# Hereditary vitamin D-resistant rickets (HVDRR): Report of four cases with successful use of intermittent intravenous calcium via peripheral route

P2-206

Saygın Abalı[1], MayukoTamura[2], Zeynep Atay[1], Pınar Isguven[3], Tülay Güran[1], Belma Haliloglu[1], Serpil Baş[1], Tsuyoshi Isojima[2], Serap Turan[1], Sachiko Kitanaka[2], Abdullah Bereket[1]

[1]Department of Pediatric Endocrinology and Diabetes, Marmara University, School of Medicine, Istanbul, Turkey
[2]Department of Pediatrics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
[3]Department of Pediatric Endocrinology, Sakarya University, School of Medicine, Sakarya, Turkey

## Background

**Hereditary vitamin D-resistant rickets (HVDRR) is a rare disease caused by mutations in *vitamin D receptor (VDR).* Patients with HVDRR are usually treated with intravenous calcium (IV-Ca) therapy via a central catheter. However, central catheter-related complications can cause important morbidity. In this report, we described four patients with HVDRR from different families. In three of these cases we used a novel therapeutic regime of intermittent IV-Ca therapy via peripheral vein.**

Table. Clinical and genetic features of patients

| | P#1 | P#2 | P#3 | P#4 |
|---|---|---|---|---|
| Age of admission at our clinic (years) | 4.3 | 9.8 | 2.7 | 1.5 |
| Laboratory at admission (SI unit) | | | | |
| Ca mg/dl (mmol/L) | 8.2 (2.1) | 7.5 (1.9) | 8.6 (2.2) | 8.2 (2.1) |
| P mg/dl (mmol/L) | 2.5 (0.8) | 3.4 (1.1) | 2.9 (0.9) | 2.2 (0.7) |
| ALP (U/L) | 6168 | 1303 | 1606 | 1655 |
| PTH pg/ml (ng/L) | 1240 | 304 | 762 | 590 |
| Age at initiation of IV Ca therapy (years) | 5.2 | 9.8 | 4.8 | 1.9 |
| Route of IV therapy | Peripheral | Peripheral | Peripheral | Peripheral-to Central |
| IV Ca dose (mg/kg/week) | 18 | 90 | 60 | 18 |
| Duration of IV Ca therapy required to healing of rickets (months) | 10 | 1 | 22 | 10 |
| Cumulative dose of IV Ca (mg/kg) | 770 | 405 | 5600 | 770 |
| *VDR mutation* | Q152X exon5 | Q152X exon5 | IVS8 as-2 A>G, homozygote (Novel) | c.67insG, p.Ile23Asp fsX20, homozygote (Novel) |

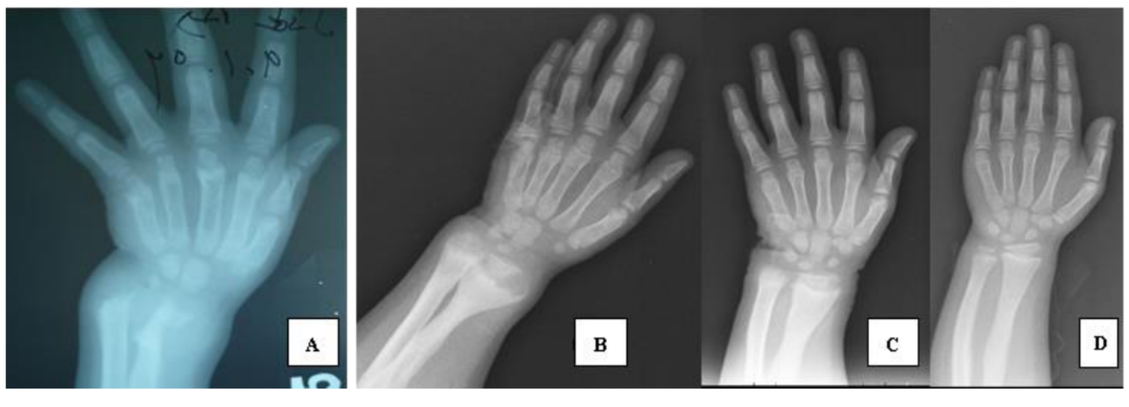


Figure. Radiologic improvement in Patient#1. A. At admission, B. After high dose oral Ca and calcitriol therapy, C. During the IV-Ca therapy, D. After IV-Ca therapy.

