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Short Communication

High Prevalence of Huntington's Disease in Cañete - Perú

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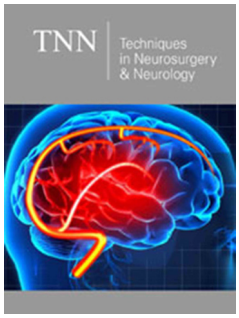

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Abstract

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 66438 inhabitants on August4th, 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 Perú [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 Perú 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 (L.T.R.) 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, percentages, 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.

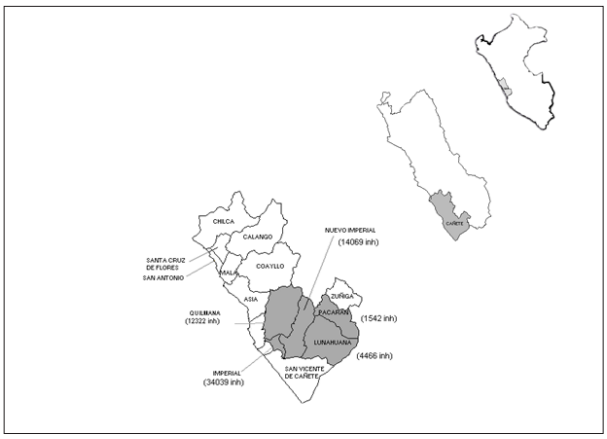

Figure 1: Cañete valley and five districts of the study.

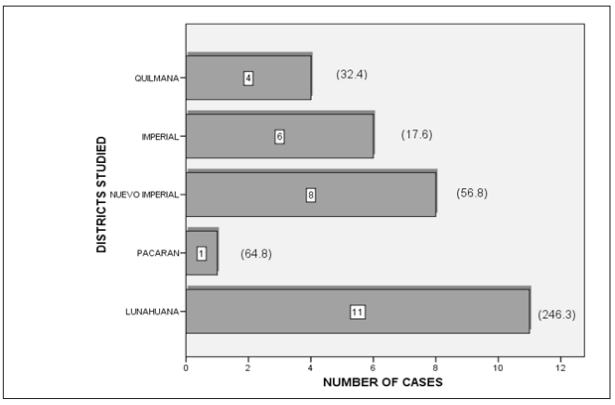

Figure 2: Huntington's disease cases and prevalence according to districts studied.

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[a] (CI 95%)
Male	17	36,8±15,7	0,473(-14,7-7,03)
Female	13	40,7±12,5	
Difference		3.9	

[a]Stadistical 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

Table 4: Relation between age at onset and sex of the affected parent.

Sex	Mean±SD Age at onset		P[a](IC 95%)
	Paternal Transmission (*)	Maternal Transmission (*)	
Male (17)	29,8±15,1 (8)	43±14,2 (9)	0,085 (-28,3-2,07)
Female (13)	42,8±11 (5)	39,3±13,9 (8)	0,652 (-12,8-19,6)

*Number of cases

aStatistical significance, SD: Standard Deviation

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 Inhabitamos
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

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

[27]. According to the results obtained in this study, Cañete might be the second largest HD population in Latin America and one of the most important ones globally. The increase in prevalence is alarming when considering the data published by Cuba et al. [16]. Such a high prevalence in this area might be due to a combination of social and geographic isolation leading to the spread of this genetic inherited disorder, which occurs when the gene is introduced in a given population with a high growth rate [12]. Interestingly, 75% of the patients had no previous diagnosis of HD, which enhances the relevance of the methodology applied in this particular study, since in other scenarios where patients have access to health care centers and communication networks a different methodology may be used, even the recent capture and recapture method used by Burguera et al. [28] in Valencia, in which case it was necessary to cross several health care information sources [29,30]. Folstein [4] conducted a study in Maryland, and reported that the pedigree follow up method enabled a more accurate identification of cases among African Americans as compared to Caucasians; the latter had more access to both radio, television and health care centers.

According to Folstein et al [20], studies conducted in the community exhibit two main sources of diagnostic error: inaccurate research in the family history, and the lack of knowledge about clinical features and course of the disease. In our study, the diagnosis issue could be solved by means of systematic interviews to the patients' relatives and a precise pedigree design; in all cases the disease had been genetically confirmed. Clinical manifestations typically include a phase characterized by mild behavioral and psychiatric disorders which develops up to 10 years before choric manifestations occur. Shiwach and Norbury [31] proved that psychiatric symptoms were common in HD before the occurrence of neurological symptoms. In our study, a third of the patients exhibited behavior disorders before or together with chorea.

All the patients in our study had typical HD, even the patient with juvenile or early onset of HD and the cases of late onset of the disease (3.3 and 23.3%, respectively) as compared to other series [32]. HD occurs at about the age of forty, which correlates with most of the results obtained in previous studies when considering juvenile, typical and late onset HD; whereas late onset HD occurs at about the age of fifty [33,34].

Conclusion

Based on the data obtained, Cañete is the second largest HD population in Latin America, and one of the largest in the world. It is vital to implement programs to provide counseling to HD patients and relatives at risk for this disease.

