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Abstract

Aim

To determine the cause and clinical profile of hypercalcemia at King Abdulaziz University Hospital (KAUH) and to compare it with studies reported in the literature.

Method

Medical records of patients with hypercalcemia over a 20-year period between January 1982 and December 2001 were studied. Patients age, sex, hospital level of recorded hypercalcemia, cause of hypercalcemia, associated comorbidities, features of diabetes mellitus and hyperparathyroidism were noted.

Results

A total of 155 patients were studied, 121 (78%) were females and 34 (22%) were males. Diabetes mellitus, hypertension and primary hyperparathyroidism were the most common causes of hypercalcemia in adults and were more common in females. 200 (70%), 100 (33%), 57 (37%) versus 10 (33%), 21 (67%), 100% cases of primary hyperparathyroidism in children. Significant difference was seen between the clinical features of hypercalcemia in adults and children. 125 (81%) versus 30 (93%) cases of hypercalcemia in adults and children were associated with diabetes mellitus. 125 (81%) versus 10 (30%) cases of hypercalcemia in adults and children were associated with hypertension. 125 (81%) versus 10 (30%) cases of hypercalcemia in adults and children were associated with primary hyperparathyroidism.

Conclusion

Hypercalcemia is mainly the consequence of hyperparathyroidism at our hospital followed by malignancy and primary hyperparathyroidism in the adult group while these causes were less common in children. The most common clinical manifestations in both children and adults are not specific unless it appears in well known associated diseases.

Key words: Hypercalcemia, Diabetes Mellitus, Hypertension, Adults, Children.

1990-1995. A strong correlation exists between diabetes mellitus (DM and PHPT. The prevalence of DM in PHPT is approximately 8% and that of PHPT in diabetics is approximately 1%. [17,18]. Insulin resistance is present in PHP, which it probably arise from the raised intracellular free calcium concentration, and if it progressed impaired glucose tolerance and DM would result [17]. Seven percent of the diabetics in our study group had PHPT. This higher prevalence could be related to the difference in the ethnic origin between the study groups. Further large studies are needed on the frequency of PHPT in diabetics in different countries. Hypertension has been noted to be present in a higher percentage of PHPT patients than in the general population [15,19]. It had been shown that increased intracellular calcium and endothelial dysfunction in PHPT may contribute to increased blood pressure observed in patients with PHPT [20,21]. half of our patients with PHPT had associated hypertension. Hypercalcemia is a relatively common complication of malignancy, occurring in approximately 10-20% of cases [22]. Malignancy was the 2nd most common cause of hypercalcemia in our hospital and there was a significantly higher mean corrected serum calcium level compared to other causes. Hypercalcemia can affect a variety of organ systems. The most common symptoms are relatively non-specific [23]. Most of our patients presented with weakness with no significant difference between children and adults.

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2.89±0.19 mmol/l and 2.87± 0.10 versus 2.89±0.20 mmol/l (p 0.7 and 0.6 respectively).

Table 2 : Clinical manifestations of hypercalcemia in adults and children

| Variable | Children N=131 N (%) | Adults N=86 N (%) | P value |
|---------------|----------------------------|-------------------------|---------|
| Weakness | 125(95) | 79(92) | 0.3 |
| Anorexia | 118(90) | 80(93) | 0.4 |
| Weight loss | 51(39) | 28(33) | 0.3 |
| Vomiting | 101(77) | 54(63) | 0.02 |
| Constipation | 9(7) | 14(16) | 0.03 |
| Polyurea | 2(2) | 13(15) | <0.001 |
| Renal colic | 1(1) | 5(6) | 0.03 |
| Renal stone | 1(1) | 5(6) | 0.03 |
| Bone ache | 7(5) | 36(42) | <0.001 |
| Bone fracture | - | 2(2) | - |
| Depression | 3(2) | 3(3) | 0.6 |
| Hypertension | 4(3) | 39(45) | <0.001 |

Table 3: Clinical manifestations of patients with primary hyperparathyroidism

| Variable | N = 8 N (%) |
|---------------|-------------|
| Weakness | 3(38) |
| Anorexia | 8(100) |
| Weight loss | 3(38) |
| Vomiting | 4(50) |
| Constipation | 2(25) |
| Polyurea | 3(38) |
| Renal colic | 1(13) |
| Renal stone | 1(13) |
| Bone ache | 5 (63) |
| Bone fracture | 1 (13) |
| Depression | 1 (13) |
| Hypertension | 4 (50) |

