Initial medical work-up in first-episode psychosis

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Purpose of the study: In recent years there were growing research regarding interventions in first-episode psychosis and patients with high risk for psychosis. Consequences are building of early intervention teams and hoped best care to psychotic patients on early phases. There are published guidelines regarding mainly treatment but few about diagnosis and medical work-up in first-episode psychosis. There are no single approach to medical work-up in first-episode psychosis but clinicians who diagnosis and treat first-episode psychosis patients should reflect on what kind of medical investigation should do. Once the diagnosis of psychotic illness, like schizophrenia, implicates absence of a medical condition that could account for the clinical picture a medical work-up is important to the diagnosis. The diagnosis of psychotic disorder also implies the subsequent treatment with antipsychotic medication and initial work-up has also the aim to ensure the safety in its use. Initial medical evaluation also make a baseline to allow monitoring of iatrogenic morbidity (metabolic problems and movement disorders). Hospital Vila Franca de Xira is a general hospital in the metropolitan area of Lisbon, Portugal, which provides medical care to a population of 245.000 persons. Department of Psychiatry is new in the hospital which begin its activity in April 2013.

Methods: A retrospective study of non-affective first-episode psychosis patients admitted to the Department of Psychiatry of Hospital Vila Franca de Xira between April 2013 and March 2015. Electronic files of each patient were analyzed and initial medical work-up studied. All medical studies including blood tests, toxicology screen, neuro-imaging and electrophysiological exams made were registered. Data were analyzed using IBM SPSS (Statistical Package for the Social Sciences) Statistics software version 21.

Table 1. Demographic and clinical characteristics of participants

Gender	
Male % (n)	33.3 (10)
Female % (n)	66.6 (20)
Mean age (years) (SD)	29.8 (9.2)
DUP (days) (SD)	520.7 (790.13)
Married % (n)	16.7 (5)
Employed %(n)	30 (9)
Students % (n)	20 (6)
Psychiatric Family History	53.3 (16)
Diagnosis % (n)	
Schizophrenia/schizophreniform disorder	20 (6)
Other Specified Schizophrenia Spectrum and Other Psychotic disorder	33.3 (10)
Brief psychotic disorder	3.3 (1)
Delusional disorder	3.3 (1)
Cannabis induced psychotic disorder	30 (9)
In-stay % (n)	70 (21)
Treatment % (n)	
First-generation antipsychotics	
Haloperidol	3.3 (1)
Zuclopentixole depot	3.3 (1)
Second-generation antipsychotics	
Risperidone	36.7 (11)
Paliperidone	6.7 (2)
Olanzapine	23.3 (7)
Aripiprazole	6.7 (2)
Risperidone long acting injectable	3.3 (1)
Paliperidone palmitate injectable	10 (3)

Table 2. Laboratory tests included on the initial medical work-up of the participants

Laboratory Tests (Units)	Number of patients performed N	Results	Normal Range
		Mean (SD)	
Haemoglobin (g/dL)	30	14.31 (1.38)	13.6-18.0
Haematocrit (%)	30	42.52 (4.54)	39.8-52.0
Leukocytes (10^3 /µL)	30	7.89 (2.72)	4.0-10.0
Platelets (10^3 /µL)	30	249.58 (77.32)	140-440
Glucose (mg/dl)	30	88,03 (11.36)	70-110
AST (UI/L)	30	25,11 (19.02)	10-41
ALT (UI/L)	30	36.65 (28.29)	24-54
GGT (UI/L)	30	49.58 (91.96)	5-55
BUN (mg/dl)	30	30 (11.45)	19.3-44.9
Creatinine (mg/dl)	30	0.89 (0.18)	0.70-1.30
Sodium (mmol/L)	30	139.58 (2.27)	136-146
Potassium (mmol/L)	30	4.22 (0.43)	3,5-5
Chloride (mmol/L)	30	103.44 (2.84)	95-108
Total Cholesterol (mg/dl)	18	164.88 (35.52)	<190
HDL (mg/dl)	18	47.64 (17.28)	28-72
LDL (mg/dl)	18	98.5 (33.65)	<115
Triglycerides (mg/dl)	18	86.35 (48.32)	32-134
Acid Folic (ng/mL)	16	4.76 (2.80)	3.0-17.0
Vitamin B12 (pg/mL)	16	391.55 (166.21)	193.0-982.0
Thyroid Stimulating Hormone (mUI/L)	23	1.47 (0.67)	0.35-5.5
Free T4 (ng/dL)	23	1.18 (0.18)	0.80-1.76
HIV test	18	All negative	
Syphilis test	20	All negative	
Hepatitis B	11	All negative	
Hepatitis C	15	All negative	
Toxicology screening			
Cannabis	15	Positive in 6 patients	
Cocaine	15	Positive in 1 patient	
Amphetamine/Methamfetamine	15	All negative	
Opiates	15	All negative	