- **In order to overcome the central-catheter related risks, we used a novel therapeutic regime of intermittent IV-Ca therapy via peripheral vein. Calcium gluconate 10% solution 1-2 ml/kg/dose diluted in 100 ml saline (0.9% NaCl solution) was given in an outpatient setting approximately three times/week, each lasting two to three hours.**
- **IV-Ca infusion via peripheral line was as effective as that via a central line and all our patients had both clinical and biochemical improvement within a few months after commencement of the therapy. In our method peripheral cannula was changed every 3-5 days.**
- **No serious complications such as infection or extravasation of Ca were noted during entire treatment period. Despite significant hypercalcuria, none of our patients developed urolithiasis or nephrocalcinosis.**
- **Another interesting observation in our patients who received IV-Ca therapy is that, despite cessation of IV therapy, their rickets remain in the remission and no patients returned to active rickets demonstrating long-lasting effect of IV Ca therapy. In our cases, the longest period was 4.5 years after cessation of therapy in Patient#1 and there was still no recurrence of active rickets.**

## Conclusion

- **We shared our experience in four children with HVDRR, two with the same previously known mutation and the other two having different novel mutations.**
- **We demonstrated that IV-Ca therapy, via peripheral route in patients with HVDRR who do not respond to high dose oral calcium treatment, is a practical method that provides a dramatic clinical benefit and healing of rickets without carrying central catheter-related risks.**

**References**

1. Malloy PJ, Feldman D. Genetic disorders and defects in vitamin D action. Endocrinol Metab Clin North Am 2010; 39: 333-46.
2. Tiosano D, Hochberg Z. Hypophosphatemia: the common denominator of all rickets. J Bone Miner Metab 2009; 27: 392-401.
3. Tiosano D, Weisman Y, Hochberg Z. The role of the vitamin D receptor in regulating vitamin D metabolism: a study of vitamin D-dependent rickets, type II. J Clin Endocrinol Metab 2001; 86: 1908-12.
4. Hochberg Z, Tiosano D, Even L. Calcium therapy for calcitriol-resistant rickets. J Pediatr. 1992; 121: 803-8.
5. Isojima T, Ishizawa M, Yoshimura K, Tamura M, Hirose S, Makishima M, Kitanaka S. Hereditary 1,25-dihydroxyvitamin D-resistant rickets (HVDRR) caused by a VDR mutation: A novel mechanism of dominant inheritance. Bone Reports 2015; 2: 68-73.
6. Tamura M, Isojima T, Kawashima M, Yoshida H, Yamamoto K, Kitaoka T, Namba N, Oka A, Ozono K, Tokunaga K, Kitanaka S. Detection of hereditary 1,25-hydroxyvitamin D-resistant rickets caused by uniparental disomy of chromosome 12 using genome-wide single nucleotide polymorphism array. PLoS ONE 10 (7)
7. Kristjansson K, Rut AR, Hewison M, O'Riordan JL, Hughes MR. Two mutations in the hormone binding domain of the vitamin D receptor cause tissue resistance to 1,25 dihydroxyvitamin D3. J Clin Invest. 1993; 92: 12-6.
8. Balsan S, Garabédian M, Larchet M, Gorski AM, Cournot G, Tau C, Bourdeau A, Silve C, Ricour C. Long-term nocturnal calcium infusions can cure rickets and promote normal mineralization in hereditary resistance to 1,25-dihydroxyvitamin D. J Clin Invest.1986; 77: 1661-7.
9. Ersoy B, Kiremitci S, Isojima T, Kitanaka S. Successful intermittent intravenous calcium treatment via the peripheral route in a patient with hereditary vitamin D-resistant rickets and alopecia. Horm Res Paediatr. 2015; 83: 67-72.

ESPE 2015
206--P2
Bone, Growth Plate and Mineral Metabolism
SAYGIN ABALI
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 7-9 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology