High Prevalence of Huntington’s Disease in Cañete - Perú

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Objective: To determine the prevalence of HD in five districts of Cañete Valley in order to develop a diagnosis, prevention and genetic counseling plan. Since HD is considered a hereditary disease with low prevalence, epidemiologic studies are scarce and lack genetic confirmation, which is nowadays necessary for the diagnosis of HD.

Methods: A first register of Cañete Valley inhabitants with HD was created in 1983. The population of this area has no access to health care or mass media, and the number of patients seeking for medical care is limited. Therefore, in 2004 we studied families systematically in five districts using the pedigree follow up method, which is ideal to determine the prevalence of genetic diseases and even more in communities like Cañete.

Results: We identified 30 genetically confirmed cases of HD (17 males, 13 females). The population of the five districts reached 66,438 inhabitants on August 4th, 2004, i.e., a minimum prevalence of 45.1 per 100,000 inhabitants. We obtained 11 pedigrees, including 1397 individuals. Twenty-four (75%) patients were newly diagnosed cases of Huntington’s disease.

Conclusion: Cañete is the second largest focus of Huntington’s disease in Latin America, and one with the highest prevalence reported worldwide

Keywords: Chorea; High prevalence; Huntington’s disease; Peru

Introduction

Huntington’s disease (HD) is an autosomal dominant neurodegenerative condition, featuring complete penetrance, anticipation, with onset at middle age [1]. It is characterized by movement and psychiatric disorders as well as cognitive impairment [2,3]. Although this condition is widespread around the world, it is more prevalent in the Northern hemisphere, e.g., in the United States [4,5]. The HD gene in these countries was inherited from European immigrants. Isolated cases of HD have been reported in Latin America in the literature. Gatto et al. [6] published a clinical series including 11 Argentine patients with a diagnosis of HD whose main initial symptom was choreic-like movements. Cruz-Coke [7] in Chile reported 10 cases of HD, which together with the previous 22 cases reported in the Chilean literature totaled 32 cases in 12 families, 2 of these families with 10 cases were immigrants. Lima and Silva et al in Brazil [8] carried out genetic testing in 44 patients with HD and in a control group.
Alonso [9] in Mexico reported his experience with 28 patients from 26 different families. Alfonso et al in Colombia, reported their experience including patients from some Colombian regions in 1995 [10,11].

No doubt, Maracaibo, in Zulia State, Venezuela is the hot spot for HD in Latin America. The number of patients with HD in this region represents the largest number of cases related to one common ancestor [12,13]. The high prevalence of HD in this region, which called the attention of the world medical community, was first reported by Negrette [14,15]. The first HD reports in the Cañete [14,15] Valley were unveiled by Cuba et al [16]; the prevalence for the Cañete province was then 31 cases per 100 000 inhabitants. In 1986 [17], the HD pedigree was studied, and Cañete was identified as the hot spot for the HD population in Peru. In 1989, Cuba and Torres [18] reported eight families with HD in Cañete, and in 1990 they reported 30 HD cases in one family only. This family was one of the 14 families assessed up to then. The authors concluded that the disease had appeared in that family 120-150 years before, to then spread from the Cañete Valley throughout Peru [19]. Learning about the prevalence of HD will lead to a better understanding of the condition in order to establish incidence rates and develop programs for improved diagnosis in Peru and more importantly, to provide adequate genetic counseling.

Methods

The pedigrees designed in 1983 were followed and updated [16,19]. A member of the family was interviewed in each case, and data were obtained to study the number of family members involved, age at the onset of symptoms, number of marriages and number of children. Once the new HD patients were identified in the new pedigrees, they underwent neurological examination. The prevalence was estimated considering the population census for the 5 districts in the Cañete Valley included in the previous study. (Quilmana, Pacaran, Imperial, Nuevo Imperial, Lunahuana) for August 2004. The districts and their populations are shown in Figure 1. Data for age, gender, age at symptom onset and family history were recorded. The patients underwent a clinical examination in their houses conducted by an experienced neurologist (LTR). The diagnosis was made according to the clinical criteria proposed by Folstein [20]. It was later confirmed by means of molecular genetic studies once the patients had signed an informed consent to undergo blood sampling and participate in the study. Systematized neurological screening was also carried out, and the Unified Huntington’s Disease Rating Scale (UHDRS) [21] used. The data were processed using the SPSS 12 statistical package for Windows. Frequency distribution, percentiles, averages, and standard deviations were used to determine the magnitude and features of the study subject. The Student’s t test for non-matched samples was performed to determine significant differences, if any, as to the age of onset of the disease in relation to the parental inheritance pattern. p < 0.05 was considered a statistically significant value; the confidence interval was 95%.

