Impact of Prolactin Hipersecrey on Glucid and Lipid Metabolisms

ELENA IONESCU[1#], BOGDAN VIRGIL COTOI[1]*, ANCA GANESCU[2#]

[1] University of Medicine and Pharmacy, 2 Petru Rares Str., 200349, Craiova, Romania

[2] University of Craiova, Faculty of Sciences, Department of Chemistry, 107i Calea Bucuresti, 200478, Craiova, Romania

Pituitary is a common terrain for the appearance of tumoral changes, representing the origin of about 15% of all intracranial tumors [13]. These tumors are, for the most part, histologically benign, as they arise from hormone secreting cells in the anterior lobe. Therefore, the aim of the paper is to specify the clinical and paraclinical clinical onset characteristics, the evolutionary peculiarities, as well as the metabolic complications secondary to the prolactin hypersecretion. The effects of prolactin-secreting pituitary tumors may occur as a result of mass effects of tumors or even hyperprolactinaemia. Because microadenomas are intrathecal, visual defects may not occur, but headaches occur more often (50%) than normal (27%) [1, 6]. A large tumor that extends beyond the limbs of the turkey can cause headaches and vision defects. The classical presentation is bitemporal hemianopsia due to the compression of the optic chiasm from a tumor that extends to the upper level. If chiasma is prefixed or if the tumor extends posteriorly, compression of a single optical system results in visual field defects similar. The lateral extension in the cavernous sinus can lead to the illness of the oculomotor function involving the cranial nerves III, IV and VI and the branches V1 and V2 of the cranial nerve V, alone or in combinations.

Keywords hyperprolactinemia, lipid metabolism, glucidic metabolism

Occasional large tumors may extend into the temporal lobe or cause apoplexy attacks.

Patients with large tumors are also at risk of compromising anterior pituitary function due to normal pituitary tissue compression, resulting in decreased GH, corticotropin, LH, FSH or tiroptropin, individually or combined [2].

GH deficiency is probably the most common, but has not been systematically studied. Hyperprolactinemia is associated with impaired pulsatile gonadotrophin release (LH, FSH), almost the same as the hypothalamic LHRH secretion. [4, 7]

Chronic hyperprolactinemia leads to decreased bone density in both males and females, and suppression of hyperprolactinemia in men and improvement in gonadal function results in increased bone density in the radial trunk but only at a small increase in bone density.

Suppression of hyperprolactinemia without restoration of gonadal function does not increase bone density [3, 8].

In hyperprolactinemia, bone mineral content in amenorrheal women is low when compared to normal-pregnant women with amenorrhoea and prolactin women, which shows that prolactin has a direct effect on bone.

Experimental part

Biochemical investigations consisted of routine investigations - blood glucose, serum cholesterol, triglycerides.

Hormonal investigations involved prolactin determination.

For this we used the Elecsys 1010 dosing system produced by the Roche Diagnostics company, equipped with the Clinical Laboratory of the County Emergency Clinical Hospital in Craiova, together with the appropriate reagent sets for determination, hPRL.

It uses electrochemiluminescence method as working method.

Electrochemiluminescence (ECL) is a form of chemiluminescence (CL) in which the light-generating reaction is preceded by an electrochemical reaction [10].

The advantages of CL are maintained, but the electrochemical reaction allows control of the moment and position of the light emitting reaction.

By controlling time, light emission may be delayed until the immune or enzyme-catalyzed reaction occurs.

Although similar control can be exerted by other detection methods, such as fluorescence, the equipment is much more sophisticated and expensive.

Position control can be used to limit light emission to a region that is precisely located relative to the detector, thus increasing sensitivity by increasing the ratio signal / noise.

A good example is the combination of ECL with magnetic field technology, which allows the tracer to be coupled by the unburned tracer without requiring an intermediate separation step.

Position control can also be used to perform multiple analytical reactions in the same specimen (biological sample) by querying each electrode in a series of analysis either sequentially or simultaneously using a position detector.

Electrochemiluminescence has been developed as a highly sensitive process in which reactive species are generated from stable precursors on the surface of an electrode.

This new technology has many distinct advantages over other detection systems: no radioisotopes are used; the tracer detection limit is very low (200 fmol / L); the dynamic quantization spectrum of the tracer is spread over 6 orders of magnitude; traversers are extremely stable compared to other chemiluminescence systems; small molecules (about 1000 Da) can be used to label haptens or large molecules, and several tracers may be coupled to proteins or oligonucleotides without affecting immunoreactivity, solubility or hybridization capacitysince chemi-luminescence is initiated electrochemically, the selectivity of the bound and unbound fractions may be based on the selectivity of the species marked to access the surface of the electrode so that separation and non-separation tests can be performed.

* email: bogdan2303776@yahoo.ro # Authors with equal contribution

Measurement is simple and fast, requiring only a few seconds.

Table 1

THE NORMAL HORMONAL VALUES OF ELECSYS DOSAGE KITS

	Mediate	Normal range
PRL	258 µUI/mL	127-637 µUI/mL

Sample collection from patients with pituitary adenomas was performed by venous puncture, prior to radical therapies.

Samples were stored in the freezer until hormonal determinations.

Statistical - mathematical processing

Data processing used EPI2000 software packages, distributed by WHO, SPSS, specialized in statistical statistical calculations, produced by SPSS, StatSoft's STATISTICA program, and MICROSOFT EXCEL's Data Analysis module together with the XLSTAT suite for MS Excel.[9]

EXCEL patient data recording produced the baseline database from which the significant aspects of this study were extracted.

The actual processing was done with the help of:

-CrossTab, BasicTables, General Tables, Correlate, Regression, and Analyst Factor, SPSS

-ANALYSIS module of the EPI2000 program specializing in the execution of graphs, tables and statistical tests.

-the nonparametric test module in the STATISTICA program for calculating the Spearman correlation coefficient

-Pivot Tables, Functions-Statistical and Chart commands from MS Excel, and commands from the XLSTAT module for making ROC curves.

In all calculations, the following statistical indicators were used:

The arithmetic mean of a series of values.

It is a simple and at the same time very synthetic indicator, being a very good indication of the value around which data is grouped together.

Write down the letter *m* or, if the set of values is denoted by a capital letter as X or Y, the average is marked with or.

The formula is the one known:

$$\overline{X} = \frac{x_1 + x_2 + \ldots\ldots\ldots x_n}{n} = m$$

*Media i*s the indicator that shows the central trend of the value series, and usually shows where the data tend to crowd.

Often, the values in the series are mostly near the average, and a smaller part of them are located to the left or right of the media.

Spreading

Values in a range of values may be more agglomerated around the average or more dispersed, i.e. at high average averages.

One way to measure these deviations from the average is to make a difference between all these values and their average.

Some deviations will be positive, others will be negative. They can not be gathered, because by summing they give the amount close to 0.

Dispersion

A way to bypass the fact that the sum of absolute deviations is 0 is the square elevation of them before they are gathered to make negative signs disappear to some and positive ones to others.

The amount obtained should be divided by the number of deviations in order to obtain an average.

In fact, for theoretical reasons, division is made at n-1.

The value thus obtained is called dispersion and is an indicator of the degree of scattering of the series.

The dispersion is denoted by D and has the formula:

$$D = \frac{(x_1 - \overline{X})^2 + (x_2 - \overline{X})^2 + \ldots\ldots + (x_n - \overline{X})^2}{n-1}$$

As we can see, the fraction counter of the dispersion definition is all the more so since the individual deviations from the mean are higher and so it is natural to consider that a high value of the dispersion shows a large scattering of the series values.

Dispersion has the disadvantage of expressing it with square meters of measure values in the series, and generally has very high values.

Standard deviation

And has the formula: σ is denoted by

$$\sigma = \sqrt{D} \text{ or } \sigma = \sqrt{\frac{(x_1 - \overline{X})^2 + (x_2 - \overline{X})^2 + \ldots\ldots + (x_n - \overline{X})^2}{n-1}}$$

This indicator is expressed in the same unit of measure as the values in the series considered and is a very accurate indicator of series scattering.

The standard deviation does not have the disadvantages of dispersion, ie the unit of measurement is the same as the values in the series, and has a value comparable to the individual deviations from the mean.

To remember:

-In roughly equal environments, the higher deviation standard series is more scattered.

-At roughly equal standard deviations, the smaller media series is more scattered.

The coefficient of variation.

It is the ratio of the standard to average deviation when the average is different from 0 and is expressed as a percentage:

$$C.V. = \frac{\sigma}{\overline{X}}$$

The appreciation with the coefficient of variation is especially true when two sets of values have very different meanings and the standard deviations may not give us a sufficiently useful indication.

The coefficient of variation is the most accurate indicator of spreading a statistical series, but it also has an inconvenience; it is all the more true since the averages are farther away than 0.