Results: Thirty patients diagnosed by their Psychiatrists as first-episode psychosis were included. Demographic and clinical characteristics are mentioned in table 1. All patients had at least some laboratory tests, 15 patients made toxicological screening test, 23 cranial computed tomography (CT scan), 2 head magnetic resonance imaging (MRI) and 1 electroencephalogram (EEG). Between laboratory tests, complete blood count (CBC), fasting blood glucose, electrolytes, renal function tests (BUN/creatinine) and liver function tests were made in all patients. Twenty-three patients underwent thyroid function tests, 18 lipid profile, 20 test for syphilis, 18 HIV test, 15 hepatitis C test and 11 hepatitis B test. Sixteen patients had vitamin B12 and acid folic dosing. None of the female patients made a pregnancy test. Mean an standard deviation (SD) from laboratory tests are mentioned in table 2. Regarding the results none of the patients had abnormalities in CBC, electrolytes or renal function tests. One patient had abnormalities in fasting glucose (132 mg/dL). Four patients had elevated AST (mean: 62 UI/L; SD: 25.44), 2 patients elevated ALT (mean: 123.5 UI/L; SD: 21.92) and 1 patient abnormal GGT (403 UI/L). Acid folic level was below normal range in 6 patients (mean: 2.1 ng/mL; SD: 0.58) and vitamin B12 in 4 patients (mean: 245 pg/mL; SD: 18.65). Total cholesterol abnormalities were found in 6 patients (mean: 208.17 mg/dL; SD: 10.44) and triglycerides in 3 patients (mean: 179 mg/dL; SD: 21.93). Six patients had positive toxicological screening for cannabis and 1 for cocaine. In neuroimaging cranial TC was done in 23 of the 30 patients studied. Nine patients revealed abnormalities: 1 patient ventricular asymmetry; 1 plagiocephaly; 2 frontal sulci accentuation; 2 parietal sulci accentuation; 1 calcification of cerebral sickle; 1 probable arachnoid granulation and 1 enlargement of perivascular interstitial just-atrial space. Of the 30 patients 2 made a head MRI to clarify some doubts in cranial CT but results did not reveal significant abnormalities. One patient made an EEG which was in normal range.

Discussion: Initial medical work-up in patients with first-episode psychosis has two main aims: 1)Exclude medical treatable disorders that could be responsible for psychotic symptoms; 2)Establishing the presence of relevant medical comorbidities (particularly important in patients who are in the beginning of psychopharmacological treatment). A problem is the differentiation between comorbidity and causality that exists in psychotic disorders. Even if a disorders/disease is discovered it is not linear that it is aetiologically relevant. Even when comorbidity is in question, it is important to diagnose it. Usually it has a negative impact in disorder. Our results illustrates that there is no consensus regarding medical work-up in first-episode psychosis. In the sample studied no organic cause was found for the psychotic disorder but some abnormalities exist. The main abnormality found were changes in lipid profile, namely in total cholesterol and triglycerides, which has impact on the antipsychotic medication chosen. In some patients the dosing of acid folic and vitamin B12 was below normal range but the exact meaning of this finding to the first-episode psychosis is quite difficult to determine precisely. However all of these patients received supplementation. Psychotic patients are considered high risk patients to infectious diseases but none of the patients in our sample had some of these analyses positive (HIV, syphilis and hepatitis B and C). We also found some abnormalities in cranial CT however none of the findings was attributed a causal link with psychotic disorder. Regarding neuroimaging 77% patients made an exam. In our sample the cranial CT was the neuroimaging technical elect for the majority of the patients. As our results reflect, majority of first-episode psychosis patients will not have identifiable disorders by neuroimaging with etiological relevance. We also agree with other authors that even a negative scan is important establishing the "functional" character of the disorder and can help patients and their families towards acceptance of a psychiatric disorder. Only in 50% (n=15) of the first-episode psychosis patients toxicology screening was done, which is quite low considering high rates of cannabis use in this population. Seven (>50%) patients of these had positive results for cannabis or cocaine. The low specificity of EEG and the medication-induced EEG changes are problems which is not advice to consider it to all first-episode psychosis patients. In our view EEG should be ordered only in patients where seizures are suspected (e.g.: history suggestive of seizures or ictal events, past head injury etc.) or suspicion of narcolepsy.

