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Case Report

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Severe intoxication by psychotropic drugs; syndrome serotoninergic

Summary

Among the intoxications by psychotropic drugs we have the serotoninergic syndrome (SS) which is an adverse pharmacological reaction of lethal character being of therapeutic use, intentional overdose, interactions of involuntary form because of drugs with activity on the serotonin receptors, this leads as a consequence a clinical picture of mild to fatal consequences including alteration of the mental state, overactivity of the autonomic nervous system, neuromuscular hyperreactivity, its diagnosis is directed in the essential clinical history, taking drugs and knowing the possible pharmacological interactions, in addition to the physical examination, support of laboratory tests and images, since this will affect its prognosis, its treatment is directed to life support measures, accompanied by pharmacological antagonists. Next, we present a case of a patient with a history of major depression, anxiety polymedicated with flouxetine, quetiapine, alprazolam, carbamazepine, causing toxicity induced by drugs that stimulated the 5-hydroxytryptimine receptors which produce affectation of the mental state, increase of the autonomic activity, neuromuscular alteration.

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Introduction

It is determined that serotonin is a neurotransmitter derived from tryptophan that has an excitatory and inhibitory function, acting on mood, eating behavior, sleep-wake cycle, temperature, gastrointestinal motility, and vascular tone.[1] The serotoninergic syndrome or overstimulation of 5-hydroxytryptamine receptors (5-HT) is characterized by a group of neuromuscular clinical manifestations, with affectation of the mental state, autonomic hyperactivity caused by serotonin toxicity induced by drugs that cause an excess of serotoninergic neuronal activity in the central nervous system with change in the peripheral serotonin receptors, this is generated in the post synaptic neuron. In turn, it can occur when sympathomimetic drugs are combined with MAOIs. The incidence of this syndrome is inaccurate since its diagnosis is clinical, it should be suspected in the evaluation of the clinical history and there are no laboratory tests that support its diagnosis. It is worth noting that experts in the field of toxicology have pushed for the use of the term serotonin toxicity (ST) or serotonergic toxicity in an attempt to abandon the inaccurate use of the term SS.[2-4] Andersen and Christiansen in 1959 observed the first cases following abrupt discontinuation of drugs associated with withdrawal symptoms treated with antidepressant drugs.[5,6]

Three hypotheses of toxicity states are determined, mild, total and toxic, which will depend on whether a single drug or several drugs are involved, as well as the combinations, the adverse events caused by serotonergic drugs caused by increased intrasynaptic concentrations of 5-HT derived from tryptophan which are found in the digestive tract, platelets and central nervous system, also the atypical antipsychotic agents that can mitigate the toxicity of 5-HT, platelets and central nervous system, also the atypical antipsychotic agents that can mitigate the toxicity of 5-HT, it should be known that the metabolism of 25 serotonergic drugs are produced in the cytochrome P-450, being 50% related to pharmacological interactions related to cytochrome P-450 inhibitors leading to the elevation of the drug concentration.[7]

Case description

26-year-old male patient with personal history: major depression and anxiety diagnosed 1 year ago treated with fluoxetine, quetiapine, alprazolam and carbamazepine, the last one added 10 days before admission. The patient presented with a clinical picture 17 hours after administration of usual medication characterized by neuromuscular changes including: hyperreflexia, rigidity of upper and lower limbs with deviation of the gaze and mydriasis, for which she went to the clinic where she presented a single episode of vomiting with bilious content, and deterioration of Glasgow 8/15, proceeding to orointubation. In this sense, the patient was received under sedoanalgesia, RASS -4, reactive mydriatic pupils, positive patellar reflexes, coupled to invasive mechanical ventilation, without vasopressor support, vital signs 126/86 mmHG, heart rate 68. The admission laboratory (hepatogram, blood glucose, coagulogram, ionogram with magnesium, calcium, phosphorus, sodium, potassium, chloride, creatine phosphokinase, erythrocyte sedimentation rate, azotemia, arterial gases and urinary sediment) did not show any abnormality, except for a leukocytosis with predominant lymphocytopenia.

Evolution

Male patient was admitted for deterioration of sensorium and signs of neuromuscular hyperactivity, due to the alteration of the hemogram, lumbar puncture was requested with normal cytochemistry, viral panel and negative culture; as well as two blood cultures, urine culture that reacted negatively. Imaging studies included a brain computed axial tomography (CT) and simple magnetic resonance imaging (MRI) which showed no lesions. In addition, toxicology for 5 psychotropic drugs was negative (marijuana, cocaine, methamphetamine, opium, MDMA). During the hospital stay, the patient presented with a single isolated febrile illness, treated with antipyretic, active cooling. Carbamazepine and quetipine were suspended. Based on the clinical picture and the pathological history, a diagnosis of serotonin

syndrome was made. Thanks to the management instituted, the patient showed improvement characterized by recovery of alertness, reversal of hyperadrenergic manifestations and correction of laboratory alterations, which made possible his extubation and discharge from the intensive care unit.

