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Research Article

Retrospective Analysis of Diabetes Comorbidity in Populations with Movement Disorders Related to Parkinson's Disease

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ABSTRACT

Background and aim of the work: Some studies during the time have shown a high comorbidity of diabetes in parkinson's disease and related disorders. This imprerssion was also detected in our clinical experience. Therefore it was decided to carry out a study about the incidence of diabetes in affected populations using the raw data collected in clinical practice. The purpose of the analysis was to establish a possible action of diabetes as a risk factor for extrapyramidal diseases.

Methods: We studied a group of 88 subjects with Parkinson's Disease (PD) of which 18 with diabetes (20.45%, about 1 in 4), a group with Essential Tremor (ET) consisting of 68 subjects of which 17 affected by diabetes (25%) and a group with Vascular Parkinsonism (VP) consisting of 21 subjects of which 5 with diabetes (23.8%).

Results: The ratios showed a relatively homogeneous distribution in the three sub-populations of the given diabetic disease. The results indicated that the statistic comparison between the various groups examined did not give any statistical significance. Similarly, the comparison between the individual groups with the pathologies examined (PD, VP and ET) and the recruited control population was not significant as regards the incidence of diabetes as comorbidity.

Conclusion: The scarce relevance in the differences between patients with diabetes and without does not exclude tout court a possible influence of the dysmetabolic disorder on extrapyramidal diseases as it is necessary to take into account biochemical factors that are difficult to measure with clinical studies.

Keywords: Parkinson's disease; Vascular parkinsonism; Essential tremor; Diabetes

INTRODUCTION

Recent clinical investigations have shown a correlation between glycemic metabolism and insulin brain levels and the pathogenesis of Alzheimer's Disease (AD) leading some authors to the definition of this disease as type III diabetes. It cannot be ruled out that a subclinical metabolic disorder may be involved in the pathogenesis as previously reported for the accumulation of beta-amyloid plaques in Alzheimer's disease, in relation to the direct influence of insulin on the integrity of brain ultra-structure [1]. For this reason the aim of the present study was to investigate whether similarly there could be a statistical link between the metabolic disorder and Parkinson's Disease (PD) or Parkinson-like diseases by comparing three groups of patients affected by PD, Vascular Parkinsonism (VP) and Essential Tremor (ET) with a control group statistically comparable in age distribution with a retrospective investigation. This purpose issued from anamnestic relatively high frequency detection of diabetes disease in its various forms while collecting clinical patients' history in the phase of access to the movement disorders out-patients clinic.

Previous studies on large populations have highlighted a possible association between diabetes and the risk of developing PD [2]. In particular, a higher incidence of Type II diabetes was detected in an extended population leading to the conclusion that PD developed more often in such patients as if diabetes or metabolic disorder was a predisposing and/or a risk factor [3-5]. The

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clinical observation over time, during a period longer than about 5 years in our outpatient's clinic seemed to suggest a high incidence of diabetes in patients with PD compared to other subpopulations; however, this observed frequency of diabetes was also detected in other subpopulations affected by movement disorders such as ET and VP. The numerical values relating to the aforementioned populations were therefore calculated with the following result: the control group was collected enrolling patients not affected by those pathologies and consisted of 147 subjects (age range 21 to 92 yrs, average age 73,61 yrs, median age 76 yrs, 68 males and 79 females) of which 38 with overt diabetes. Note that the diagnosis of diabetes reported consisted in raw data analysis and does not take into account the type of diabetes as well as the duration and degree of compensation over time and possible complications.

The group considered as "control" collected patients affected by other movement disorders-including Restless Leg Syndrome patients in whom diabetes cannot be excluded as a co-pathogenic factor due to peripheral neuropathy. Moreover it has to be noticed that the control population was considered referring to a criterion that stands out from which adopted in research studies collecting "healthy adult subjects", because elderly people are generally affected by multiple diseases and therefore hardly strictly 'healthy'; on the other hand it was necessary to make an age homogeneous group comparison, in other words the concept of healthy subject in advanced age is certainly an abstraction not adherent to clinical practice, being the majority of older people affected by various often clinically silent diseases, especially those commonly known as aging diseases (among which the most widespread is ATS). In particular, it was included in the control population a group of subjects suffering from pathologies definable as neurodegenerative or even affected by vascular brain disease and composing a homogeneous group as concerns mean and median age, who had an age distribution similar to the groups examined (PD, ET, VP).

MATERIALS AND METHODS

The group with PD consists of 88 subjects (age range 56-97 yrs, average age 76,34 yrs, sex M 38 F 50) of which 18 with diabetes or 20.45% (about 1 in 4) has diabetes. The group with ET consists of 68 subjects (age range 30-94 yrs, average age 73, 86, sex M 39 F 29) of which 17 affected by diabetes or 25%. Finally the group with VP consists of 21 subjects (age range 58-92 yrs, average age 79,52, sex M 11 F 10) of which 5 with diabetes or 23.8%.

The ratios show a relatively homogeneous distribution in the three sub-populations of the given diabetic disease with the aforementioned limits. Therefore as a consequence of our observation at the moment it is not possible to establish at a clinical level that the diabetes-taken as an isolated risk factor-could be a predisposing factor to the single PD but it is not possible to exclude that it can concur together with other factors to the onset of degenerative diseases that involve generically movement disorders (ET and other Parkinsonisms).

