FGF-23 and Hyperphosphatemia in Dialysis Dependent Chronic Kidney Disease Patients

Abstract

Introduction

Kidney disease (CKD). Aim was to evaluate Fibroblast Growth Factor (FGF-23) metabolism, in dialytic CKD patients.

Methods

Results

as compared to their recruitment levels.

Conclusion

Keywords:

Hyperphosphatemia, Mineral bone Disease; Secondary hyperparathyroidism

Abbreviations: CKD: Chronic Kidney Disease; iFGF23: intact Fibroblast Growth Factor-23; eGFR: Estimated Glomerular Filtration Rate; iPTH: Intact Parathyroid Hormone; SHPT: Renal Disease; Ca: Calcium; P: Phosphorus BALP: Bone Alkaline Phosphatase

Introduction

Dialysis dependent chronic kidney disease (CKD) has become a worldwide public health problem. It is known to increase patient morbidity and mortality risks which can cause major economic strain on the health-care systems. A population based study has in India was 160 per million population (p.m.p.) in the year 2008

\[ D_2 \text{Calcitriol}/ \text{Active Vitamin } D \], which can enhance intestinal phosphorus absorption. \[ 1,25 \text{(OH)}_2 \text{D} \], a phosphaturic hormone, hypophosphataemic rickets [6]. FGF-23 induces urinary phosphate

Arun Halankar\(^1\), Sandhya Sivaraman\(^2\) and Kavita Shalia*\(^*\)

\(^1\)Department of Nephrology, Sir H N Reliance Foundation Hospital and Research Centre, India

\(^2\)Ph.D. Student, Sir H N Hospital and Research Centre, India

\(^*\)Sr Scientist, Sir H N Medical Research Society, India

*Corresponding author:

Medical Research Society, Court House, L T Road, Mumbai

Kavita.shalia@fnshospital.org

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its later amendments or comparable ethical standards. Patient collection.

Dialysis Protocol

Recruitment of Study Population

Materials and methods

Enrollment of Study Population

Study population was selected as per the inclusion and

Also patient who were likely to conduct a kidney transplant biochemical tests.

Ethical Consideration
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while Sevelamer hydrochloride is a non-absorbable, synthetic
the two phosphate binders on an equal basis. At six month Total
recruitment and at six month.
Methodology of Research Tests

assay based on coated tube separation. Samples and calibrators
were studied by either Pearson or Spearman Correlation test.

Results and Discussion
Recruitment Data

Methodology of Research Tests

Statistical Analysis

Follow up Data

Citation:
at six month as compared to their recruitment levels. iFGF-23 and C-terminal FGF-23 levels at six month in dialytic CKD patients data (Table 6).

Discussion

In the present study, it was observed that plasma FGF-23 dialytic CKD patients as compared to the controls. A similar line provided in vitro and in vivo evidence that the isolated C-terminal
the diseased condition. In the present study it was observed that

P levels in dialytic CKD patients. The above mentioned increase in

Table 1

|                  | Control          | Recruitment CKD Stage 5 |
|------------------|------------------|-------------------------|
| **M/F**          | 32/34            | 31/17                   |
| **Age (years)**  | 41.4±10.5        | 42.6±12.4               |
| **Weight (kg)**  | 65.2±15.4        | 55.4±14.0               |
| **Body Mass Index** (BMI) (kg/m²) | 25.2±5.2 | 22.3±4.72               |
| **Smoking**      | -                | 13(27%)                 |
| **Alcohol**      | -                | 21(44%)                 |
| **Diabetes**     | -                | 27 (56%)                |
| **Hypertension** | -                | 26(54%)                 |

Table 2: Biochemistry Data.

| Routine Biochemical Tests | Control | Recruitment CKD Stage 5 |
|--------------------------|---------|-------------------------|
| Blood Urea Nitrogen (BUN) (mg/dl) | 9.50 (8/12) | 49.5 (38/58.8) |
| Creatinine (mg/dl)       | 1.0 (1.0/1.0) | 7.0 (6.0/8.0) |
| Estimated Glomerular Filtration Rate (ml/min/1.73m²) | 102±26.2 | 9.2±3.38 |
| Albumin (mg/dl)          | 4.53±0.84 | 3.51±0.37 |
| Globulin (mg/dl)         | 2.95±0.51 | 3.12±0.54 |
| Total Protein (mg/dl)    | 7.51±0.66 | 6.6±0.54 |
| Calcium (Ca) (mg/dl)     | 9.46±0.47 | 9.2±0.84 |
| Corrected Calcium (Cr.Ca) (mg/dl) | 9.07±0.63 | 9.56±0.79 |
| Phosphorous (P) (mg/dl)  | 4.31±1.74 | 6.5±2.22 |
| Corrected Ca x P (mg²/dl²) | 38.8±14.7 | 59.0±23.8 |

NS non-significant
**Table 3:** Six Month Follow up Biochemistry Data.