Result

Frequency of the disease

Eleven pedigrees were obtained including a total of 1397 individuals. Three new cases were found corresponding to two pedigrees previously studied by Cuba et al. [18] Further information was obtained for four generations for these cases. For the remaining 9 pedigrees information was obtained for at least five generations. Thirty patients were identified according to the pedigree follow up method. One patient, with a clinical diagnosis of HD from a family with genetic confirmation of the disease refused to participate in the study; therefore, this patient was not considered for the prevalence estimate. According to the National Institute of Statistics and Informatics and the population projections made for the years 1999-2005, the population in the 5 districts for the prevalence day (Figure 1), August 4, 2004, was 66438, which implies a minimum prevalence of 45.1/100 000 inhabitants. The cases per study area and their corresponding prevalence values are shown in Figure 2.

Figure 1: Cañete valley and five districts of the study.

Figure 2: Huntington’s disease cases and prevalence according to districts studied.

Age and gender

All the patients were of mestizo origin, (mixed race Amerindian and white parentage origin), 17 (56.7%) were male and 13 (43.3%)
were female: age range 23-71 yrs, mean age 43.2. The age and gender distribution are shown in Table 1. Of the 30 cases, 24 (75%) were first diagnosed by a neurologist.

Age of onset of clinical manifestations and time of the disease

The mean age of onset of clinical manifestations was 38.5 years (SD 14.3); the mean age for males was 36.8 years (SD 15.7) and, for females 40.6. (SD 12.6) (Table 2). In one patient (3.3%) onset of the disease occurred before the age of 20. The distribution of the stratified age of onset and gender is shown in Table 3. As for the inheritance pattern, 13(43.3%) patients reported having inherited the disease from their fathers, whereas 17(56.7%) inherited the condition from their mothers. No, de novo mutation was observed. The distribution of the age of onset depending on the parent involved appears in Table 4.

Table 1: Age and gender distribution at diagnosis.

| Age at Diagnosis | Male | Female | Total |
|------------------|------|--------|-------|
| 20-29            | 4    | 2      | 6     |
| 30-39            | 5    | 1      | 6     |
| 40-49            | 2    | 7      | 9     |
| 50-59            | 2    | 1      | 3     |
| 60-69            | 3    | 2      | 5     |
| ≥70              | 1    | 0      | 1     |
| Total            | 17   | 13     | 30    |

Table 2: Age of onset according to sex.

| Sex       | Cases | Mean±SD | P* (CI 95%) |
|-----------|-------|---------|-------------|
| Male      | 17    | 36.8±15.7| 0.473(-14.7-7.03) |
| Female    | 13    | 40.7±12.5|
| Difference|       | 3.9     |

*Statistical significance; SD: Standard Deviation.

Table 3: Age of onset by stratified groups according to sex.

| Age at onset of symptoms | Male | Female | Total |
|--------------------------|------|--------|-------|
| <20                      | 1    | 0      | 1     |
| 20-29                    | 7    | 2      | 9     |
| 30-39                    | 2    | 6      | 8     |
| 40-49                    | 3    | 2      | 5     |
| 50-59                    | 2    | 1      | 3     |
| 60-69                    | 2    | 2      | 4     |
| Total                    | 17   | 13     | 30    |

Clinical manifestations

Either the patients or their relatives were asked about three manifestations of the onset of the disease during the interview. Chorei-like movement disorders were present in 30 cases (100%), although some patients exhibited behavior disorders before or together with the chorei movements. Nine patients (30%) presented psychiatric disorders as the initial symptom; 8 of them had irritability, and one of them lacked motivation. None of these patients, even those with a late onset of the condition, presented dementia as the initial symptom. One patient (3.3%) developed the juvenile or early onset, though with rather atypical symptoms featuring involuntary movements involving the upper limbs and behavior disorders including irritability. In this case the patient had a paternal pattern of inheritance. One patient (3.3%) had memory impairment as the initial symptom.

Discussion

Table 5: HD prevalence around the world.

| Countries                          | Prevalence per-100 000 Inhabitantes |
|------------------------------------|-------------------------------------|
| United States (Minnesota)          | 5,4                                 |
| Canada (Manitoba)                  | 8,4                                 |
| United Kingdom (South Wales)       | 7,6                                 |
| France (Limousin)                  | 7,0                                 |
| Australia (Victoria)               | 4,6                                 |
| Venezuela (Zulia, Maracaibo)       | 700,0                               |
| Perú (Cañete)                      | 45,1                                |

*Number of cases
aStatistical significance, SD: Standard Deviation

The prevalence of HD in the world ranges between 4 and 7/100 000 inhabitants [22]. Palo et al. [23] estimated the prevalence in Finland was 0.5 per 100 000 inhabitants, whereas in Western countries the prevalence ranges between 3 and 7 cases per 100 000 inhabitants. Incidence among the Japanese [24], South Africans [25] and African Americans [12] is the lowest. However, the prevalence of HD is over 15/100 000 cases in some countries, mainly in Western Europe [26]. The distribution of HD prevalence in different regions of the world is shown in Table 5. The prevalence in Lake Maracaibo, Venezuela, reaches 700 per 100 000 inhabitants.
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