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Yun-XiaoJian Wu, Assistant editor
Baishideng Publishing Group, Inc.

January4th 2024

Manuscript No: 90261

A new method of local adjuvant therapy with bicarbonate Ringer's solution for tumoral calcinosis

Dear Yun-XiaoJian Wu

Thank you very much for your email and the reviewer's comments regarding our manuscript. We have revised our manuscript according to the reviewer's suggestions.

Very Respectfully,

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Response to Reviewers' Comments

Reviewer #1 comment

Thank you for providing me with the opportunity to review the manuscript. The study demonstrates good methodological quality and addresses an important topic in the field of orthopedics.

Abstract:

The aim section does not accurately reflect the study's objective. Please correct it.

Response:

We have amended the manuscript.

Original manuscript: Abstract

Aims: Calcium phosphate crystals are mainly composed of hydroxyapatite, which is highly infiltrative to tissues, thus making complete resection difficult.

Amended manuscript: Abstract

Aims: Calcium phosphate crystals are mainly composed of hydroxyapatite, which is highly infiltrative to tissues, thus making complete resection difficult. An adjunct method to remove or resolve the residual crystals during the operation is necessary.

Reviewer #1 comment

Introduction

It would be helpful if you could provide a brief explanation of why patients with CKD develop tumoral calcinosis, as you started discussing parathyroidectomy without mentioning its involvement.

Response:

We have amended the manuscript to explain the mechanism underlying tumoral

calcinosis in the parathyroidectomy section.

Original manuscript: INTRODUCTION

Tumoral calcinosis has a primary type with no associated disease, which is associated with a genetic abnormality, and a secondary type that is associated with other disorders, especially chronic renal failure ^[1, 6]. The prevalence of tumoral calcinosis has been reported to range from 0.5%-3% among dialysis patients ^[7-9]. Regardless of the etiology, hyperphosphatemia is associated with tumoral calcinosis. The role of repeated joint microtrauma has also been suggested to cause tumoral calcinosis ^[10].

Medical treatment for tumoral calcinosis in hemodialysis patients includes dietary phosphorus restriction, calcium-free phosphate binders, and frequent dialysis with low-calcium dialysis solutions; however, these treatments are usually ineffective ^[7, 11, 12]. Surgical resection is only used when these treatments are insufficient ^[13]. Surgical resection of tumoral calcinosis lesions has been the primary treatment, but because surgery is not curative, a subtotal parathyroidectomy is increasingly being performed ^[2, 7, 14-17]. Following a parathyroidectomy, calcified tissue is significantly resorbed; however, bone renewal is reduced following parathyroidectomy because of lower parathyroid hormone (PTH) levels, resulting in increased circulating calcium and promotion of vessel and soft tissue calcification ^[18-20].

Amended manuscript: INTRODUCTION

Tumoral calcinosis has a primary type with no associated disease, which is due to a genetic abnormality, and a secondary type that is associated with other disorders, especially chronic renal failure ^[1, 6]. The prevalence of tumoral calcinosis has been reported to range from 0.5%-3% among dialysis patients ^[7-9]. The exact mechanisms underlying tumoral calcinosis are unclear. The role of repeated joint microtrauma has been suggested to cause tumoral calcinosis ^[10]. Previous studies have reported that elevated calcium phosphate production is closely associated with soft tissue calcification ^[11, 12]. Regardless of the etiology, hyperphosphatemia is associated with tumoral calcinosis. Medical treatment for tumoral calcinosis in hemodialysis patients includes dietary phosphorus restriction, calcium-free phosphate binders, and frequent dialysis with low-calcium dialysis solutions; however, these treatments are usually ineffective ^[7, 13, 14].

Surgical resection is only used when these treatments are insufficient ^[15]. Surgical resection of tumoral calcinosis lesions has been the primary treatment but

surgical resection is not curative. In contrast, it has been reported that tumoral calcinosis is reduced or resolved with improved systemic symptoms following parathyroidectomy [16-18]. Parathyroidectomy is effective for tumoral calcinosis patients, especially patients with secondary hyperparathyroidism [5]. Following a parathyroidectomy, calcified tissue is significantly resorbed; however, bone renewal is reduced following parathyroidectomy because of lower parathyroid hormone (PTH) levels, resulting in increased circulating calcium and promotion of vessel and soft tissue calcification [19, 20].

Reviewer #1 comment

Material

Do you believe that Bicanate specifically has the capacity to dissolve tumoral calcinosis? If not, and any bicarbonate Ringer's solution can be used, it is better not to mention the commercial name.

Response:

Any bicarbonate Ringer's solution can be used. We have amended the entire manuscript and eliminated the commercial name.

Reviewer #1 comment

Case presentation

Abbreviations must be written in full the first time they appear in the text (e.g., Ca⁺⁺).

Very interesting case and I appreciate the technique used.

Response:

We have amended the entire manuscript to satisfy the queries.