| Routine Biochemical Tests                  | Recruitment | 6th Month Follow Up |
|-------------------------------------------|-------------|---------------------|
| Blood Urea Nitrogen (BUN) (mg/dl)         | 49.5 (38.0/58.8) | 49.0 (38.0/69.0)   |
| Creatinine (mg/dl)                        | 7.0 (6.0/8.0)   | 8.0 (6.0/9.0)      |
| Estimated Glomerular Filtration Rate (ml/min/1.73m²) | 9.01±3.20       | 9.17±3.70          |
| Albumin (mg/dl)                           | 3.51±0.37     | 3.58±0.32          |
| Globulin (mg/dl)                          | 3.12±0.54     | 3.13±0.86          |
| Total Protein (mg/dl)                     | 6.61±0.54     | 6.73±0.64          |
| Calcium (Ca) (mg/dl)                      | 8.91 ±0.92     | 9.22 ±0.88         |
| Corrected Calcium (Cr.Ca) (mg/dl)         | 9.52±0.81      | 9.82±0.81          |
| Phosphorous (P) (mg/dl)                    | 6.45±2.20      | 4.45±1.26          |
| Corrected Ca x P (mg²/dl²)                | 58.6 ± 24.3    | 42.4 ± 14.8        |
| **NS non-significant**                    |              |                    |

**Table 4:** Six Month Follow up Data Continued.

|                                    | 6th Month Follow Up |
|------------------------------------|---------------------|
| Intact Parathyroid                 | 126 (100/320)       |
|                                    | ↑,                  |
| Total Fibroblast Growth Factor -23 (FGF-23) | 0.0 (0.0/2.1)   | ↑               |
| Intact Fibroblast Growth Factor -23 (iFGF-23) |                    | ↓,              |
| C Terminal Fibroblast Growth Factor -23 (FGF-23) |                | ↓               |
| Bone Alkaline Phosphatase          |                    | ↓               |
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Table 5: Left Ventricle Function Data.

|                        | Recruitment | 6th Month Follow Up |
|------------------------|-------------|---------------------|
| Left Ventricular Mass Index (LVMI) (g/m²) | 160 (127/214) | 157 (127/199) NS |
| End Diastolic volume (EDV) (ml) |            | ↓                   |
| End Systolic Volume (ESV) (ml) |            |                     |
| Stroke Volume (SV) (ml) |            |                     |

Table 6: Bone Mineral Density Data.

|                        | Median Percentiles 25/75 | Median Percentiles 25/75 |
|------------------------|-------------------------|-------------------------|
| FOREARM T Score SD     | -3.1 (-4.1/-2.3)        | -3.2 (-4.7/-2.6) p = 0.02 ↓ |
|                        |                         |                         |
| Z Score SD             | -2.95 (-4.07/-1.9)      | -3.2 (-4.7/-2.6) p = 0.02 ↓ |
|                        |                         |                         |
| FEMORAL NECK T Score SD| -1.15 (-2.2/-0.52)      | -2.2 (-2.95/-1.9) NS     |
|                        |                         |                         |
| Z Score SD             | -1.15 (-2.2/-0.52)      | -1.4 (-2.2/-0.8) p = 0.01 ↓ |

Table 6: Bone Mineral Density Data.

|                        | Median Percentiles 25/75 | Median Percentiles 25/75 |
|------------------------|-------------------------|-------------------------|
| LUMBAR SPINE T Score SD| -2.2 (-3.1/-1.52)       | -1.9 (-3.0/-1.5) NS     |
|                        |                         |                         |
| Z Score SD             | -1.4 (-2.2/-0.72)       | -1.4 (-2.2/-0.45) NS    |

NOTE: In the general population T-score ≤ -2.5 SD=OSTEOPOROSIS, T-score -1.0 TO -2.49 SD = OSTEOPENIA, Z Score above – 2.0 is considered normal acc. to International Society for Clinical Densitometry.

SHPT and 1, 25 (OH)₂ D deficiency are common complications among the long-term dialytic CKD patients. [22,23] SHPT is characterized by increased synthesis and secretion of PTH, mainly due to disturbances of calcium, phosphate and vitamin D metabolism. In addition, data suggests that FGF-23, plays a central role in the pathogenesis of SHPT by inhibiting 1 alpha hydroxylase which results in the reduction of calcitriol. [12,13] In agreement with the above findings, a significant reduction in the 1, 25 (OH)₂ D levels and significant increase in the levels of iPTH was observed in the present study. Hyperphosphatemia is considered a potent contributing stimulus for the development of SHPT, metastatic calcifications and renal osteodystrophy [5]. Thus managing phosphate levels in dialysis patients is a multi-interrelated task, involving the indispensable action of FGF-23, serum PTH and vitamin D.

However, optimal phosphate control in dialysis patients is extremely challenging [24]. Despite the significant increase in the levels of iPTH and phosphaturic hormone FGF-23, hyperphosphatemia were observed in CKD stage 5 patients. These dialysis patients were thus prescribed with phosphate binders and followed up for a period of six months. Multiple clinical studies have demonstrated that Sevelamer Hydrochloride lowers serum phosphorus levels among patients with ESRD and is generally well tolerated [25,26]. Apart from Sevelamer, several clinical trials have shown that Lanthanum is another effective and well tolerated phosphate binder among healthy volunteers as well as hemodialysis patients. [27,28] In the present study there was randomisation between the two phosphate binders among the patients. These patients were also provided with calcium carbonate and calcitriol tablets depending on their...
serum calcium and vitamin D levels. Calcium carbonate has been as compared to the baseline levels was observed in these CKD-

Acknowledgement

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Conclusion

Thus in the present study in the dialytic CKD patients as compared to controls, serum P, C-terminal and iFGF-23 levels were 

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