

CENTRAL ANTITUSSIVE EFFECT OF CODEINE IN ANESTHETIZED RABBIT

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Codeine represents commonly used drug to suppress cough. Central antitussive effect of codeine has been confirmed in number of animal studies. However, available data related to antitussive activity of codeine in rabbits are very limited. Effect of codeine on mechanically induced tracheobronchial cough, single expiratory responses (expiration-like reflex induced by tracheobronchial stimulation), and sneeze reflex were examined on 20 pentobarbitone anesthetized spontaneously breathing rabbits. Increasing doses of codeine (Codeinum Dihydrogenphosphate, Interpharm) were injected intravenously (i.v.; 0, 0.15, 0.76, and 3.78 mg/kg of codeine dissolved in saline, 0.25 ml/kg) or intracerebroventricularly (i.c.v.; 0, 0.015, 0.076, and 0.378 mg/kg of codeine dissolved in artificial cerebrospinal fluid, 0.033 ml/kg). Both i.v. and i.c.v. injection of codeine led to the dose dependent reduction of coughing, however, at markedly different dosages. Tracheobronchial stimulation evoked lower number of coughs ($p < 0.05$; $p = 0.001$ for i.v. and i.c.v. injection of codeine, respectively), but not the number of single expiratory responses compared to control (reflex responses after the vehicle injection). Cough expiratory efforts (expiratory esophageal pressure and abdominal muscles electromyographic moving average amplitudes) were also diminished ($p < 0.05$) by codeine. The effective cumulative dose for 50% reduction of cough number was 3.9 mg/kg and 0.11 mg/kg during i.v. and i.c.v. administration, respectively, representing about 35 fold higher efficacy of i.c.v. in comparison with i.v. application. No significant changes in analyzed temporary parameters of cough were detected, however, the tendency to prolong the quiescent periods of the cough expiratory phase and the total cough cycle durations were observed. No significant changes in single expiratory responses as well as no alteration in sneeze reflex were seen. Our results on anesthetized rabbit confirm the central antitussive effect of codeine. Very low sensitivity of sneeze and possibly expiration reflex to codeine were proved, too. We have validated the experimental model of anesthetized rabbit for studies on central antitussives.

Key words: Codein, Tracheobronchial Cough, Sneeze, Expiration Reflex, Airway Defense.

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