THE CARDIOTOXIC EFFECTS OF PSYCHOTROPIC MEDICATION

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ABSTRACT

It has long since been recognized that the use of certain psychotropic drugs such as neuroleptics, antipsychotics, antidepressants and anxiolytics, is associated with a risk of cardiac arrhythmias and sudden death. In addition, antiepileptics and drugs used for kinetic disorders can also have cardiotoxic effects on some patients (pimozide for example). Sudden cardiac death is generally defined as an unexplained cardiac arrest, which

usually occurs as a result of a cardiac arrhythmia, which can occur within an hour of the symptoms' onset

Key words: antipsychotic drugs, cardiovascular accident, tachyarrhythmias, arrhythmia, antipsychotics.

INTRODUTION

We should pay particular attention to the patient's comorbidities, especially to the ischemic heart disease and to hypertension, in patients receiving agents with multiple targets; these comorbidities need to be carefully monitored and controlled before and during the treatment (Haddad et al 2004, Wallace et al 2001, Ghadirian et al 1982, Wirshing et al 2002, Alviret, 1993, Hold et al 1999).

The identification of the uncertainty zones, associated with the diversity of the patients from the clinical trials also merits special attention, as well as the perspectives' limitation regarding the long-term survival data and the therapeutic and monitoring strategies (Holmberg et al 2002, Huie et al 1994, Hurly et al 1984, Ishak et al 1984, Johansson et al 2000).

The use of multiple target agents – conversion inhibitors for example– induces a cardiac dysfunction that remits itself, in time (Johnson et al 1972, Jorge-Riviera et al 2000, Markuja et al 2007).

Patients who recover from coma often have hallucinations, delusions, disordered movements of the extremities and dysarthria. EKG is sometimes suggestive appearance (Mark et al 2005, Martikainen et al 1986).

Sinus tachycardia is usually present. In severe cases, increase the PR interval and QRS duration (Martinez et al 2002).

In patients with severe poisoning and bradycardia ventricular arrhythmias occur, especially in those with hypoxia. Death occurs by cardiorespiratory depression and severe acidosis (Soares et al 2003, Tammenman et al 2002).

Treatment consists in freeing the airways, providing ventilation and supportive therapy. Supervision and continuous observation is necessary because the condition can quickly worsen (Kleinberg et al 2007).

MATERIALS AND METHODS

We examined 40 patients with psychiatric issues, two group selected, clinically suspected of having coronary disease, that were scheduled for coronary angiographies in the interventional cardiology department of Oradea's Clinical County Hospital.

They were monitored for 24 months, during which several suicide attempts were registered. All patients that were analyzed in the studio had their weight and height measured, as well as their body mass index (BMI), systolic and diastolic blood pressure, heart rate and they also had electrocardiographies performed on them.

Lab analyses were performed, which determined the levels of the total cholesterol, triglycerides (TG), high density lipoproteins (HDL), low density lipoproteins (LDL), uric acid (UA) and glycosylated hemoglobin (hemoglobinA1c). All study patients had their GIM, carotid-femoral PWV and ABI measured.

Univariate analysis was used to describe the variables using frequency tables and simple percentage values for discrete variables and average (minimummaximum), and graphical representation by plotting histograms and box type plotters for continuous variables. Bivariate analysis was used for discrete variables using contingency tables and chi square test. Student test (t test), with or without the Mann-Whitney test were used for continuous variables.

RESULTS AND DISCUSSIONS

The treatment of the cardiac dysfunction induced by them justifies the aggressive intervention with the standard utilized methods in the treatment of

other types of HF; the observation period of asymptomatic patients can include the evaluation of the systolic function, 6 months after the beginning of the treatment, annually thereafter, and then every 1-2 years, for life. Any CV events occurring during the observation period justify a stricter monitoring.

The medication study	Asymptomatic decrease in LVEF (≥5% 40%)	Severe CHF /death event
quetiapine vs fluoxetine	12,5%-7,8%	1.2%-0,15%
Quetiapine+trazodone- vs- quetiapine+fluoxetine	15,3%-11,1%	0,45%-3,21%

Table 1 The cardiotoxicity induced the psychotropic medication



Fig. 1 The average age of patients in the 2 groups



Fig. 2. The average age of female and male patients in the 2 groups



Fig. 3. Reason for hospitalization of patients in the 2 groups

The figure above shows the frequency of administration of psychotropic drugs and antiarrhythmic drugs used by the population sample.

The use of isolated or in the form of drug combinations. None of the patients in the study did not use digitalis.

