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Case Report

Drug Intoxication with Colchicine in Successful Suicide Act

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Abstract

Male 30 years old made a suicide act and took 50-tab colchicine of 1 mg each, 14-tab Lonarid-N of 400 mg paracetamol/10 mg codeine/50 mg caffeine, 6-tab Algofren/ibuprofen of 400 mg and 10-tab of paracetamol of 500 mg each. His medical history has lack of G6PD, smoker p/10 year. Those tablets were taken 24 hours before he came to the hospital. He came to the hospital because of vomiting and continuous diarrhea. He entered into the internal medicine department for five hours and while his situation was not getting better, entered in the ICU department. He was supporting with all the technical-mechanical and pharmacological means but the patient died after being 27 hours in the ICU.

Keywords: *Drug Intoxication; Colchicine; Suicide Act*

Introduction

Colchicine is an alkaloid extracted from autumnal Colchicum plant and it is use for prevention of gout, familial Mediterranean fever and in increased Uric Acid. It is absorbed with oral administration usually and it is widely distributed to intracellular elements, primarily metabolized by liver especially enterohepatic re-circulation and excreted by the kidneys.

Case Report

Male 30 years old came in the emergency department because of vomiting and diarrhea for 12 hours. His medical history has lack of G6PD, smoker p/10 year and a referring psychologic disorder with no official, through national electronic medical prescriptions, evidence. First vital sights in the emergency department from ECG: sinus tachycardia 144 pulse/min, BP: 100/80 mmHg Sat: 88% FiO_2: 21% T: 37,4 C from the first blood exams: WBC: 49400, Hb: 17,6, Plt: 226000, INR: 2,26, APTT: 55,5, Glu: 64, Ur: 40, Gr: 2,09, SGOT: 189, SGPT: 33, Alp: 339, CPK: 712, CPK-MB: 76, LDH: 3698, CRP: 10,38, total bilirubin: 0,4, indirect bilirubin: 0,4 chest X-ray: normal, upper abdominal echo: normal., ABGs: ph: 7,43, pCO_2: 33,3, pO_2: 57,8, K: 3,7, Na: 142, lac: 23, HCO_3: 23,4, cBase: -1,8. FiO_2 21%. The patient witnesses that, before 24 hours he took in order to suicide, 50-tab colchicine of 1 mg each, 14-tab Lonarid-N of 400 mg paracetamol/10 mg codeine/50 mg caffeine, 6-tab Algofren/ibuprofen of 400 mg and 10-tab of paracetamol of 500 mg each.

He entered in the department of the internal medicine, he supporting all his vital parameters and internal med on call, contacted with the National Intoxication Institute for further instructions of management, in order to indicate the proper antidot for the situation. The instructions were, that no antidot for the colchicine exists and for the paracetamol the antidot is NAC: N acetyl-L cysteine, which it should give the 1st dose 150 mg/kg the 1st hour, 50 mg/kg for the next 4 hours and 100 mg/kg for the next 16 hours as and it was given. Also, the

instructions were for no stomach lavage with nasogastric catheter. Echo of the upper abdominal was made with normal founding's from the liver, pancreas and kidneys was done.

For the next 4 hours the patient was with tachypnea, difficulty fluid management while the vomiting and the diarrhea continue with low urine output. The instructions for giving NAC to patient started in the department of the internal medicine. The patient entered in the ICU for close observation of his vital parameters. A new chest X-Ray was made (Figure 1), arterial catheter was placed for invasive measured of the blood pressure, central vein catheter for better fluid management, fluid balance. BP: 110/60 mmHg, 130 pulse/min, the next ABGs was: ph: 7,41, pCO_2: 33,7, pO_2: 65 FiO_2: 28% and from the blood exam, WBC: 45200, Hb: 17,5, Plt: 244000, PT: 23,9, INR: 2,01, APTT: 48,5, Glu: 85, Ur: 31, Cr: 1,45, SGOT: 151, SGPT: 27, Alp: 279, CPK: 560, CPK-MB: 63, LDH: 2678. His tachycardia remained so it starts b1-blocker in esmocard-lyo in dose 60 - 120 ml/h, gastroprotection, antibiotic protection of the first line (cefoxitin-wide range of antibiotics), his Glasgow Coma Scale is 15, his respiratory rate over 25 so he was put in mask Venturi 40%, as with the fluid management the blood pressure remain stable, his urine output increased and vomiting and diarrhea was reduced.