In environments very close to 0 it looses fidelity and is not intended to be used. This is especially true when the series values are negative and positive, and for this reason the average can be close to 0.

If repeated samples are taken from the same population, statistical measures of central trend and variability (mean, standard deviation) may vary from one sample to another.

The degree of variation depends both on the variation in population and on the size of the sample.

Sample media may be distributed approximately normally if the size of the sample is large enough.

LOT	<20	20-29	30-39	40-49	50-59	60-69	>70	Total
PRL	1	5	10	7	3	1	0	27

Table 2
DISTRIBUTION OF ADENOMAS ACCORDING TO SECRETION AND AGE GROUP

The standard deviation of sample MEDIOLES is called a standard error of average and has the formula:

$$S.E. = \frac{\sigma}{\sqrt{n}} = \sqrt{\frac{D}{n(n-1)}}$$

The standard media error is sometimes incorrectly used to summarize the data. Unlike the standard deviation, it does not show the variability that occurs within a sample (batch).

Results and discussions

We analyzed the age group structure of the entire batch of patients with PRL-secreting adenomas.

The age group distribution of PRL secreting adenomas has a higher incidence in young people: 20-29 years -5 cases (6.25%), 30-39 years 10 cases (12.5%), 40-49 7 cases (8.75%) (table 2).

The minimum age in the study group was 18 years for PRL secreting tumors, the maximum of 60 years, and the mean age was 37.93 at a standard deviation of 10.11 (table 2, fig. 1).

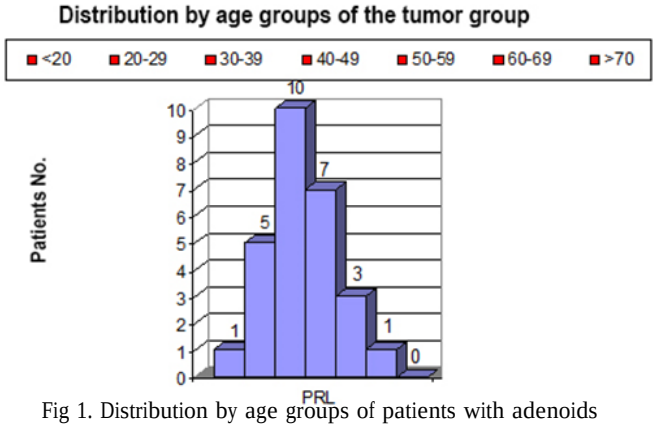

Fig 1. Distribution by age groups of patients with adenoids

Tumors	PRL
Number	27
Minimum	386
Maximum	9360
Average	2229.19
St.Dev.	2202.38
C.V.	98.80

Table 3
MINIMUM, MEAN AND MAXIMUM PRL VALUES

Maxim prolactin - 124200

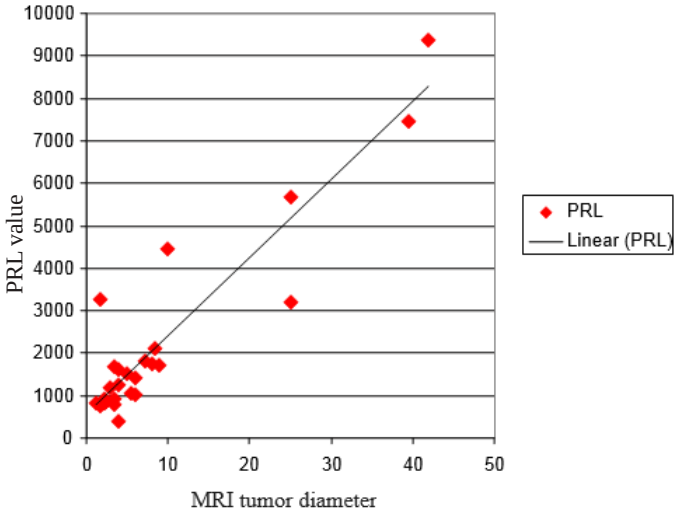

Fig. 2. Correlation of tumor volume-secretion by PRL

PRL determinations have shown a wide range of values.

Confirmation that pituitary adenomas were prolactinomas was made on a single criterion that prolactin should be greater than 637 microU / mL (PRL dosages were done in a laboratory having normal values between 127-637 microU / mL), although the literature includes a number of divergences of opinion. On the validity of this minimum value of prolactin as a unique diagnostic criterion for a prolactin, when the pituitary adenoma has already been imagistically detected.

Serum prolactin was dosed in 27 patients, the median PRL score was 2229.19 microU /mL with a range of 386 to 9360 microU / mL (table 3).

