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Diagnostic process and management of schizophrenia in Spain: the ACEE project

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Introduction. Although schizophrenia has a great impact on the health care, social and family levels, there is little epidemiological information on patients with schizophrenia, its diagnosis and treatment in Spain. The ACEE (Abordaje Clínico de la Esquizofrenia en España; Clinical Approach to Schizophrenia in Spain) study was designed with the primary objective of defining the management of schizophrenia in Spain from the perspective of current clinical practice.

Methods. ACEE is a descriptive cross-sectional multicenter observational study with data collected in the setting of current clinical practice by means of a specifically designed questionnaire.

Results. A total of 1,937 patients have been studied (83 % pertaining to the public sector and 17 % to private one). Most subjects had paranoid schizophrenia in the stabilization phase, and did not work because of their illness. Most (96%) were receiving antipsychotic treatment and 55% also received some non-drug treatment. Negative symptoms were more frequent than positive symptoms (88 % versus 63 %). Significant differences were observed for type of patients and diagnostic procedures involved between the public and private health care sectors.

Conclusions. The ACEE study shows that schizophrenic patients attending Spanish psychiatric centers are mainly single, non-working males who are living in their family setting. Treatment basically consists of antipsychotics combined with other drugs, and few complementary examinations are performed.

Key words:
Schizophrenia. Diagnosis. Treatment. Observational study.

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Diagnóstico y manejo de la esquizofrenia en España: el proyecto ACEE

Introducción. A pesar de tratarse de una enfermedad con una gran repercusión sanitaria, social y familiar, en España se dispone de escasa información epidemiológica sobre los pacientes con esquizofrenia, su diagnóstico y tratamiento. El estudio ACEE (Abordaje Clínico de la Esquizofrenia en España) se ha diseñado con el objetivo principal de conocer en la práctica clínica habitual el manejo de la esquizofrenia en España.

Método. El ACEE es un estudio observacional, descriptivo, transversal, multicéntrico, con datos recogidos en el curso de la práctica clínica habitual mediante un cuestionario diseñado específicamente.

Resultados. Se han analizado un total de 1.937 pacientes (83 % del sector público y 17 % del privado). La mayoría presenta una esquizofrenia paranoide en fase de estabilización y no trabaja debido a su enfermedad. El 96 % está sometido a tratamiento con antipsicóticos y un 55 % recibe además algún tipo de terapia no farmacológica. Se presentan con mayor frecuencia síntomas negativos que positivos (88 frente a 63 %). Existen diferencias significativas entre el tipo de pacientes y el procedimiento de diagnóstico entre el sector público y el privado.

Conclusiones. El ACEE muestra que el perfil del paciente atendido por esquizofrenia en las consultas psiquiátricas españolas es mayoritariamente varón, soltero, viviendo sin trabajo en un entorno familiar, tratado básicamente con fármacos antipsicóticos combinados con otras medicaciones y al que se practica un reducido número de exploraciones complementarias.

Palabras clave:
Esquizofrenia. Diagnóstico. Tratamiento. Estudio observacional.

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INTRODUCTION

Schizophrenia is a significant health problem in every country of the world[1]. Its treatment has greatly advanced in recent years thanks to a better understanding of psychiatric

symptoms, to advances in the field of neuroscience and to modification of different social beliefs and attitudes. In recent years, clinical research, on its part, has focused on early detection of the disease and on comorbidity aspects with other diseases[2]. Modern treatments have made out-patient monitoring of patients possible over long phases of the disease. Years earlier, patients with schizophrenia remained in long stay closed institutions most of the time.

However, at present, wide controversies focused on diagnosis and treatment of schizophrenia continue to exist. The different approach models to this disease complex, clinical subtypes or differentiation of symptoms make up examples of still on-going discussions[3,4]. Choice of first drug treatments is also not exempt of controversy in spite of the data provided by clinical trials and dissection of evidence based medicine. As a whole, it is possible to perceive great difficulty to transfer the results from all these investigations to the daily clinical practice. Enthusiasm regarding constant progression in investigations contrasts with an outstanding incapacity of psychiatry to translate these advances into better care of patients affected by the disease[5,6].

This may be why many treatment guides, consensuses, protocols, expert's recommendations, etc. have been developed in an attempt to homogenize diagnostic and therapeutic decisions of schizophrenia based on scientific evidence as much as possible[7]. In spite of these efforts, there are still noticeable divergences and even contradictions in the health care setting or in geographic distribution: hospitals, health care sites, public or private clinics in the treatment of schizophrenia in different countries. Few studies exist on how psychiatric professionals adapt their work to these recommendations of health care organizations or of scientific societies. Thus, in a first essential step, it is necessary to know the real management of schizophrenia in a certain setting or country. That is why the ACEE (Clinical Approach to Schizophrenia in Spain) project was done, that is, in order to approach daily diagnosis and treatment of schizophrenia in Spain, evaluating the clinical practice of Spanish psychiatrists in their public and private consultations of a country with an estimated population of 40 million inhabitants.