Discussion

Hypercalcemia is a relatively common clinical problem. The major causes of hypercalcemia are PHPT and malignancy [4]. PHPT is more common in ambulatory patients without clinical evidence of malignancy

and account for almost all hypercalcemia in these patients (>90%). In hospitalized patients hypercalcemia can be a sign of a serious disease, malignancy is the most common cause and it account for 58%-65% of cases while PHPT account for 25% [3-6]. In another study conducted by Greaves et al [7], 50% (81of162) of hospitalized hypercalcemia had chronic renal failure. To some extent the cause of hypercalcemia is population specific and tuberculosis account for 6% of cases in Hong Kong hospital [8]. Chronic renal failure was the commonest cause of hypercalcemia in our hospital followed by malignancy and PHPT in the adult group while the frequency of these disorders were much lower in children. The different distribution of specialities cause different hospital population and the high frequency of hypertension and diabetes in patients admitted to our hospital [9,10] could account for the high frequency of chronic renal failure as a cause of hypercalcemia. Our study didn't show significant difference in sex distribution or the mean corrected serum calcium between children and adults which is also reported by Aishan and his co-worker [2].

PHPT is the third most frequent endocrine disorder [11]. The prevalence of PHPT varies in different countries. Although it has been reported to be 0.1% in American population, it is far less in Japanese population [12]. PHPT was more common in females in their 5th decade, which is consistent with what had been reported by others [13-15]. PHPT presents in markedly different ways depending on the country in which it is studied. In United States, it typically presents as asymptomatic hypercalcemia and the classical clinical manifestations of stone and bone disease is not common while in China weakness and easy fatigability are always present, and clinical manifestations of stone and bone disease are present in 42% and 60% respectively [16]. Our study showed predominance of abdominal symptoms and boneache. Routine screening of serum calcium and the development of sophisticated assay of PTH can lead to earlier detection of asymptomatic PHPT. Inaba et al [12] has reported that the proportion of APHPT patient rose from 10-20% to approximately 45% of all PHPT in

Introduction

Hypercalcemia is one of the most commonly diagnosed metabolic disorders. The prevalence of hypercalcemia shows a large variation in hospital population ranging from 0.17% to 2.92%, while in normal population it range from 1.07% and 3.9% [1,2]. The most frequent cause of hypercalcemia in hospitalized patients is malignancy followed by primary hyperparathyroidism while in ambulatory patients, it is primary hyperparathyroidism followed by transient hypercalcemia [1,3].

The aim of our study is to determine the causes and clinical profile of hypercalcemia at King Abdulaziz University Hospital (KAUH) and to compare our findings with those reported in the literature.

Method

Laboratory records of patients seen at KAUH between January to December 2000 were reviewed. Medical records of patients with hypercalcemia (corrected serum calcium > 2.6 mmol/l) on 2 separate occasions were retrieved. Serum calcium was measured using the Colorimetric assay with endpoint determination and sample blank. The following data were collected, patient's age, sex, nationality, level of corrected serum calcium and the cause of hypercalcemia. The clinical presentation of each patient was also recorded as well as the presence of diabetes and hypertension. Statistical analysis was done using the SPSS 9.1. Mean +/- standard deviation (SD) was determined for quantitative data and frequency was determined for categorical variables. For continuous variables t test was used if comparing 2 groups. Chi-square was used to analyze group differences for categorical variables. P value <0.05 was considered significant.

Results

A total of 217 patients were included in the study with mean age of 20.38 years (one week- 80 years) and mean corrected serum calcium of 2.89 +/- 0.19 mmol/l. One-hundred and thirty one of 217 (60%) were less than 13 years and 86 of 217 (40%) were more than 13 years. As shown in (Table-1), no significant difference was found in sex distribution or mean corrected serum

Table 1: Comparison between children and adults with hypercalcemia according to some variables

| Variable | Children N=131 N (%) | Adults N=86 N (%) | P value |
|--------------------------------------|----------------------------|-------------------------|---------|
| Sex (M : F) | 67:64 (1:1) | 42:44 (1:1) | 0.7 |
| Nationality (S:NS) | 64:67 (1:1) | 32:54 (1:1.7) | 0.09 |
| Calcium level (mean in mmol/l +/-SD) | 2.88 +/- 0.16 | 2.89 +/- 0.23 | 0.7 |
| Causes: | | | |
| PHPT | - | 8(9) | - |
| Malignancy | 21(16) | 30(35) | <0.001 |
| Chronic renal failure | 10(7) | 39(45) | <0.001 |
| Others | 100(76) | 10(12) | <0.001 |

