جدول ۲. مقایسه عوامل پیش‌بینی سرم و ادرار در گروه‌های مورد مطالعه

<table>
<thead>
<tr>
<th>Biochemical tests</th>
<th>Deferiprone group</th>
<th>Deferasirox group</th>
<th>Deferoxamine group</th>
<th>Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (mL/min/1.73 m²)</td>
<td>126.06 ± 37.22</td>
<td>124.06 ± 35.87</td>
<td>131.8 ± 36.36</td>
<td>128.86 ± 33.24</td>
<td>0.965</td>
</tr>
<tr>
<td>Serum Cr (mg/dl)</td>
<td>0.72 ± 0.11</td>
<td>0.7 ± 0.07</td>
<td>0.74 ± 0.14</td>
<td>0.7 ± 0.08</td>
<td>0.705</td>
</tr>
<tr>
<td>Urine albumin (mg/dl)</td>
<td>8.6 ± 7.11</td>
<td>5.73 ± 2.43</td>
<td>9.36 ± 7.71</td>
<td>10.13 ± 5.76</td>
<td>0.089</td>
</tr>
<tr>
<td>Cys C (mg/dl)</td>
<td>0.79 ± 0.16</td>
<td>0.82 ± 0.13</td>
<td>0.79 ± 0.18</td>
<td>0.71 ± 0.09</td>
<td>0.185</td>
</tr>
<tr>
<td>B₂₆-MG</td>
<td>1.9 ± 0.56</td>
<td>2.57 ± 0.98</td>
<td>2.23 ± 0.6</td>
<td>1.73 ± 0.44</td>
<td>0.035</td>
</tr>
<tr>
<td>Urine P (mg/dl)</td>
<td>63.8 ± 31.84</td>
<td>40.06 ± 29.11</td>
<td>42.06 ± 20.28</td>
<td>48.73 ± 21.18</td>
<td>0.122</td>
</tr>
<tr>
<td>Serum P (mg/dl)</td>
<td>5.22 ± 0.88</td>
<td>5.08 ± 1.17</td>
<td>5.78 ± 1.51</td>
<td>5.90 ± 0.43</td>
<td>0.211</td>
</tr>
<tr>
<td>Urine sodium (mg/dl)</td>
<td>137.26 ± 56.84</td>
<td>122.26 ± 51.82</td>
<td>111.33 ± 44.37</td>
<td>118.53 ± 47.53</td>
<td>0.596</td>
</tr>
<tr>
<td>Serum sodium (mg/dl)</td>
<td>136.46 ± 0.83</td>
<td>135.8 ± 1.42</td>
<td>134.66 ± 1.47</td>
<td>133.33 ± 0.97</td>
<td>0.001</td>
</tr>
</tbody>
</table>

جدول ۳. مقایسه GFR بین دفراسیروکس و ادرار

<table>
<thead>
<tr>
<th>Biochemical tests</th>
<th>Deferiprone (Group A)</th>
<th>Deferasirox (Group B)</th>
<th>Deferoxamine (Group C)</th>
<th>Controls</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>B₂₆-MG</td>
<td>1.9 ± 0.56</td>
<td>2.57 ± 0.98</td>
<td>2.23 ± 0.6</td>
<td>1.73 ± 0.44</td>
<td>NS</td>
</tr>
<tr>
<td>Serum Na</td>
<td>136.46 ± 0.83</td>
<td>135.8 ± 1.42</td>
<td>134.66 ± 1.47</td>
<td>135.33 ± 0.44</td>
<td>0.004 NS</td>
</tr>
</tbody>
</table>

بحث

مطالعه حاضر به تغییرات ترکیب همکاران گزارش‌کننده به عنوان گروه‌های مختلف به سبب افزایش سدیم سرم و ادرار در گروه‌های مورد مطالعه (درفراسیروکس و کنترل) نشان داد (p<0.05). مقایسه حمام‌های شلیک‌وری در مورد آنها نشان داد که عدد سدیم سرم در گروه دفراسیروکس و گروه کنترل تفاوت اقلیدسی گروه دفراسیروکس نشان داد (p<0.05).
حال، کرون و همكاران نشان داد که سمت کلیوی در فلوکسامین و استه به در این اثر با با کاهش دوز دارو و افزایش مصرف مایعات قابل پیش‌بینی است. [17] چنان تحقیقاتی ممکن است به دلیل تفاوت در جمعیت و درمان باشد.

از انجایی که کارشناسان سرم اغلب GFR عملکرد کلیه را بررسی می‌کنند و در مطالعه حاضر، سیستاتین C در مقدار خاص، سیستاتین C در سرم در بن گروه‌های مورد مطالعه تفاوت معنی‌دار نداشت. با این حال، سطح آن در گروه دیفرسیروکس کاهش یافت. لذا، وظیفه فیزیولوژیک، بالاتر از سطح آن در گروه دیفرسیروکس کاهش یافت. این نتایج نشان می‌دهد که در حالی که گروه‌های دیفرسیروکس و دفورکسامین ممکن است نشان دهنده اختلال عملکرد کلیه باشد، این نتایج با مطالعاتی که سیستاتین C را در ارزیابی تصمیم‌گیری کلیه تأثیر زده‌اند. [41]

یافته‌های ما نشان داد که β2M در اکونومو و همکاران و ظفری و همکاران با مطالعه حاضر مطابقت داشت. [7، 13] البته این نتایج نشان می‌دهد که افزایش سیستاتین C، ممکن است نشان دهنده اختلال عملکرد لوله‌های پری و رثایی اولیه است. علاوه بر این، به نظر می‌رود که افزایش سیستاتین C، ممکن است نشان دهنده اختلال عملکرد لوله‌های پری و رثایی اولیه است. 

نتیجه‌گیری

بر اساس نتایج این مطالعه، با میکروگلوبولین‌های آلوده (B2M) و سدیم سرم در میان‌هایی که شلاتور در پایه یافته این اثر با با کاهش دوز دارو، افزایش مصرف مایعات قابل پیش‌بینی است. [17] چنان تحقیقاتی ممکن است به دلیل تفاوت در جمعیت و درمان باشد. در این اثر با با کاهش دوز دارو و افزایش مصرف مایعات قابل پیش‌بینی است. [17] چنان تحقیقاتی ممکن است به دلیل تفاوت در جمعیت و درمان باشد.
References