More than 3500 psychiatrists work in Spain, most in the public sector and some of them also coordinating their work in a private clinic. When this study was begun, Spanish psychiatrists had easy access to guides, protocols and recommendations of experts from Spain and other European countries and from the United States[8-10].

MATERIAL AND METHODS

ACEE is a pure, descriptive, cross-sectional, multicenter, national scope study in which 500 psychiatrists had to include the first four patients diagnosed of schizophrenia who came to their office during the enrolment period (June-October 2003). Most of the psychiatrists (72%) had been working more than 10 years in the profession. Each psychiatrist, after receiving an informed consent, included the patients in the study by a specifically designed question-naire. This questionnaire detailed sociodemographic data, background, clinical characteristics (mean time of disease course, most frequent symptoms, disease phase, comorbidity) and treatment regimes.

After considering the categoric variables included, sample size needed to be able to obtain a 95% confidence interval with minimum accuracy of 5% was calculated. This calculation was 1,600 patients, a number that increased to 1,920 patients after considering possible loss of 20% of the patients enrolled. According to the health care distribution in Spain, it was calculated that the initial percentage of patients treated in a public consultation and private consultation should be 80%-20% and a number of patients was established for each one of the regional communities of the Spanish state based on the official data of the population of each one of them in the year 2002.

There were three primary objectives of the ACEE project: *a)* describe the socio-demographic characteristics of the schizophrenic population; *b)* describe the present clinical profile of the schizophrenic patient in Spain, and *c)* know and compare the diagnostic and treatment guidelines (drug and non-drug) of the specialists in psychiatry in Spain according to the type of health care site.

Statistical analysis

A database defined and analyzed through the SAS V8.0 program was constructed with the information collected for each patient with the questionnaire.

Frequency distributions and percentages for the qualitative variables with their corresponding confidence intervals and means, standard deviation and range for quantitative variables were calculated. The different groups were compared by the chi-square test or corresponding alternative tests were applied to contingency tables in the case of qualitative variables and with the Student's *t* test of comparison of means in the case of quantitative variables.

RESULTS

A total of 1969 patients were enrolled, 1937 of whom were evaluable. A total of 83% of the sample belonged to patients from public sector consultations and 17% to private ones. Almost 70% of the patients enrolled were male and mean age was 37.6 years. Most of the patients were single (79%), lived in a family setting (89%) and did not work (73%) due to their disease. Sixty percent of the schizophrenic patients were seen in a single public or private psychiatric facility without using other health care resources. Most

of the patients included in the sample had a disease evolution greater than 5 years (77%). This guarantees the stability of the diagnosis and increases its reliability. A total of 23.1% had family background of first grade schizophrenia.

The ACEE study demonstrated a decrease in the proportion of patients who have a laboratory test or physical examination as a diagnostic complementary examination. One percent of the sample underwent neuroimaging tests and 27% underwent an electroencephalogram (table 1). Most of the sample had paranoid schizophrenia in stabilization phase, and were enrolled in the study through a routine visit. As a whole, negative symptoms are more frequent than positive ones, globally standing out social withdrawal, affecting blunting, apathy and delusional ideas, in the latter case above the perception alterations (table 2).

Psychiatric comorbidity practically affects half of the sample (anxiety, affective and sleep disorders), there being greater associated morbidity of psychotic depression in women (8.05% versus 5.6% of men) and of anxiety disorders (14.3% versus 10.4%). On the contrary, a greater association of the masculine gender with personality disorders was detected (5.7% versus 3%). When these comorbidities were observed by age, an inverse relationship of presence of «phobias and obsessions» and «anxiety disorders» (the greater the age, the less presence of these disorders) is observed. On the other hand, non-psychiatric comorbidity reaches 25% of the patients (mainly hypercholesterolemia and diabetes). More than one third of the patients have substance abuse disorder (table 3).

From a health care perspective, 96% of the patients (almost all if we consider that 4% of patients are newly diagnosed) receive drug treatment and 55% a concomitant non-drug treatment. Individual psychotherapy (25%), rehabilitation (19%), and occupational therapy (18%) stand out in the latter case, with considerably lower values for family psychotherapy (5%) (table 4).

Table 1 Complementary diagnostic tests

Complementary test	
Blood analysis	1,335 (68.9 %)
Physician examination	1,220 (63 %)
Neurologic examination	909 (46.9 %)
Electrocardiogram	534 (27.6 %)
Electroencephalogram	523 (27 %)
CT scan	152 (7.8 %)
Magnetic nuclear resonance	133 (6.9 %)
Others	111 (5.7 %)
SPECT/PET	19 (1 %)

Table 2 Subtype of clinical profile

Diagnosis of schizophrenia	
Paranoid schizophrenia	1,314 (68.4 %)
Hebephrenic schizophrenia	70 (3.6 %)
Catatonic schizophrenia	8 (0.4 %)
Undifferentiated schizophrenia	138 (7.1 %)
Residual schizophrenia	268 (13.9 %)
Simple schizophrenia	71 (3.7 %)
Other schizophrenia	31 (1.6 %)
Without specification	12 (0.6 %)
Paranoid/residual schizophrenia	11 (0.6 %)
Paranoid/hebephrenic schizophrenia	1 (0.1 %)
Disease phase	
Acute phase	140 (7.2 %)
Condition with active symptoms	554 (28.7 %)
Stabilized	1,239 (64.1 %)
Condition in the visit	
Patient who is diagnosed of schizophrenia for the first time	74 (3.8 %)
Patient with previous diagnosis of schizophrenia who comes to routine visit	1,586 (82.4 %)
Deterioration	172 (8.9 %)
Patient with schizophrenia who comes to consultation to modify medication	61 (3.2 %)
Others causes	52 (2.6 %)
Disease symptoms	
Positive	1,229 (63.4%)
Delusional ideas	861 (44.4 %)
Hallucinations	527 (27.2 %)
Conceptual disorganization	512 (26.4 %)
Hostility	262 (13.5 %)
Excitement	255 (13.2 %)
Negative	1,699 (87.7 %)
Apathy	855 (44.1 %)
Affective blunting	971 (50.1 %)
Social withdrawal	1,276 (65.9 %)
Absence of spontaneity and fluency in conversation	767 (39.6 %)
Poverty of speech	783 (40.4 %)
Abulia	578 (29.8 %)

In drug treatment, 65% of the patient received antipsychotic monotherapy, 30% two drugs and 5% three or more antipsychotics. During the 6 months prior to the study visit, antipsychotic treatment was modified in 34% of the patients, changing the drug (49%), the dose (44%) or adding a new drug (26%). The most frequent causes for the change were relapse or clinical deterioration (38%), lack of improvement (29%), adverse reaction (21%) or lack of compliance (14%). The most frequent adverse reaction related with

Table 3 Comorbidity

Psychiatric comorbidity: 867 (44.8 %)
- Depression: 221 (25.5 %)
- Post-psychotic depression: 124 (14.3 %)
- Anxiety disorders: 225 (25.9 %)
- Phobias and/or obsessions: 149 (17.2 %)
- Personality disorders: 97 (11.2 %)
- Cognitive disorders: 127 (14.7 %)
- Sleep disorders: 220 (25.4 %)

Non-psychiatric comorbidity: 491 (25.3 %)
- Arterial hypertension: 70 (14.3 %)
- Hypercholesterolemia: 172 (35 %)
- Hypertriglyceridemia: 100 (20.4 %)
- Diabetes: 61 (12.4 %)

Comorbidity due to drugs abuse: 731 (37.9 %)
- Alcohol: 232 (11.8 %)
- Tobacco: 550 (28.2 %)
- Amphetamines: 14 (0.7 %)
- Hallucinogens: 9 (0.5 %)
- Cocaine: 52 (2.7 %)
- Cannabis: 192 (9.9 %)
- Opiates: 17 (0.9 %)
- Others: 37 (1.9 %)

the use of antipsychotics is weight gain (33 %, this increase being greater than 5 kg in 57 % of the cases), fatigue and somnolence (21 %), extrapyramidal effects (14 %), mouth dryness (13 %) and sexual dysfunction (12 %). There was no data (analysis) regarding some of their lipid or glucose parameters in between 41 % and 43 % of the patients. In addition to antipsychotics, 70 % of the patients received other concomitant drug treatments, 66 % drugs for the central nervous system (mainly anxiolytics, antidepressants and anticholinergics) and 11 % another type of treatment.