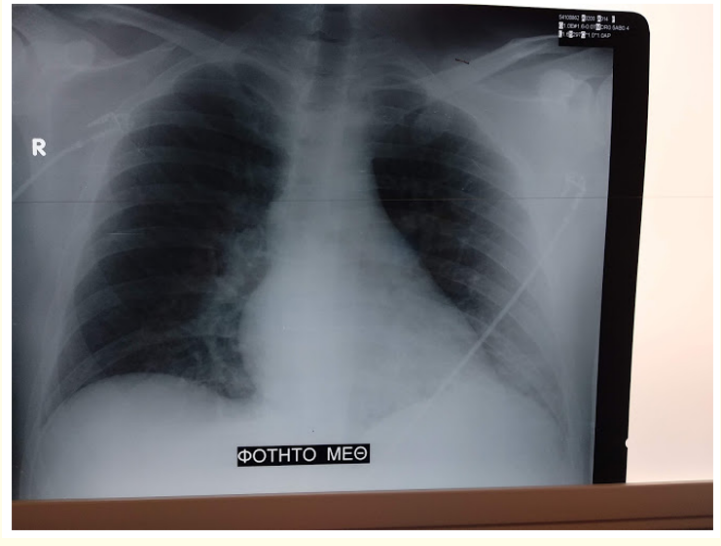

Figure 1: *In the ICU as the patient enters in the ICU with a small turn on the left. Reduce ventilation on the left down lobe.*

The next morning the ICU department made a new consulting, of the gastroenterology's hospital for further instructions or interpretations from a hepato-transplantation center for the pharmacology intoxication. No other interventions were consulted to be done and as the patient hat hemorrhage from the medical interventions and prolonged INR and APTT, he transfused with 6 fresh frozen plasma although the patient was with lack of G6PD and 2gr of tranexamic acid was also given. As the time passed the patient was hemodynamic unstable, a noradrenaline started as he also hats hallucinations. Intubation was decided (Figure 2), he was putted in mechanical ventilation- Volume control model 550 ml, peep: 5, rf: 14, FiO_2: 100% with O_2 fraction lower of 200, ABGs before intubation ph: 7,23, pCO_2: 50, pO_2: 55, Hb: 10.7, glu: 94, lac: 64, cBase: -6, HCO_3: 18,5 after intubation ABGs: 7,37, pCO_2: 22,4, pO_2: 88, glu: 82, lac: 47, Hb: 14.5, K^+: 4.4, Na^+: 140, cBase: -9.8, HCO_3: 17.7. Sedation with dexdor/dexmedetomidine at first was set, while the noradrenaline support was increased from 10 - 15 γ/kg/min to 25 - 35 γ/kg/min and still continued increasing. The fresh frozen plasma which was given hat no effective use. The hemodynamic status of the patient went worse hat need of bolus use of adrenaline and ephedrine and the noradrenaline was 80 γ/kg/min, deep sedation with midazolam was chosen but didn't helped. Solution of Mannitol 20% with 12 amp. Furosemide of 20 mg each was set in order to increase the urine output. The next ABGs: ph: 7.19, pCO_2: 47, pO_2: 117 with FiO_2 100%, lac: 56, cBase: -9.2, HCO_3: 16.5, N/S: 0,9% solution addition was given to the patient as $NaHCO_3$: 8,4% every 8 hours to the patient to fix the metabolic acidosis. Cardiology consulting was made after the 2nd chest X-Ray (Figure 2) and a trans-thorax echocardiography/echo assessment was done, with no pathology elements and EF > 55% as the dose of the b1-blocker was over 120 ml/min.

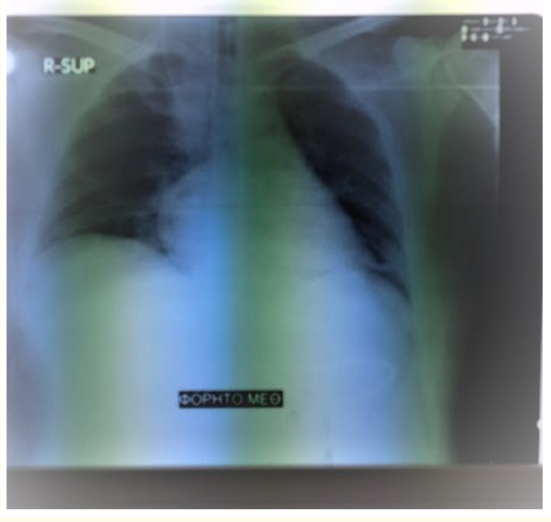

Figure 2: *After 12 hours in the ICU better ventilation with mechanical help and after the cardiology consultation.*

The metabolic acidosis wasn't correcting, the saturation was getting worst with FiO_2 100%, peep > 5, worst of hemodynamic stability with increasing the solution of noradrenalin, reducing of the patient urine output although the urine solution keep supporting, pupils reactive to light but still increasing the hemodynamic support so that it was no compatible to add continuous mechanical renal replacement also extracorporeal elimination with hemodialysis and hemoperfusion is ineffective because of the large volume of distribution [1]. The condition of the patient was getting worst and he died 27 hours after his entrance in the ICU.