Conclusions: There is no optimal work-up in first-episode psychosis, it should be individualized regarding medical history and clinical picture. However general guidelines regarding tests in first-episode psychosis could help to standardize the evaluation of these patients. In our sample of first-episode psychosis patients no medical causes for psychosis were found, but abnormalities in laboratory findings affected the choice of psychopharmacological treatment. Table 3 shows our proposal for medical work-up in first-episode psychosis. Finally table 4 summarizes main current guidelines.

Table 3. Medical work-up in first-episode psychosis

Physical Exam (including neurological exam)
Vital signs
Weight, height, BMI, waist circumference
ECG (if cardiac risk)

Laboratory tests
Complete blood count
Renal function tests
Liver function tests
Electrolytes
Fasting glucose
Lipid profile
TSH, fT4
Syphilis serology
HIV test
Vitamin B12

Neuroimaging
Magnetic resonance imaging (prefered over CT)

Considered if indicated by clinical picture
Electroencephalogram (EEG)
Heavy metal testing
Chest X-ray
Lumbar puncture

Table 4. Some current guidelines regarding work-up in first-episode psychosis

	NICE 2013 UK	Australian and New Zealand clinical practice guidelines 2005 Australia and New Zealand	Canadian Psychiatric Association, 2005 Canada	American Psychiatric Association, 2004 USA
Physical Exam	Medical history and full physical examination, weight, waist circumference, pulse, blood pressure	Physical exam including neurological exam, weight and height/body mass index	Physical exam including neurological exam, vital signs, body mass index, waist circumference	Physical exam including neurological exam, vital signs, weight and height/body mass index
Laboratory tests	Fasting blood glucose, glycosylated hemoglobin (HbA1c), blood lipid profile and prolactin levels ECG if indicated	Fasting glucose (and/or HbA1c), lipid profile, toxicology screen	Complete blood count, electrolytes, renal and liver function tests Thyroid function tests Syphilis test Hepatitis tests, if indicated HIV test, if indicated Toxicology screen	Complete blood count, electrolytes, BUN/creatinine, liver function tests Thyroid function tests Pregnancy test (women of child-bearing age) Syphilis test Hepatitis C if indicated HIV, if indicated Toxicology screen Heavy metal screen if indicated
Neuroimaging (NICE, 2008)	CT or MRI not recommended as a routine part of the initial investigations; only performed if indicated by clinical picture	MRI	CT or MRI	CT or MRI if indicated
Neurophysiology/Neurocognitive assessment		Neurocognitive assessment		Electroencephalogram if indicated
Medical monitoring	Follow-up overall physical health Weight and waist circumference Pulse and blood pressure Fasting blood glucose, HbA1c and lipid profile	Full physical check-ups, including weight, blood pressure, lipid profile, ECG, and fasting blood glucose	Fasting glucose, lipid profile ECG Prolactin level if clinically indicated Evaluate for potential extrapyramidal symptoms Ocular evaluation	Fasting glucose, lipid profile ECG if indicated Prolactin level if indicated Evaluate for potential extrapyramidal symptoms Ocular evaluation if indicated

Adaptated from Freudenreich, O *et al*., 2009

Disclosure
No potencial conflict of interest

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