Men and women show differences in some aspects in regards to their disease profile. Women are seen in a higher proportion in private sites (20 % vs 16 % for men; $p<0.05$), and are older at the time of the visit (40 years vs 36 years; $p<0.001$), they are married in higher proportion then the men (19 % vs 8 %; $p<0,001$) and have a higher level of studies. On the other hand, they were diagnosed of schizophrenia at a later age and have a higher rate of direct family background (mother and siblings) (table 5). Furthermore, women have a lower proportion of negative symptoms of the disease (especially «absence of spontaneity and conversation fluency» and «poverty of speech»), they are treated with antipsychotics in lower proportion, and they receive fewer non-drug treatments (and more specifically «rehabilitation» and «occupational therapy») (table 5).

The differences between patients seen in public or private sites are significant in some cases. Patients are seen at older ages in public sites (38 years vs 36; $p<0.005$), have a lower level of studies and work or study in a lower percentage. A total of 68 % of patients in private sites are seen in only one health care facility versus 58 % of the patients in the public sector ($p<0.001$), where we find a higher use of other health care resources and non-drug treatments. Time from diagnosis is significantly higher in the public than in the private sector and more complementary diagnostic examinations are performed in all their range in the private sector. In

Table 4 Treatment of schizophrenia

Drug treatment: 1,853 (95.6 %)
- Atypical antipsychotics: 1,728 (81.9 %)
- Depot antipsychotics: 461 (23.8 %)
- Typical antipsychotics: 377 (19.5 %)

Treatment form
- One drug: 1,203 (65.5 %)
- Two drugs: 547 (29.8 %)
- Three or more drugs: 86 (4.7 %)

Non-drug treatment: 1,068 (55.9 %)
- Individual psychotherapy: 494 (25.5 %)
- Group psychotherapy: 110 (5.7 %)
- Family psychotherapy: 96 (5 %)
- Rehabilitation: 363 (18.7 %)
- Training in social skills: 261 (13.5 %)
- Occupational therapy: 353 (18.2 %)
- Community support activities: 212 (10.9 %)

Table 5 Differences between men and women ($p<0.05$)

	Men (n = 1,334)	Women (n = 596)
Age at time of diagnosis	23.2 ± 5.7	25.6 ± 7.9
Family background	280 (21.1 %)	163 (27.6 %)
Mother	61 (4.6 %)	41 (6.9 %)
Siblings	117 (8.8 %)	73 (12.2 %)
Symptoms		
Negative signs	1,185 (88.8 %)	508 (85.2 %)
Absence of spontaneity and fluency in conversation	550 (41.2 %)	213 (35.7 %)
Poverty of speech	567 (42.5 %)	213 (35.7 %)
Treatment		
Drug treatment	1257 (94.2 %)	574 (96.3 %)
Non-drug treatment	765 (57.3 %)	299 (50.2 %)

private health care, patients in acute phase with fundamentally positive symptoms are seen more frequently on the contrary to the public health care network. Finally, more patients are treated with monotherapy in the public sector.

The profile of patients with positive symptoms differs, among other things, from those of patients with negative symptoms in that the former are younger at the time of the visit (table 6). Patients with exclusively positive symptoms were hospitalized more than patients with negative symptoms the last year (33% vs 15%). Further, they differ in that they come to the psychiatrist due to worsening of the disease in a greater proportion than those who have negative symptoms, the majority of whom generally come for a routine visit. Finally, patients with positive symptoms were diagnosed of paranoid schizophrenia more (89% vs 57%) and less of residual, simple or undifferentiated schizophrenia than patients with negative symptoms.

DISCUSSION

The ACEE shows that the patient seen for schizophrenia in the Spanish psychiatric consultations is mostly male, single, living without work in a family setting, seen at the onset of the disease in the public or private sector and makes a progressively greater use of complementary public and therapeutic services as the disease advances; with comorbidity with sleep, affective and anxiety disorders, has clinical characteristics with «negative» symptoms more frequently than the «positive», always receives drug treatment and, in 55%, concomitant non-drug treatments.

Table 6 Differences between patients with positive symptoms and negative symptoms ($p < 0.05$)

	Patients with exclusively positive symptoms (n = 164)	Patients with exclusively negative symptoms (n = 634)
Age (mean ± SD)	36.2 ± 10.9	38.3 ± 10.8
Clinical history data		
Patients hospitalized in last year	55 (33.5%)	96 (15.2%)
Cause of coming to psychiatry		
Patient who is diagnosed of schizophrenia for the first time	9 (5.6%)	5 (0.8%)
Deterioration	37 (23.1%)	2 (0.3%)
Patient with previous diagnosis of schizophrenia who comes to routine visit	107 (66.9%)	597 (94.6%)
Time greater than 5 year since diagnosis	120 (73.2%)	493 (78.0%)
Subtype of schizophrenia		
Paranoid	141 (85.9%)	361 (57.4%)
Residual	6 (3.7%)	133 (21.1%)
Simple	2 (1.2%)	39 (6.2%)
Undifferentiated	5 (3.0%)	51 (8.11%)