A confirmation of the lack of significance between diabetes comorbidity (raw data) and PD is given by the statistical analysis performed comparing the subpopulations in the study and the group taken as a control; this comparison was made with the chi-square calculator test. This is a chi-square calculator test for a contingency table with four rows for the considered groups' values and two columns for the studied parameters, similarly to a previous methodology adopted to evaluate the incidence of cerebrovascular disease comorbidity.

In fact, in previous studies the frequent observation of CVD in some subpopulations of patients with movement disorders has led to a positive finding of a different distribution of CVD comorbidity between PD and other movement disorders.

RESULTS

The chi-square statistic, p-value and statement of significance appear beneath the table. Blue means you're dealing with dependent variables (Table 1).

Table 1: The chi-square statistic is 0.9172. The p-value is 0.821281. The result is not significant at $p<0.05$.

Results			
	Diabetes yes	Diabetes no	Row totals
Control group	38 (35.39) [0.19]	109 (111.61) [0.06]	147
PD group	18 (21.19) [0.48]	70 (66.81) [0.15]	88
VP group	5 (5.06) [0.00]	16 (15.94) [0.00]	21
ET group	17 (16.37) [0.02]	51 (51.63) [0.01]	68
Column Totals	78	246	324 (GrandTotal)

The results are evident in Table 1 where it is shown that the statistic comparison between the various groups examined for what concerns the incidence of diabetes does not give any statistical significance. Similarly, the statistical comparison between the groups with the pathologies examined PD, VP and ET compared individually with the recruited control population does not show any significance as regards the incidence of diabetes as comorbidity.

Therefore the statistical analysis carried out on these particular populations does not seem to address a clinical link between overt diabetes and movement disorders. However, considering the impression in clinical practice of a certain frequency of diabetes, it was of interest to define the estimated percentage of diabetes prevalence in the subjects examined.

The calculation of the prevalence rate of diabetes in the parkinsonisms is shown in Table 2: in the PD group 20.45% of 88 subjects have diabetes (raw data), in the group with VP 23.81% of 21 subjects is affected by diabetes (raw data) and finally in the group with ET 25.00% of 68 subjects is affected by diabetes (raw data) (Table 2).

Table 2: Calculation of the prevalence rate of diabetes in the Parkinsonism.

Percentage of diabetes comorbidity			
	Diabetes yes	**Diabetes no**	**Row totals**
Control group	38	109	(147) 25.84%
PD group	18	70	(88) 20.45%
VP group	5	16	(21) 23.81%
ET group	17	51	(68) 25%

Note that the necessarily smaller number of subjects that compose the subpopulations does not correspond to a large difference in percentage of the diabetic disease. It is noteworthy that in vascular forms one would expect diabetes to be more incident as one of the most important vascular risk factors. For this reason, the percentage of incidence considered in a smaller group of 20 patients (VP) can be assessed in comparison to the percentage observed in the other larger population.

DISCUSSION

From the statistical results diabetes, which is a well-known vascular risk factor, does not apparently seem to represent a direct risk for PD development instead, at least relying on our raw data. On the contrary, previous studies ascertained that cerebrovascular disease has a significant comorbidity role for PD, even with raw data [6,7]; in fact, in those studies, the exact timing and distribution of vascular damage was neglected to make possible the statistic processing at that given time. This leads to deduce that, whether a possible correlation beyond the indirect atherogenic\hypoxic risk factor of diabetes on PD onset and cerebrovascular disease should be considered a predisposing condition [6,7] some unknown biochemical mechanism should be called in question for insulin\glycaemia disruption regarding a direct influence of diabetes on PD [8].

According to a clinical impression commonly detected in specialist practice there is a high frequency of diabetes in the various forms expressed in terms of type, severity and duration in patients with movement disorders, particularly PD. To achieve the aim to sensibly assess the real influence of metabolic disturbances on degenerative movement disorders it should be necessary to extend in number the statistical sample and to carry out a more detailed analysis of the aforementioned parameters of diabetes; particularly in relation to the timing of onset of movement disorders with respect to the duration and type and possible degree of complication of diabetes itself. These studies should be supported with chemical and anatomic investigation about the interaction of hormones, glycaemia and specific brain areas, as previously shown regarding the presence of insulin receptors in hippocampus and other basal ganglia areas.

CONCLUSION

In this study, we have a high degree of uncertainty due to various factors that are difficult to clearly define within the taken groups of subjects, such as the onset and duration of the diabetic disease. In fact, factors that cannot be measured with the common standard parameters used in clinical practice but operating in a subclinical way could be implicated; for example the highest insulin level that precedes the hyperglycaemia even for many years. This was observed in Alzheimer's disease. Glycemia, blood cholesterol and cortisol levels can be even slightly higher than the physiological parameters for extended periods of time. It will probably be necessary to integrate clinical studies with biochemical, *in vitro* and metabolic studies to achieve a good level of certainty on the possible direct incidence of dismetabolic impairment and/or insulin levels influence on the pathogenesis of neurodegenerative diseases and related movement disorders.

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