S= Saudis, NS= Non-Saudi, PHPT= primary hyperparathyroidism, others = thyrotoxicosis, immobilization, infantile hypercalcemia, transient hypercalcemia, associated with congenital anomalies, tuberculosis

calcium level between children and adults. Chronic renal failure was the commonest cause of hypercalcemia in adults followed by malignancy and primary hyperparathyroidism (PHPT) while in children these were less common causes. The mean age of patients with PHPT was 52 +/- 7.8 years with male: female ratio 1:1.7. Weakness, anorexia and vomiting were common clinical features in both children and adults while renal and bone symptoms were more in adults compared to children with hypercalcemia (Table-2). In patients with PHPT, anorexia, vomiting and bone ache were common clinical features (Table - 3). Diabetes was diagnosed in 28 of 86 (33%) of the adult group. Two of 28 (7%) of the diabetics had associated PHPT versus 6 of 189 (3%) non-diabetics had PHPT (p 0.1). Hypertension was found in 4 of 8 (50%) patients with PHPT. The level of corrected serum calcium was high in patients with malignancy as a cause of hypercalcemia compared to other causes, 3.02 +/- 0.3 mmol/l versus 2.87 +/- 0.15 mmol/l (<0.001). While no significant difference was found in those with PHPT or chronic renal failure and other causes of hypercalcemia, 2.87 +/- 0.18 mmol/l versus

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Original

Hypercalcemia At King Abdulaziz University Hospital: Causes And Clinical Profile

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ملخص

الهدف: دراسة المظاهر الاكلينيكية و أسباب ارتفاع مستوى الكالسيوم في الدم في مستشفى جامعة الملك عبد العزيز و مقارنتها بالأبحاث المنشورة.
الطريقة: تمت دراسة ملفات المرضى الذين يعانون من ارتفاع مستوى الكالسيوم في الدم في الفترة ما بين يناير إلى ديسمبر ٢٠٠٠م. تم تسجيل العمر، الجنس، الجنسية، مستوى الكالسيوم في الدم، أسباب ارتفاع مستوى الكالسيوم في الدم، المظاهر الإكلينيكية، وجود مرض السكري و ارتفاع ضغط الدم.
النتيجة: كان المجموع الكلي للمرضى الذين تم دراستهم ٢١٧ مريض منهم ١٣١ (٦٠٪) أطفال و ٨٦ (٤٠٪) بالغين. الفشل الكلوي المزمن، الأورام السرطانية، و زيادة إفراز الغدة الجار درقية من أهم أسباب ارتفاع الكالسيوم في الدم لدى البالغين بينما وجدت بنسب أقل لدى الأطفال ولم توجد أي حالة إفراز الغدة الجار درقية لدى الأطفال، و كانت النسب ٨٦/٣٩ (٤٥٪)، ٨٦/٣٠ (٩٪) لدى البالغين مقارنة بـ ١٣١/١٠ (٧٪) ، لدى الأطفال.
الضعف العام، قلة الشهوة للطعام، التقير من أهم المظاهر الإكلينيكية لدى البالغين و الأطفال و كانت النسب ٨٦/٧٩ (٩٢٪) ، ٨٦/٨٠ (٩٣٪)، ٨٦/٥٤ (٦٣٪) لدى البالغين و ١٣١/٢٥ (٩٥٪)، ١٣١/١٠ (٧٧٪) لدى الأطفال.
الخاتمة: أوضحت الدراسة أن الفشل الكلوي المزمن من أهم أسباب ارتفاع مستوى الكالسيوم في الدم في مستشفىنا يليه الأورام السرطانية و زيادة إفراز الغدة الجار درقية لدى البالغين ولكنها بنسبة أقل لدى الأطفال. وجد أيضا أن أعراض زيادة مستوى الكالسيوم في الدم هي غير محددة سواء لدى البالغين أو الأطفال وهذا يتفق مع ما سبق نشره.

Abstract

Aim

To determine the cause and clinical profile of hypercalcemia at King AbdulAziz University Hospital (KAUH) and to compare our findings with those reported in the literature.

Method

Medical records of patients with hypercalcemia seen at KAUH in the period between January to December 2000 were studied. patient's age, sex, nationality, level of corrected serum calcium, cause of hypercalcemia, clinical presentation, presence of diabetes mellitus and hypertension were recorded.

Results

A total of 217 patients were studied, 131/217 (60%) were children and 86/217 (40%) were adults. Chronic renal failure, malignancy and primary hyperparathyroidism were the commonest causes of hypercalcemia in adults and they were less common in children, 39/86 (45%), 30/86 (35%), 8/86 (9%) versus 10/131 (7%), 21/131 (16%) and no cases of primary hyperparathyroidism ($p < 0.001$). Weakness, anorexia and vomiting were common clinical features in both children and adults, 125/131 (95%), 118/131 (90%), 101/131 (77%) versus 79/86 (92%), 80/86 (93%), 54/86 (63%) (p 0.3, 0.4, 0.02 respectively).

Conclusion

Chronic renal failure is the commonest cause of hypercalcemia in our hospital followed by malignancy and primary hyperparathyroidism in the adult group while these causes were less common in children. The most common clinical manifestations in both children and adults are non specific which is comparable with those reported in the literature.

Key words: Hypercalcemia. Causes. Clinical Features. Adults. Children

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