It is very difficult to incorporate research results into the clinical practice in all the medical specialities, but especially in psychiatry. Are the data provided by epidemiological, clinical studies and controlled trials sufficient to modify patient care?[11] If the answer is yes, why aren't they incorporated into the daily clinical practice?[12]. Epidemiological data offer the first example. The sociodemographic profile of patients diagnosed of schizophrenia presently under treatment in Spain, as occurs with many clinical studies, differs from the epidemiological values of the studies in the general population that speak of a similar male/female rate. There are no fixed enrolment criteria in the ACEE on the contrary to clinical studies with drug treatment, in which some elements such as possible pregnancies may advise against the enrolment of female patients.

Evidence based medicine, impeccable formulation which in essence only applies what should be criteria of strict scientific rationality, is hindered by quite a few difficulties: the studies have different methods, there are serious problems to evaluate, for example, psychosocial treatments[13]. The variety of symptoms manifested in different functional areas constitutes a significant clinical problem. Increase of guides and protocols also do not appear to be accompanied by real modifications in the clinical practice. The slowness of its elaboration processes does not seem to provide sufficient explanation. It is necessary to establish the agreement existing between the real practice and the guides or existing consensuses based on this evidence based medicine and see if there are minimum standards of quality in all the care of patients with serious and chronic mental disorders such as schizophrenia[14]. Only in this way would it be possible to elaborate programs aimed at modifying the practice in those points in which this agreement is less or in which there are a greater number of scientific proofs whose translation to the daily clinical practice is not incorporated by the specialists.

The Patient Outcomes Research Team (PORT) project in the United States[15,16] for the treatment of schizophrenia was followed-up in a sample of 700 patients to determine the grade in which their treatment adapted to the criteria recommended by the consensus. The level of practical agreement with the recommendations was low or very low in almost all of them. Agreement was somewhat higher in the aspects of drug treatment than in psychosocial treatments, and in the rural areas compared with the urban ones. PORT is, as far as we know, the only study of these characteristics. Its review[17] seven years later affirms the need for more stu-

dies on the etiopathogeny of the associated neurocognitive deficits, of treatments aimed more specifically at the functional alterations and of making treatments with proven scientific criteria available to the patients, most of whom do not usually have access. One of the last consensuses that has appeared[18] has previously taken into account the large majority of similar guides published and has concluded that both early detection and comprehensive treatment of the first episodes as well as continued care during the 3 to 5 years of evolution of the disease are a priority. The Australian-New Zealand consensus considers that psychosocial interventions should be available for all the patients from the first moment and that prevention of physical complications in the schizophrenic patients is another priority in which the participation of the primary health care physicians is fundamental. The most recent up-date of the Texas Proejct[19] affirms that only a small part of the research makes it possible to respond to the large questions posed by the sequence and type of drug treatment used in schizophrenia.

In the ACEE, we observe more patients in the initial phases of the disease who are treated in the private sector while the opposite occurs as the disease course time passes. The data indicate that there is a progressive transfer of patients from the private care sector to the public one as the disease becomes chronic. The public sector in Spain has almost all the community health care services existing in the country.

In regards to treatment, deinstitutionalization makes it necessary to develop new care systems to accommodate care to the schizophrenic patients with the growing complexity of community treatment[19-21]. Explicit determinations of the key components of the integrated treatment are needed to make them accessible to patients and family members. Finally, studies on care quality should reflect the care offered to mental patient and the relationship between use of these services and characteristics or phases or subtypes of the disease. The ACEE project has obvious limitations: only psychiatrists willing to collaborate in a study of these characteristics participated, even though the time from the diagnosis did not use standardized instruments to typify the disease nor evaluation scales and the care facilities existing in a certain area or regional community may condition a good part of the daily clinical practice, especially that referring to treatments and complementary support services, that are so important in certain phases of a disease such as schizophrenia.

To try to resolve the controversies in the diagnosis and treatment of schizophrenia, these works must be stressed, extending them in time and implementing systems for quality control of the care given to persons suffering this disease. Research should be aimed at the symptoms, deterioration, care systems and drug and non-drug treatments[22,23]. In the future, it should be evaluated up to what point the recommendations, guides and protocols existing in all the countries, obviously also in Spain, adapt to the real practice and they are going to change or not at the rhythm of the advances in the psychiatric research.

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