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Effect of Amantadine on Serumic Levels of ALT, AST and ALP in Native Poultry

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Abstract: Clinical trials have documented that amantadine hydrochloride is effective drug for the prophylaxis and treatment of influenza A virus infection. Newsday use of amantadine for treatment of influenza has been increased. The aim of present study was to determine the effect of Amantadine on serumic levels of ALT, AST and ALP in native poultry. About 10 adult hens weighing between 2 and 2.5 kg were used for the study. In first steps one blood sample were taken. In secondary steps amantadine (orally) with dose of 25 mg kg^{-1} for 4 consecutive weeks were administrated. Blood samples in days of 1, 3, 7, 14, 21 and 28 after administration from every hen were taken and after centrifugation serums for seral titration of ALT, AST and ALP by standards kits were used. In fact study according to results of present study a significance in serumic levels of AST in 21, 28 and ALP in 3 , 7, 14, 21, 28 after orally amantadine administration were observed.

Key words: Amantadine, poultry, ALT, AST, ALP, Iran

INTRODUCTION

Clinical trials have documented that amantadine hydrochloride (Galbraith, 1975; Hoffman, 1980; Jackson and Stanley, 1976; Monto *et al*., 1979; Van Voris *et al*., 1981) and its a nalog rimantadine hydrochloride (Dawklns *et al*., 1968; Hoffman, 1980; Rablnovich *et al*., 1969; Van Voris *et al*., 1981; Wingleld *et al*., 1969) are effective drugs for the prophylaxis and treatment of influenza A virus infection. However, widespread use of amantadine has been limited in part by concern about its side effects. Most studies of amantadine prophylaxis have documented minimal toxicity at a dosage of 200 mg day^{-1} (Jackson *et al*., 1967; Monto *et al*., 1979; Peckinpaugh *et al*., 1970) but the frequency and severity of side effects increase with increasing dosage (Jackson *et al*., 1967; Jackson and Stanley, 1976; Schwab *et al*., 1972). Rimantadine has been considered to be better tolerated in humans than amantadine (Hoffman, 1980) although, conflicting results have been reported from studies of their relative toxicities (Peckinpaugh *et al*., 1970).

Amantadine has been used as an antiparkinsonian drug since, 1969 (Schwab *et al*., 1969). For several years its main indications have been the treatment of early Parkinson's Disease (PD) or as adjunct therapy for more advanced PD patients on stable doses of carbidopa/levodopa. Recently, there has been a renewed interest in its use after discovery of its antidyskinetic effects (Blanchet *et al*., 1998; Metman *et al*., 1998). Study on side effects of amantadine in animals is very low but in human some of this side effects is consist of severe allergic reactions (Rash, hives, itching, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips or tongue), aggression, agitation, confusion, depression, fainting, fast or irregular heartbeat, fever, hallucinations, memory loss, mental or mood changes, muscle problems (e.g., spasms, uncontrolled movements), paranoid thoughts, personality changes, seizures, severe or persistent drowsiness or trouble sleeping, shortness of breath, sore throat, swelling of hands, legs, feet or ankles, thoughts of suicide, trouble urinating, unusual anxiety or irritability and vision changes.

MATERIALS AND METHODS

About 10 adult hens weighing between 2 and 2.5 kg were used for the study. They were kept under standard laboratory conditions and were fed with standards feeds and drinking water *ad libitum*. Ethical committee in accordance with animal experimentation and care has approved all animal procedures. In first steps one blood sample from wing vein of every hen were taken. In secondary steps amantadine (orally) with dose of 25 mg kg^{-1} for 4 consecutive weeks were administrated. Blood samples in days of 1, 3, 7, 14, 21 and 28 after administration from every hen were taken and after centrifugation serums for seral titration of ALT, AST and ALP by standards kits were used. Values were represented as mean±SEM. Data were analyzed by one-way Analysis of Variance (ANOVA) followed by Dunnett's test using Statistical Package for Social Sciences (SPSS) version 10. $p<0.05$ was considered significant.