CONCLUSIONS

Seven deaths were recorded as a result of self-medication with overdoses of tricyclic antidepressant drugs. Death occurred due to the cardiac electromechanical dissociation, as a result of overdosing on trimipramines or amitriptyline; the overdose was confirmed by the toxicological analysis, during the Tricyclic antidepressants treatment determine insulin resistance and increase the plasmatic lipid levels, irrespective of the effect on the body weight. At the same time, the treatment with antidepressants such as amitriptyline or doxepin significantly determines the increase of the body weight and this effect is mainly responsible for the non- compliance to the treatment.

REFERENCES

1. Hold, K. M., Borges, C. R., Wilkins, D. G., 1999, Detection of nandrolone, testosterone, and their esters in rat and human hair samples, J. Anal Toxicol, 23(6):416-23.

2. Holmberg, L., and Berg-Kelly, K., 2002, Health, health-compromising behaviour, sexuality and involvementin pregnancy among 18 year- old Swedish males: a cross-sectional survey, ActaPaediatr, 91(7):838-43.

3. Huie, M. J., 1994, An acute myocardial infarction occurring in an anabolic steroid user, Med Sci Sports Exerc, 26(4):408-13.

4. Hurley, B. F., Seals, D. R., Hagberg, J. M., 1984, High- densitylipoprotein cholesterol in bodybuilders v powerlifters. Negative effects of androgen use. JAMA, 252(4):507-13.

5. Ishak, K. G., Zimmerman, H. J., 1987, Hepatotoxic effects of the anabolic/androgenic steroids, Semin Liver Dis, 7(3):230-6.

6. Johansson, P., Hallberg, M., Kindlundh, A., 2000, The effect on opioid peptides in the rat brain, after chronic treatment with the anabolic androgenic steroid, nandrolone decanoat, Brain Res Bull, 51(5):413-8.

7. Johnson, F. L., Lerner, K. G., Siegel, M., 1972, Association of androgenicanabolicSteroid therapy with development of hepatocellular carcinoma, Lancet, 2(7790):1273-6.

8. Jorge-Rivera, J. C., McIntyre, K. L., Henderson, L. P., 2000, Anabolic steroids induce region- and subunit-specific rapid modulation ofGABA(A) receptor-mediated currents in the rat forebrain, J Neurophysiol, 83(6):3299-309.

9. Makhija, N. J., 2007, Childhood abuse and adolescent suicidality: a direct link and an indirect link through alcohol and substance misuse, Int J Adolesc Med Health, 19(1):45-51.

10. Mark, P. B., Watkins, S., and Dargie, H. J., 2005, Cardiomyopathy induced by performance enhancing drugs in a competitive bodybuilder, Heart, 91(7):888.

11. Martikainen, H., Alen, M., Rahkila, P., 1986, Testicular responsiveness to human chorionic gonadotrophin during transient hypogonadotrophic hypogonadism induced by androgenic/anabolic steroids in power athletes, J. Steroid Biochem, 25(1):109-12.

12. Martinez-Sanchis, S., Aragon, C. M., Salvador, A. 2002, Cocaineinduced Locomotor activity is enhanced by exogenous testosterone, PhysiolBehav 76(4-5)

13. Soares-Weiser KV, Joy C., 2003, Miscellaneous treatments for neuroleptic- induced tardive dyskinesia. Cochrane Database Syst Rev.; (2):CD000208.

14. Tammenmaa IA, McGrath JJ, Sailas E, Soares-Weiser K., 2002, Cholinergic medication for neuroleptic-induced tardive dyskinesia. Cochrane Database Syst Rev.; (3):CD000207.

15. Kleinberg DL, Davis JM, de Coster R, Van Baelen B, Brecher M., 1999, Prolactin levels and adverse events in patients treated with risperidone. J Clin Psychopharmacol; 19(1):57–61.

16. Howard L, Kirkwood G, Leese M., 2007, Risk of hip fracture in patients with a history of schizophrenia. Br J Psychiatry; 190:129–134.

17. Haddad PM, Wieck A., 2004, Antipsychotic-induced hyperprolactinaemia. Drugs; 64(20):2291–2314.

18. Wallace M., 2001, Real progress—the patient's perspective. Int Clin Psychopharmacol; 16(suppl 1):S21–S24.

19 Ghadirian AM, Chouinard G, Annable L., 1982, Sexual dysfunction and plasma prolactin levels in neuroleptic-treated schizophrenic outpatients. J Nerv Ment Dis. 1982;170(8):463–467.

20 Wirshing DA, Pierre JM, Marder SR, Saunders CS, Wirshing WC., 2002, Sexual side effects of novel antipsychotic medications. Schizophr Res.; 56(1–2):25–30.

21. Alvir JM, Lieberman JA, Safferman AZ, Schwimmer JL, Schaaf JA., 1993, Clozapine-induced agranulocytosis, Incidence and risk factors in the United States. N Engl J Med.; 329(3):162–167.