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DESOGESTREL ENHANCE VENTILATION IN ONDINE PATIENTS. ANIMAL DATA SUGGEST THE INVOLVEMENT OF SEROTONIN, A NEUROTRANSMITTER

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BACKGROUND. The Ondine's curse is a neurorespiratory disease characterized by a sleep-hypoventilation associated with the absence or important decrease of the respiratory response to CO_2. A serendipitous observation led to propose that desogestrel, a potent progestive used for contraceptive purpose, could induce a recovery of the respiratory response to CO_2 (Straus et al., 2010). The effect of desogestrel on the resting ventilation was not yet described.

OBJECTIVE. Aim of this work was to determine if desogestrel enhance the resting ventilation in Ondine patients and, in that event, to determine the underlying mechanisms in mice by the use of pharmacological and histological techniques.

MAIN RESULTS. Retrospective analysis of the resting ventilation of the two Ondine patients who displayed a respiratory response to CO_2 under desogestrel (Straus et al., 2010) evidenced that the contraceptive enhanced their resting respiratory frequency leading to a decrease in their expired CO_2 level. In mice, the increase in respiratory frequency was also evidenced. Use of *ex vivo* iolated nervous system preparations permitted to determine that the active biological metabolite of desogestrel, the etonogestrel, increased the respiratory frequency by a mechanism involving neurons of the medulla oblongata that release serotonin, a brain neurotransmitter. On these preparations, the increase in respiratory frequency was not observed when the action of serotonin was blocked.

CONCLUSION. Thus, observations suggest that desogestrel enhance the resting ventilation of Ondine patients by a stimulant effect on their respiratory frequency. Data obtained in mice that suggest implication of medullary neurons releasing serotonin, permit to dedicate investigations designed to test if the ventilation of Ondine patients is reinforced when desogestrel is associated with drugs mimicking or enhancing the action of serotonin.