The blood exams of the patient are presenting, as the changed in his hospitalization in the ICU department: 15/01/2020.

08:00	14:45	15:45	21:00
WBC: 48400	6500	4400	15100
Neutrophils: 91%	71%	73%	81%
Lymphocytes: 7.5%	21%	25.5%	16.5%
Monocytes: 0.5%	0.8%	0.6%	0.8%
Hb: 16.4	10.7	10.2	9.9
Plt: 159000	6600	68000	75000
PT: 36	32	-	30.5
INR: 3.00	2.7	-	2.55
APTT: 78.5	86	-	105.8
D-dimmers	Hight	Not-determinate	Not-determinate
Fibrinogen	90	-	110
Glu: 85	90	86	66
Ur: 51	64	68	72
Cr: 1.99	2.08	3.00	3.36
Na^+: 145	144	142	143
K^+: 4.7	4.00	4.5	4.9

Cholesterol: 119	-	-	-
Triglyceride: 295	-	-	-
SGOT: 212	136	150	185
SGPT: 31	22	32	48
ALP: 570	369	200	86
γGT: 44	-	-	-
Total proteins: 6.8	3.9	-	-
CPK: 987	-	-	3928
CK-MB: 104	-	-	267
Ca^{+2}: 9.0	7.0	-	7.1
Amylase: 119	-	-	-
CRP: 15.31	-	-	-
LDH: 4262	2925	-	3107
Total bilirubin: 0.6	-	-	1.5
Direct bilirubin: 0.3	-	-	0.9

Table 1

Colchicine intoxication through the bibliography

Colchicine is an alkaloid extracted from autumnal Colchicum plant and it is use for prevention of gout, familial Mediterranean fever and in increased Uric Acid. It is absorbed with oral administration usually and it is widely distributed to intracellular elements, primarily metabolized by liver especially enterohepatic re-circulation and excreted by the kidneys. The usual adult oral adult dose is from 0.6 mg/day to 2.4 mg/day, high fatality dose as reported after ingestion a 0.5 mg/kg. An acute dose of about 0.8 mg/kg of colchicine is presumed to be fatal. The mechanisms of toxicity are by binding to tubulin and disrupting the microtubular network, the cells experience impaired protein assembly which decreased endocytosis and exocytosis, altered the cell morphology, arrest mitosis and interrupted cardiac myocyte conduction and contractility. All the above leads to multi -organ failure, the clinical features are facing three phases: 1) 10-24h after ingestion with gastrointestinal symptoms 2) 24h-7 days after ingestion have multi-organ dysfunction and death 3) a recovery time for those cases which after ingestion with no fetal dose have improvement. If patient survive beyond the second stage, the third stage starts after a week [2]. Therapy with gastric lavage may indicated for the cases with no more than 60 minutes time ingestion of the colchicine and a use of activated charcoal, continue with supportive treatments although an experimental treatment with Fab fragment antibodies for colchicine poisoning was used [3].

Discussion

The ingestion of colchicine more of 0,5 mg/kg is fetal and if medical help is on time, then as the bibliography shows not always the patient survives. The colchicine is an old and effective medication against the gout, the Mediterranean fever among others treatments. The mechanisms of toxicity are by binding to tubulin and disrupting the microtubular network, the cells experience impaired protein assembly which decreased endocytosis and exocytosis, altered the cell morphology, arrest mitosis and interrupted cardiac myocyte conduction and contractility. All the above leads to multi-organ failure, the clinical features are facing three phases: 1) 10-24h after ingestion with gastrointestinal symptoms 2) 24h-7 days after ingestion have multi-organ dysfunction and death 3) a recovery time for those cases which after ingestion with no fetal dose have improvement. If patient survive beyond the second stage, the third stage starts after a week.

Conclusion

Overdose of Colchicine is a live-threatening condition as it is binds to the intracellular protein tubulin cause disturbed mitosis in all tissues and it is following by multi-organ failure.

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