Discussion

Serotonergic syndrome is a potentially fatal pathology due to a pharmacological reaction by the combination of a serotonergic agent and an antidepressant selective serotonin uptake inhibitor (SSRI), is attributed as a clinical situation characterized by a classic triad of autonomic hyperactivity, neuromuscular abnormalities and alterations in mental status, but may have variable symptoms of the autonomic nervous system such as tachycardia, diarrhea, chills, hyperthermia, myoclonias, neuromuscular alterations, hyperreflexia, tremors, muscle rigidity, and in severe cases from psychomotor agitation, hypotonia, delirium, convulsions, clunus, bilateral Babinsky's signs, shock, coma and death. alteration of the sensorium with lethal behavior, in addition to severe conditions, hyperthermia that can reach more than 40 degrees Celsius.[7,8] This syndrome occurs mainly due to the administration of monoamine oxidase inhibitors such as tramadol in combination with SSRIs. Serotonergic activation in the central and peripheral nervous system is characterized by autonomic and neuromuscular mental dysfunctions and the 5'HT (hydroxytryptamine) receptors would be responsible for the symptomatology, besides serotonergic drugs are metabolized by cytochrome P 450 enzymes, therefore an alteration in these enzymes decreases the metabolism to some drugs and could have a tendency to the development of S.S.[9,10] In this pathology the diagnostic criteria could be determined by the presence of at least three of the ten clinical features such as agitation, tremor, mental status changes such as confusion, hypotonia, myoclonus, fever, hyporeflexia, diarrhea, diaphoresis.[6,10] Its recognition is directed to clinical perception, since the supporting diagnostic methods such as clinical laboratory and images do not provide definitive support, it is supported with parameters of clinical criteria of toxicity such as Sternbach, Hunter and Radomski, among these the Hunter criterion with a sensitivity of 84% and specificity of 97%. There are no diagnostic tests for this syndrome, but nevertheless, hemogram, electrolytes, liver enzymes, renal profile, toxicological analysis, uro analysis, creatine phosphokinase and lumbar puncture should be included for its initial evaluation, if there is alteration, the severity associated to organic failure could be determined.[2,11] In the case of renal failure, its etiology is due to drugs such as antidepressants, narcotic agents, antibiotics (linezolid), triptans (anti-migranous), antitussives, dietary supplements and analgesics.[13] Taylor et al. in a retrospective evaluation at the Mayo Clinic showed an incidence of 3% in patients taking ISRA and linezolid.[14] Grenha et al. and among the antidepressant drugs most associated with serotonergic syndrome are fluoxetine, paroxitone, fluxoxoxacin, which may be due to intentional or accidental intoxication.[15] The combination of analgesic such as fentanyl opioid used in postoperative patients including those of cardiac surgery that between 5 to 25% may present vasoplegia are also included, Katzianer et al, Schumacher et al, present cases associated to sertarlin, escitalopram, in combination with fentanyl, and methylene blue.[16] Pedavally et al.[17] determined that in a group of patients admitted to intensive care, 33% developed serotonin syndrome when they received antidepressants, opiates (fentanyl) including antiemetics. This is related to our patient who ingested an antidepressant in combination with an anticonvulsant. It is necessary to take into account differential diagnoses such as malignant hyperthermia, meningitis, autoimmune encephalitis, toxicity of anticholinergic drugs.

In relation to its management as a fundamental part clinical suspicion, then identify and suspend the drugs causing serotonin syndrome, fundamental to the stabilization of vital signs, the basis of treatment will depend on the severity, in mild cases with the discontinuation of the drug will be sufficient, in moderate cases, assessment and treatment directed hemodynamics and aggregation of serotonin antagonists including cryptoheptadine is estimated, the percentage of patients with mild SS 70% recover completely 24 hours after discontinuation of the drug, 40% will require admission to intensive care and about 25% require intubation with assisted mechanical ventilation, Chima et al.,[18] presented a case of vasospasm caused by serotonin antagonist (sumatriptan) which was reversed with cryptoheptadine. In the most severe cases it is a true emergency that adds complications such as severe hyperthermia, disseminated vascular coagulation, rhabdomyolysis, respiratory distress syndrome, requiring mechanical ventilation, sedation and intensive care, agitation should be restricted in agitated patients as these may cause lactic acidosis, the first line of sedation are benzodiazepines as they control agitation and hyperadregernic state. It also helps to reduce the temperature due to the reduction of muscle contraction and autonomic hyperactivity. As mentioned the incorporation of the serotonin antidote (cycloheptadine) at doses of 12 mg at the beginning, then 2 mg every 2 hours until clinical improvement and an alternative maintenance dose of 8 mg every 6 hours.[18-20]

Conclusion

In emphasizing this syndrome, it should be made clear that health personnel must take into account the range of pharmacological interactions and identify potentially lethal drugs, determine the use of drugs or drugs with serotonergic action, early assessment of neurological findings, autonomic and neuromuscular hyperactivity, determining that this disorder can be life-threatening and thus support and treatment should be given promptly.

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None.

Conflicts of interest

Authors declare that there is no conflicts of interest.

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