Six-months treatment with cabergoline in 10 acromegalic patients .

Dr .Abbas Mahdi Rahmah
C.A.B.M. FRCP(Edinburgh)
National Diabetes Center –Almustansyria university

يعتبر تضخم الاطراف من امراض الغدد الصم الناجمة عن ورم الغدة النخامية الذي يفرز كميات كبيرة من هرمون النمو.ان هذا المرض يقلل العمر ومن اهم اسباب الوفاة امراض جهاز الدوران.تم دراسة حالة عشرة مرضى من المصابين بتضخم الاطراف و الذين تعالجون في المركز الوطني لعلاج و بحوث السكري (الجامعة المستنصرية) خلال النصف الاول من عام ٢٠٠٦ وكان الجميع مرضى فعال ، ثلاثة منهم اورام الغدة النخامية صغيرة اما الباقون فكان ورم الغدة النخامية كبيرة.
تمت دراسة مستوى هرمون النمو و السكري على مدى ساعتين بعد تناول ٧٥ غم من سكر الغلوكوز و تبين بان هرمون النمو و السكر كانا عاليين و لكن و بعد تناول حبة كابركولين ٠,٥ غم بواقع حبتان كل اسبوع و على مدى ستة اشهر. في نهاية الدراسة حصل هبوط ملحوظ في هرمون النمو و السكر في دم المرضى بعد اجراء فحص السكر المطول مثلما اجري في بداية الدراسة
ستنتج من ذلك ان دواء الكابركولين قد نجح في تخفيض هرمون النمو و سكر الدم و الامر ستدعي اجراد دراسة مماثلة على نموذج اكبر من المرضى و على مدى اطول من الزمن اضافة الى البحث عن امكانية تصغير حجم ورم الغدة النخامية باستعمال الدواء المشار اليه (الكابركولين) .

Abstract

Acromegaly is an endocrine disease caused by hypersecretion of growth hormone from pituitary adenoma , its annual incidence is 4 per million per year while its prevalence approaches 60 per million .The disease is known to reduce life expectancy and the main cause of mortality is cardiovascular.The mainstay of treatment is hypophysectomy however pharmacotherapy with dopamine agonists (bromocreptine ,cabergoline) and long acting octreotide represent other modalities of treatment after failure of surgical treatment or for patients in whom surgery is not feasible or contraindicated.

Aim

The main objective of this study is to look for any reduction of plasma growth hormone (GH) , and plasma glucose by using cabergoline .

Methods

Ten acromegalic patients with active acromegaly were treated wih the dopamine agonist ,cabergoline over aperiod of 6 months , and the target is to lower their GH , and plasma glucose.

Results

Cabergoline use results in obvious decrement in both GH and plasma glucose in the fasting state and after taking a glucose load of 75 grams orally .These results were achieved in patints with pituitary microadenoma , or macroadenoma , and in those who failed to achieve cure after being exposed to trans-sphenoidal hypophysectomy.

Key wards :Acromegaly,Cabergoline ,Growth hormone.

Introduction

Acromegaly is an insidious chronic disease caused by unrestrained hypersecretion of growth hormone (GH) , insulin like growth factor -1 (IGF-1) and it is associated with increased morbidity and mortality with reduced life expectancy mostly due to cardiovascular disease(1)

Epidemiological studies have shown that the increased mortality is reversed to normal rate in patients achieving normal GH levels (i.e. <2.5 ng /ml) regardless of the therapeutic approach used(2,3)

Neurosurgery(NS) is usually considered the first treatment of choice .Pharmacotherapy has been used to reduce GH/IGF-1 hypersecretion in patients unsuitable or unwilling to undergo NS or after its failure or in selected cases as primary therapy(4,5)

Cabergoline is found to useful in reducing GH levels in patients with acromegaly and specifically in those with pituitary adenomas cosecreting GH(5)

Aim of the study

The study was conducted to find out the effect of cabergoline on GH response to oral glucose tolerance test(GTT) in patients with acromegaly .

Patients and methods

Ten acromegalic patients were enrolled in the study .They attended The National Diabetes Center (NDC) during the period from 2-January-2006 to 6-August -2006. The patients are 7 males and 3 females , their age range from 38 to 41 years with a mean of 39.5 years .The mean duration of their illnesswas 8 years.All the studied subjects have pituitary macroadenoma except 2 males who have microadenoma .Three patients have been treatedwith trans-sphenoidal hypophysectomy .

