Modification of naloxone-induced withdrawal signs by ascorbic acid in morphine-dependent guinea-pigs

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Abstract

Background&Objective: Ascorbic acid, an antioxidant vitamin, is found throughout the mammalian central nervous system. Although, the centeral role of ascorbic acid is unclear, but there is good evidence that ascorbic acid modulates opiate withdrawal syndrome. This study was done to determine the effect of ascorbic acid (A.A.) on naloxone-induced withdrawal signs in morphine-dependent guinea-pigs.

Materials&Methods: In this experimental study, male guinea-pigs (300-400 g; 8-10 animals/group) were rendered dependent on morphine by subcutaneous (s.c.) injections of morphine sulfate 3 times a day for 3 days, and withdrawal signs were induced by intraperitoneal (i.p.) administration of naloxone (15 mg/kg) 2 h after the tenth injection of morphine sulfate on day 4; then animals were placed individually into a cylindrical glass (25 cm in diameter, 180 cm height) and the withdrawal signs were recorded over a 60-min period.

Results: Chronic pretreatment of guinea-pigs with A.A., 200 mg/kg, s.c. 3 times daily for 3 days, reduced withdrawal jumping, digging, writhing, rearing, face-washing, head and body shakes, penile licking and diarrhea. The mixed dopamine D1/D2 receptor agonist apomorphine (0.5 mg/kg, s.c.) markedly antagonized the inhibitory effect of A.A. on the withdrawal signs. The effect of apomorphine was blocked by the dopamine D1 receptor antagonist SCH23390 (0.5 and 1 mg/kg, i.p.) but not by the dopamine D2 receptor antagonist sulpiride (50 mg/kg, s.c.) nor the peripheral dopamine receptor antagonist domperidone (1 mg/kg, s.c.).

Conclusion: It is concluded that chronic administration of ascorbic acid inhibits opiate withdrawal, via a central dopamine D1 receptor mechanism.

Key Words: Ascorbic acid- Withdrawal syndrom- Morphine- Naloxone- Dopamine- Guinea-pigs