

A Study of Tetany among The Saudi Population

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ABSTRACT

Aim of the work: studies mentioning etiological distribution of tetany are rare and responsiveness concerning it is poor among physicians so, we tried to describe different causes of tetany beyond the decrease in total serum calcium level. **Methods:** patients with overt or latent tetany were assessed clinically and from laboratory investigations. Initial examinations completed were serum calcium, potassium and arterial blood gas analysis. Both ionized and total calcium were evaluated and corrected according to serum albumin level. Depending on initial reports, additional tests were completed for example, alkaline phosphatase, serum phosphate, parathyroid hormone and magnesium levels; and urine potassium, calcium and chloride levels. **Results:** Gitelman's syndrome (GS), Bartter's syndrome (BS), recurrent vomiting, anxiety hyperventilation, vitamin D3 deficiency (VDD), idiopathic hypoparathyroidism (IHP), postoperative hypoparathyroidism (PHP), acute pancreatitis, tumor lysis syndrome (TLS) and hypomagnesemia were the different causes of tetany identified. Out of 106 patients, total serum calcium was normal in 82 patients with metabolic or respiratory alkalosis (GS, BS, recurrent vomiting, and anxiety hyperventilation). Total calcium was low only in 24 patients (in VDD, IHP, PHP, acute pancreatitis, TLS and hypomagnesemia). Ionized calcium was low in all patients. GS was the most common (38%). Recurrent vomiting (19%), anxiety hyperventilation (13%), and VDD (11%) were also common. PHP was less common (4%); acute pancreatitis, TLS, hypomagnesemia and IHP were uncommon. **Conclusion:** tetany has diverse etiologies. Both metabolic and respiratory alkalosis caused a decrease in ionized calcium and are responsible for the majority of cases of tetany. Causes other than decreased total calcium should be kept in mind for early etiological diagnosis of tetany.

Keywords: hyperventilation, hypocalcemia, Gitelman's syndrome, vitamin D3 deficiency, vomiting.

INTRODUCTION

Tetany is categorized by variable combinations of features comprising cramps, muscle twitching, circumoral numbness, paresthesias of hands and feet, laryngeal stridor, carpopedal spasm, and convulsions (due to cerebral vasoconstriction). Trousseau sign (carpopedal spasm observed following application of inflated blood pressure cuff over brachial artery 20 mmHg above systolic blood pressure for 3 min) and Chvostek sign (twitching of circumoral muscles with tapping on facial nerve below zygomatic process 2 cm anterior to earlobe) unmask latent tetany in patients with numbness, tingling and cramps in extremities. The reduction in serum calcium causing tetany is well known^[1]. Nonetheless, decrease in ionized calcium is more significant than total calcium level, as it is the biologically active component. In different causes of tetany, total serum calcium can be normal when ionized calcium was low^[1]. Awareness regarding the etiological spectrum of tetany is very poor amid physicians. Studies on the etiological distribution of tetany are rare in

literature. We conducted this study to identify the relative frequencies of different causes of tetany and to make the primary care physicians aware about the different causes of tetany beyond the decrease in total serum calcium level.

METHODS

Both female and male patients admitted as inpatients in general medical ward in King Abdulaziz hospital over 2 years period with symptoms or signs of overt or latent tetany were comprised in this study. Patients with movement disorders or epilepsy were excluded from the study to avoid confusion.

Basic demographic data of the patients were gathered. For creating the etiology of tetany, detailed history of patients was taken containing current and past h/o recurrent vomiting, weakness of limbs, anxiety disorder, abdominal pain, thyroid and neck surgeries, presence of polyuria and polydipsia, h/o drug intake, chemotherapy for malignant disorders, and family h/o similar disorders. The detailed clinical examination was completed to discover

any features for example, loss of muscle power, malignancies, hyperventilation, scar mark of thyroidectomy (to exclude accidental parathyroidectomy) and abdominal tenderness. Features of any autoimmune disorder like vitiligo were searched. After history taking and clinical examination, laboratory examinations were completed to reach the diagnosis. Initial examinations done were serum calcium, albumin, arterial blood gas (ABG) analysis, serum sodium, and potassium levels. Both ionized and total serum calcium levels were assessed and corrected according to serum albumin levels. Depending on the initial investigation reports, additional tests were done, for example, serum phosphate, alkaline phosphatase (ALP), intact parathyroid hormone (iPTH) and serum magnesium levels and urinary potassium, calcium, and chloride levels. Serum magnesium was evaluated when possibility of either Gitelman's syndrome (GS) or Bartter's syndrome (BS) was considered and when calcium infusion failed to correct tetany. Tetany as a result of Vitamin D3 deficiency (VDD) was diagnosed in the presence of diminished serum calcium and phosphate and increased ALP level and confirmed after evaluation of 25hydroxy (25(OH))cholecalciferol level. Hypoparathyroidism (idiopathic