The statistical calculation did not include the amount of 124.200 microUI / mL encountered in a patient with macroprolactinoma 32.7 / 28 / 32.2 mm diameter with left cavernous sinus invasion, with intra-parapituitary displacement mainly left and with Excessive minimal extension.

This value was not included in the statistical study due to the enormous difference from the other PRL values in the study group (6).

From the graph above (fig. 2), we can conclude that there is a direct correlation between the dimensions of the measured MRI tumor and the secretion of prolactin (the larger the tumor, the higher the amount of hormone), because the right regression has a clear ascendant slope.

This is also evidenced statistically by Pearson's correlation coefficient r having a value of 0.923, well above the significance threshold of ± 0.381 of r for 27 subjects (25 degrees of freedom).

In the group studied were 27 cases of prolactinomas, of which 5 macroprolactinomas (PRL over 4468 microU / mL), 18.5%.

Considering this correlation, we highlighted a higher incidence of microprolactinoam in women compared to males, and a higher incidence of macroprolactinomas in males [6].

This fact confirms the data in the literature, which recorded a higher incidence of macroprolactinoam in men, the major causes being late presentation to the doctor or minimization of sexual dysfunction.

Following glucose dosing, glycemic levels in the PRL-secreting group of adenomas are observed. There is no clear evidence of direct involvement of PRL in diabetes pathogenicity [11].

However, hyperprolactinemia has been documented for insulin resistance, explaining the increase in its secretion. It was hypothesized that, under normal conditions, PRL is not diabetes, this effect being only apparent in pancreatic beta dysfunction subjects [2,5].

glycemic	PRL
Number	27
Minimum	35
Maximum	102
Average	82.56
St.Dev.	13.76
C.V.	16.67

Table 4
DETERMINATION OF BLOOD GLUCOSE IN PATIENTS WITH PROLACTIN-SECRETING ADENOMAS

Using the Student's t test to highlight the difference in blood glucose, we obtained the following results (table 4).

- there is a very high statistically significant difference (p = 0.00019, much lower than the 0.001 threshold) between the mean blood glucose levels for subjects with prolactin secretory tumors.

Prolactin modifies lipid metabolism, but this effect does not correlate with the degree of overweight, demonstrating instead that hyperprolactinemia itself is the primary cause of lipid disorders, while obesity is only a secondary aggravating phenomenon [5]

Taking into account the cholesterol level established by NCEP (Adult Treatment Guidelines 1993 - Greespan, 2001), the number of patients with cholesterol greater than 200mg / dL, its minimal, mean and maximum value is illustrated in table 5 .

The mean cholesterol level in patients with prolactin was 192.15 mg / dL (table 5).

CHOLESTEROL	PRL
Number	27
Minimum	149.00
Maximum	252.00
Average	192.15
St.Dev.	25.28
C.V.	13.16

Table 5
CHOLESTEROL IN PATIENTS WITH PRL-SECRETING ADENOMAS

Performing the Student's t test to highlight the difference in the mean cholesterol values, we obtained the following results (table 5).

- there is a statistically significant difference (p = 0.0045, less than the threshold of 0.01) between cholesterol mean for subjects in the subtype of prolactin secretory tumors.

Performing the Student's t test to highlight the difference between the triglyceride values averaged the following results (table 6).

triglycerides	PRL
Number	27
Minimum	56.00
Maximum	185.00
Average	123.80
St.Dev.	45.40
C.V.	36.68

Table 6
TRIGLYCERIDE DOSING

- there is a statistically significant difference (p = 0.049, less than the threshold of 0.05) between triglyceride averages for subjects with prolactin secretory tumors.

Conclusions

Pituitary adenomas represent 15% of the intracranial tumors, being more common in women (70% women versus 30% men) and having a peak incidence between 30-40 years (prolactinomas).

The age group distribution of PRL secreting adenomas has a higher incidence in young people: 20-29 years -5 cases (6.25%), 30-39 years 10 cases (12.5%), 40-49 7 cases (8.75%).

We highlighted a higher incidence of microprolactinoam in women compared to males, and a higher incidence of macroprolactinomas in males.

Following glucose dosing, glycemic levels in the PRL-secreting group of adenomas are observed.

Prolactin alters lipid metabolism, but this effect does not correlate with the degree of overweight, demonstrating in turn that hyperprolactinemia itself is the primary cause of lipid disorders, while obesity is only a secondary aggravating phenomenon.

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