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Table 1: Seral titration of ALT, AST and ALP

Time after administration	0	1	3	7	14	21	28
Level of serum ALT (U L^{-1})	96.50±0.67	96.5±0.67	96.66±1.05	96.5±0.67	93.66±2.74	96.33±0.42	96±0.63
		p = 1.000	p = 1.000	p = 1.000	p = 0.663	p = 1.000	p = 1.000
Level of serum AST (U L^{-1})	117.50±1.11	120±0.00	117.5±1.11	120±2.23	120.83±2.00	125±2.7	127.5±1.11
		p = 0.996	p = 1.000	p = 0.996	p = 0.981	p = 0.028	p = 0.019
Level of serum ALP (U L^{-1})	39.16±0.83	37.5±1.11	45.83±0.83	45.83±0.83	45.83±0.83	50±1.29	51.66±1.05
		p = 1.864	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.000

p-value compared with day of 0

RESULTS AND DISCUSSION

Seral titration of ALT, AST and ALP by standards kits were calculated and in Table 1 have been shown. In human deaths have been reported from overdose with Amantadine. The lowest reported acute lethal dose was 1 g. Because some patients have attempted suicide by overdosing with Amantadine, prescriptions should be written for the smallest quantity consistent with good patient management. Acute toxicity may be attributable to the anticholinergic effects of Amantadine. Drug overdose has resulted in cardiac, respiratory, renal or central nervous system toxicity. Cardiac dysfunction includes arrhythmia, tachycardia and hypertension. Pulmonary edema and respiratory distress (including Adult Respiratory Distress Syndrome-ARDS) have been reported; renal dysfunction including increased BUN, decreased creatinine clearance and renal insufficiency can occur. Central nervous system effects that have been reported include insomnia, anxiety, agitation, aggressive behavior, hypertonia, hyperkinesia, ataxia, gait abnormality, tremor, confusion, disorientation, depersonalization, fear, delirium, hallucinations, psychotic reactions, lethargy, somnolence and coma. Seizures may be exacerbated in patients with prior history of seizure disorders. Hyperthermia has also been observed in cases where a drug overdose has occurred. There is no specific antidote for an overdose of Amantadine. However, slowly administered intravenous physostigmine in 1 and 2 mg doses in an adult 2 at 1-2 h intervals and 0.5 mg doses in a child 3 at 5-10 min intervals up to a maximum of 2 mg h^{-1} have been reported to be effective in the control of central nervous system toxicity caused by amantadine hydrochloride. For acute overdosing, general supportive measures should be employed along with immediate gastric lavage or induction of emesis. Fluids should be forced and if necessary, given intravenously. The pH of the urine has been reported to influence the excretion rate of Amantadine. Since, the excretion rate of Amantadine increases rapidly when the urine is acidic, the administration of urine acidifying drugs may increase the elimination of the drug from the body. The blood pressure, pulse, respiration and temperature should be monitored. The patient should be observed for hyperactivity and convulsions if required, sedation and anticonvulsant therapy should be administered. The patient should be observed for the possible development of arrhythmias and hypotension if required, appropriate antiarrhythmic and antihypotensive therapy should be given. Electrocardiographic monitoring may be required after ingestion since, malignant tachyarrhythmias can appear after overdose. Care should be exercised when administering adrenergic agents such as isoproterenol to patients with an amantadine overdose since, the dopaminergic activity of Amantadine has been reported to induce malignant arrhythmias. The blood electrolytes, urine pH and urinary output should be monitored. If there is no record of recent voiding, catheterization should be done. Also in one study has been reported that amantadine was effectivein the treatment PD-related symptomsfor at least 1 year in 40% of patients (Singer *et al*., 2006). In fact study according to results of present study a significance in serumic levels of AST in 21, 28 and ALP in 3 , 7, 14, 21, 28 after orally amantadine administration were observed.

CONCLUSION

Now a days use of amantadine for treatment of influenza has been increased; of course study on effect of amantadine on serumic level of ALT, AST and ALP has not been reported therefore the goal of present study was to determine the effect of Amantadine on Serum ALT, AST and ALP in native poultry.

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