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References

1. Walker FO (2007) Huntington's disease. Lancet 369: 218-228.
2. Martin JB, Gusella JF (1986) Huntington's disease. Pathogenesis and management. N Engl J Med 315(20): 1267-1276.
3. Martin JB (1999) Molecular basis of the neurodegenerative disorders. N Engl J Med 340(25): 1970-1980.
4. Folstein SE, Folstein M, Chase GA, Wahl WE, Donnell A (1987) Huntington disease in maryland: clinical aspects of racial variation. Am J Hum Genet 41(2): 168-179.
5. Critchley M (1973) Great britain and the early history of huntington's chorea. Adv Neurol 1: 13-18.
6. Gatto E, Micheli F, Fernández M, Giannaula R, Casas (1994) Análisis de una serie clínica: corea de huntington evaluación clínica. Rev Chil Neuro Psiquiat 32: 127-128.
7. Cruz-Coke R (1987) Epidemiología genética de corea de huntingtonen chile. Rev Med Chile 115: 483-485.
8. Lima E SilvaTC, Guerra H, Bertuzzo C, Lopes CI (2000) Molecular diagnosis of huntington disease in brazilian patients. Arq Neuropsiquiatria 58: 11-17.
9. Alonso M, Nieto D (1985) Aspectos clínicos y genéticos de la enfermedad de huntington. Rev Inv Clin 37: 125-130.
10. Alfonso HS, Daza J, Carboneli C (1995) Correlación clínico molecular y caracterización de la Enfermedad de Huntington en familias de Juan de Acosta y otras regiones colombianas. Acta Neurol Colomb 32: 300.
11. Alfonso HS, Daza J, Carboneli C (1996) Caracterización de las secuencias polimórficas de tripletes CAG y CCG del gen de la Enfermedad de Huntington en familias colombianas. Acta Neurol Colomb 12: 70-75.
12. Harper P (1991) Huntington's disease major problems in neurology 2da ed. Londres: Saunders.
13. Negrette A (1963) Corea de Huntington (Estudio de una sola familia investigada a través de varias generaciones). Maracaibo, Venezuela.
14. Okun M, Thommi N (2004) Americo negrette (1924 to 2003): diagnosing huntington disease in Venezuela. Neurology 63(2): 340-343.
15. Young A, Shoulson I, Penney J, et al. (1986) (1986) Huntington's disease in Venezuela: neurologic features and functional decline. Neurology 36(2): 244-249.
16. Cuba JM, Castro C, Benzaquen M (1983) Sobre la epidemiología de la corea de huntington en el Perú. Rev Neuropsiquiatría 46: 114-120.
17. Cuba JM (1986) A focus of huntington's chorea in Peru. Rev Neurol 142: 151-153.
18. Cuba JM, Torres L (1989) Huit arbres généalogiques de chorée de huntington au Peróu. Rev Neurol 145: 482-484.
19. Cuba JM, Torres L (1990) Estudio de una familia con Corea de huntington en cañete. Rev Neuropsiquiatria 53: 94-102.
20. Folstein S, Leigh JI, Folstein M (1986) The diagnosis of Huntington's disease. Neurology 36(10): 1279-1283.
21. Huntington Study Group (1996) Unified huntington's disease rating scale: reliability and consistency. Mov Disord 11(2): 136-142.
22. Harper PS (1986) The prevention of Huntington's chorea. JR Coll Physicians Lond 20(1): 7-14.
23. Palo J, Somer H, Ikonen E, Karila L, Peltonen L (1987) Low prevalence of

Huntington's disease in Finland. Lancet 2(8562): 805-806.

24. Narabayashi H (1973) Huntington's chorea in Japan: review of the literature. Adv Neurol 1: 150-152.

25. Silber E, Kromberg J, Temlett JA, Krause A, Saffer D (1998) Huntington's disease confirmed by genetic testing in five African families. Mov Disord 13(4): 726-730.

26. Bates G,Harper P, Jones L (2002) The Epidemiology of Huntington's Disease. In Harper P. ed. Huntington's Disease. London: Oxford University Press. 251-280

27. Avila-Giron (1973) Medical and social aspects of huntington's chorea in the state of zulia, Venezuela. In: Barbeau A, Chase TN, et al. (Eds.), Advances in Neurology. New York, USA, pp. 261-266.

28. Burguera JA, Solís P, Salazar A (1997) Estimación de la prevalencia de la enfermedad de huntington por el método captura- recaptura en la Comunidad Valenciana. Rev Neurol 25: 1845-1847.

29. Hook EB, Regal RR (1993) Effect of variation in probability of ascertainment by sources (variable catchability) upon capture-recapture estimates of prevalence. Am J Epidemiol 137: 1148-1166.

30. Hook EB, Regal RR (1992) The value of capture-recapture methods even for apparent exhaustive surveys. The need for adjustment for source of ascertainment intersection in attempted complete prevalence studies. Am J Epidemiol 135: 1060-1067.

31. Shiwach R (1994) Psychopathology in Huntington's disease patients. Acta Psychiatr Scand 90(4): 241-246.

32. Solís M, Palau F, Burguera JA (1995) Enfermedad de Huntington: estudio clínico y genético en una población española. Neurologia 10: 362-366.

33. Wexler NS, Lorimer J, Porter J (2004) Venezuelan kindreds reveal that genetic and environmental factors modulate Huntington's disease age of onset. Proc Natl Acad Sci 101(10): 3498-3503.

34. Conneally M (1984) Huntington disease: genetics and epidemiology. Am J Human Genet 36(3): 506-526.