hypoparathyroidism [IHP] or postoperative hypoparathyroidism [PHP]) was diagnosed in the presence of decreased serum calcium, increased phosphate, and decreased/inappropriately normal iPTH. Hyperventilation induced tetany was diagnosed if ABG presented respiratory alkalosis. Recurrent vomiting (as the cause of tetany) was diagnosed in the presence of metabolic alkalosis with reduced urinary chloride level. GS was diagnosed if metabolic alkalosis was associated with hypokalemia, hypomagnesemia, decreased urinary calcium, and increased urinary potassium and chloride levels. BS was diagnosed in the presence of metabolic alkalosis associated with hypokalemia with or without hypomagnesemia and increased urinary calcium, potassium, and chloride levels. After different causes of tetany were identified, frequency of different etiologies and their salient features were tabulated. SPSS was used for data analysis. For description of data, we used percentage (%), mean value, 95% confidence interval (CI) and standard deviation.

RESULTS

A total of 106 patients were included in this study. Female patients were 54 and male patients were 52.

calcium was low only in 24 (22.6%) patients (including VDD, IHP, PHP, acute pancreatitis, TLS, and hypomagnesemia). Ionized calcium was low in all 106 (100%) patients. Overt tetany (44 cases, 41,5% of total) was connected with spontaneous carpopedal spasm. All the latent cases (62 cases, 58,5% of total) had Trousseau sign positive, but Chvostek sign was positive only in 12 cases (11,3% of total). GS was the most common cause of tetany (37%), followed by recurrent vomiting with metabolic alkalosis (19%). Anxiety hyperventilation was common (14%), particularly in females with features of overt tetany. VDD (11%) was linked with latent tetany in the majority (10 out of 12 patients). PHP cases were due to the removal of parathyroid glands throughout total thyroidectomy and had persistent hypocalcemia after 6 months of surgery. TLS case had nonHodgkin's lymphoma (NHL) and developed tetany during chemotherapy and succumbed to death.

Table 1: shows the demographic characteristics of studied patients with tetany (n=106)

Parameters	N
Males	52
Females	54
Mean Age (years)	36
Working	69
Not working	37

Table 1 showed emographic characteristics of patients with tetany (n=106).GS, BS, recurrent vomiting, anxiety hyperventilation, VDD, IHP, PHP, acute pancreatitis, tumor lysis syndrome (TLS), and hypomagnesemia were the different causes of tetany identified.

Table 2 showed the frequencies of different causes of tetany and some of their salient features. Total serum calcium was normal in 82 (77,3%) patients with metabolic and respiratory alkalosis including GS, BS, recurrent vomiting, and anxiety hyperventilation. Total serum

Table 2: frequencies of different causes of tetany

Etiologies	Male - female (N)	%	Total serum calcium	Ionized serum calcium (mmol/L)	Overt versus latent tetany (Male-Female)
Gitelman's syndrome	22-18	37,7%	9.21±0.25	0.79±0.07	12-28
Bartter's syndrome	4-4	7,5%	9.09±0.26	0.81±0.05	2-6
Recurrent vomiting	12-8	18,9%	9.10±0.21	0.85±0.05	8-12
Anxiety hyperventilation	2-12	13,2%	9.20±0.25	0.74±0.06	12-2
Vitamin D3 deficiency	6-6	11,3%	6.52±0.45	0.79±0.05	2-0
Acute pancreatitis	2-0	1,9%	5,96	0.69	2-0
Tumor lysis syndrome	2-0	1,9%	5,59	0.68	2-0
Idiopathic hypoparathyroidism	0-2	1,9%	6,74	0.91	0-2
Postoperative hypoparathyroidism (removal of parathyroid glands during thyroidectomy)	0-4	3,8%	6.09±0.59	0.74±0.07	2-2
Hypomagnesemia	2-0	1,9%	5,49	0.71	2-0

DISCUSSION

Serum calcium level was expressed as total serum calcium, corrected calcium (measured total Ca [mg/dL] + 0.8 * [4.0 – serum albumin (g/dL)]) and ionized calcium. The total calcium concentration in plasma was 8.7–10.2 mg/dl (2.2–2.6 mmol/L). Fifty percent of plasma calcium was ionized, 40% was bound to proteins (90% to albumin) and 10% was bound to anions (e.g., phosphate, carbonate, citrate, lactate and sulfate). Normal ionized calcium level was 1.12–1.32 mmol/L (4.5–5.3 mg/dL). Tetany was typically realized when ionized calcium level was lower than 1.1 mmol/L or corrected total serum calcium level falls below 7.0 mg/dL. Reduction in corrected total serum calcium was frequently related with reduced ionized calcium. Ionized calcium was the biologically active component responsible for tetany. Alkalosis increased calcium binding to albumin, which decreased ionized calcium. Hence, tetany might arise even in the presence of normal total serum calcium. GS was the most common reason of tetany in the current study. Tetany is a significant feature of GS apart from hypokalemic paralysis and other features of dyselectrolytemia^[2]. In GS and BS, decreased ionized calcium may be due to metabolic alkalosis precipitates tetany. Conversely, it may be aggravated by related hypomagnesemia. Hypomagnesemia was nearly always linked with GS and 20% of BS patients had hypomagnesemia. In GS, total serum calcium was usually normal. Nonetheless, rare case reports showed hypocalcemic tetany in GS^[3]. BS