All patients do not fulfill the definition of cure on the basis of high basal fasting GH , and the paradoxical response to glucose load during oral glucose tolerance test (GTT)support the fact that they deserve treatment.

The patients were examined fully and subjected to oral GTT with GH assay before using cabergoline and 6 months after being kept on cabergoline 0.5 mg twice weekly .

The results of glucose and GH levels before using cabergoline were compared with those after using cabergoline and the target was to reduce these parameters.

Results

As shown in table 1 ,table 2,the use of cabergoline for 6 months results in marked reduction of GH and plasma glucose in the fasting state , 1 hour , and 2 hours after 75 grams oral glucose ingestion during a formal oral GTT in acromegalic patients with pituitary macroadenoma.

TABLE 1.GH levels during oral GTT before , and after the use of cabergoline in 3 acromegalic patients with pituitary macroadenoma.

GH (ng/ml)	Before cabergoline	After cabergoline	Percentage reduced
Basal	87.5	44	43.5
1 hour	73.7	37	36.7
2 hour	61.9	28.8	33.1

TABLE 2. plasma glucose during oral GTT in 3 acromegalic patients with pituitary macroadenoma before and after using cabergoline.

Plasma glucose (mg/dl)	Before cabergoline	After cabergoline	Percentage reduced
Basal	193	102	91
1 hour	265	181	84
2 hour	145	167	22

In patients with microadenoma the results of GH response to oral GTT before and after using cabergoline are evident in table 3.

TABLE 3. GH response to oral GTT in acromegalic patients with pituitary microadenoma before and after the use of cabergoline in 3 acromegalic patients.

GH (ng/ml)	Before cabergoline	After cabergoline	Percentage reduced
Basal	53	36	17
1 hour	56	36	20
1 hour	52	29	23

In patients with microadenoma the use of cabergoline results in decrement of plasma glucose 2 hours after the oral glucose load but the fasting glucose and the plasma glucose 1-hour after the glucose load revealed mild increment as shown in table 4.

TABLE 4.Oral GTT before and after the use of cabergoline in 3 acromegalic patients with pituitary microadenoma.

Plasma glucose mg/dl)	Before cabergoline	After cabergoline	Percentage change
Basal	101	105	+1.05
1 hour	122	132	+1.32
2 hour	142	110	_32

Patients who have been treated with trans-sphenoidal hypophysectomy in whom cure has not been achieved ,thus they were treated with cabergoline , the effect of cabergoline on their GH was evident in table 5, and its effect on plasma glucose during the formal GTT was shown in table 6 .The use of cabergoline reduces both GH , and plasma glucose in the fasting state and after the oral glucose load .

TABLE 5. GH levels during formal GTT in 3 acromegalic patients who have been treated with hypophysectomy before and after being treated with cabergoline

GH (ng/ml)	Before cabergoline	After cabergoline	Percentage decrease
Basal	121	78.2	42.8
1 hour	105	70.9	34.1
2 hour	94	54.7	39.3

TABLE 6. Plasma glucose in 3 acromegalic patients- who have been treated with hypophysectomy-before and after using cabergoline.

Plasma glucose(mg/dl)	Before cabergoline	After cabergoline	Percentage decrease
Basal	97	92.3	8.7
1 hour	199	146.6	52.4
2 hour	163	136	27

Discussion

The use of cabergoline is found to be useful in reducing GH , and plasma glucose levels in patients with acromegaly whether they have microadenoma or macroadenoma , its benefit extends to acromegalic patients who have been treated withtrans-sphenoidal hypophysectomy as they fail to achieve cure after such surgical procedure.Dopamine agonists are proved to be useful in acromegalic subjects(6).

Cabergoline ,an orally active dopamine agonistused to treat hyperprolactinemia , also reduces serum GH in acromegalic subjects , and in those with pituitary adenomas that secrete variety of hormones and cosecrete GH(7).

Conclusion

The use of cabergoline is found to be useful in acromegalic patients by reducing GH and plasma glucose in the fasting state and after glucose load irrespective whether the patient has pituitary macroadenoma ,or macroadenom , or failed to achieve cure after trans-sphenoidal hypophysectomy.

Recommendation

It is recommended to conduct similar studies by enrolling a large sample of acromegalic patients, and to follow them over a long period of time to look for the effect of cabergoline on the pituitary adenoma size , and its effect on morbidity and mortality.

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