was comparatively rare than GS especially in adults and tetany was less frequent. Though, tetany had been reported in literature in BS cases^[4]. We have likewise found BS patients with tetany (8%). The second most common cause of tetany in the current study was metabolic alkalosis as a result of recurrent vomiting. In a case series, tetany was caused by surreptitious vomiting leading to metabolic alkalosis and BS was accepted by low urinary chloride level^[5]. Anxiety hyperventilation leads to respiratory alkalosis and is a vital cause of tetany and reports were prevalent particularly after spinal anesthesia^[69]. Anxiety hyperventilation was correspondingly common in our study (13%) having overt tetany in 12 out of 14 patients and was predominant in females. Hypocalcemia and tetany by reason of VDD were similarly common^[10]. Malnutrition, malabsorption disorders, for example, Celiac disease, decreased sunlight exposure and urbanization was associated with VDD^[11]. Saudis are disposed to VDD. In the current study, VDD was responsible for tetany in 11% of patients. Pancreatitis is a common cause of hypocalcemia. Mechanism of hypocalcemia in acute pancreatitis is not well recognized. It was assumed to be attributable to saponification of calcium by free fatty acids typically in areas of fat necrosis or dissolved or suspended in ascitic fluid^[12]. Hypocalcemic tetany has a bad prognostic significance in acute pancreatitis^[13]. TLS can cause acute kidney injury (AKI). AKI causes hyperphosphatemia that may cause metastatic deposition of calcium phosphate

leading to hypocalcemia and tetany. In the current study, two NHL patient developed tetany throughout chemotherapy caused by TLS.

IHP is infrequent cause of hypocalcemic tetany [14]. If immune etiology is recognized, it is called autoimmune hypoparathyroidism [15]. Autoimmune hypoparathyroidism can arise in isolation or as a part of a polyglandular endocrinopathy [15, 16]. Hypoparathyroidism was associated with hypocalcemia, hyperphosphatemia and low or inappropriately normal iPTH levels. Only single case of IHP was seen in our study with latent tetany who presented at the second decade of life (18 years of age). Thyroid surgery is a vital cause of tetany caused by hypoparathyroidism regardless of major surgical advances. Transient hypocalcemia was common (range, 19%–38% after thyroidectomy) [15, 16]. Nonetheless, hypoparathyroidism and hypocalcemia may be permanent in 0%–6% cases after total thyroidectomy [15, 17]. Hypoparathyroidism may be due to unintentional removal or harm of the parathyroid glands or their vascular supply during thyroidectomy or neck surgery. Persistent hypocalcemia with low or unsuitably normal PTH levels 6 months after surgery confirms permanent hypoparathyroidism. In the current study, four PHP cases with persistent hypocalcemia were found and they were as a result of the removal of parathyroid glands throughout total thyroidectomy. Chronic alcoholism can lead to tetany by hypomagnesemia [18]. Nonetheless, hypomagnesemic tetany was infrequently described [19]. Chronic alcohol consumption can result in hypomagnesemia by decreasing renal tubular reabsorption and causing malabsorption from the gastrointestinal tract. Hypomagnesemia causes peripheral parathyroid hormone resistance and impairs parathyroid function and accordingly causes hypocalcemia. In case of tetany because of hypomagnesemia, patient replies to magnesium injection, but not to calcium treatment. Hypomagnesemia likewise reasons kaliuresis causing hypokalemia which can aggravate symptoms of tetany. Many drugs can result in hypocalcemia, comprising bisphosphonates, cisplatin, antiepileptics, aminoglycosides, diuretics, and proton pump inhibitors [20]. Hypocalcemia can progress with bisphosphonate treatment, particularly in individuals with inadequate 25(OH) cholecalciferol levels. Nevertheless, druginduced hypocalcemia was absent in the current study.

Different acute emergencies such as sepsis can lead to dyselectrolytemia and acidbase disorders,

and thus, tetany can improve in these situations. In the current study, we did not get such cases. Hungry bone syndrome causing tetany after parathyroidectomy in hyperparathyroidism was not found in the current study. Generally, hypokalemia causes tetany in relationship with alkalosis. Though, hypokalemia has similarly been reported to cause tetany in the absence of alkalosis [21]. Isolated hypokalemia causing tetany was absent in the current study. In the current study, the majority of VDD cases (10 out of 12 patients) had latent tetany. As the process of developing VDD was prolonged, calcium level decreases slowly. Patients got time to be diagnosed early in latent tetany stage. Neuromuscular irritability may also be less because of slow changes of serum calcium level.

CONCLUSION

Tetany had dissimilar etiologies. Both metabolic and respiratory alkalosis caused a decrease in ionized calcium and were responsible for the majority of cases of tetany. Causes other than decreased total serum calcium ought to be kept in mind for early and proper diagnosis and management of tetany and underlying disorders.

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