Objective: To investigate expression of cleaved caspase-3 in the lacrimal gland of female mice of hyperprolactinemic mice female. Design: 40 adult female mice were randomly divided into two groups: In experiment I (induced hyperprolactinemia), the female mice were randomized in two groups of 20 animals each as follows: control group (Ctr1, 0.2 mL of saline solution), and experimental group (HPrl1, 200 µg/day of metoclopramide). Drugs were subcutaneously administered during 50 consecutive days. After 50 days was performed examination of the vaginal smear on the 50th day and the animals were subsequently euthanized in proestrus phase (10 animals/group), their blood collected, and the lacrimal glands were removed. In experiment II, carried out to analyze the lacrimal glands in pregnancy, the estrus females were placed together with males for mating. Two groups of 20 animals each were formed control pregnant (Ctrl2) and experimental pregnant (Hprl2) and the treatments continued. From the 6th of gestation, the animals were euthanized, their blood collected, and the lacrimal glands removed. Plasma was isolated for prolactin (ELISA), estrogen, and progesterone (RIA) measurements. Afterwards, the lacrimal glands were removed and fixed in 10% formaldehyde and were processed for immunohistochemical analysis for the semiquantification of cleaved caspase-3. Statistical analysis was carried out by ANOVA (p<0.05). The photomicrographs were collected using Axion vision (Zeiss, Germany) and the semiquantification analysis from ImageLab® (Software Informatics Ltd., Brazil). Results: The expression of caspase 3 was located in the lacrimal glandular acini and higher in the group of animals treated metoclopramide proestrus phase and pregnant compared to other groups. Serum prolactin levels were higher whereas the levels of estradiol and progesterone were lower in the animals that received metoclopramide compared to controls. Conclusion: Our data showed that the metoclopramide-induced hyperprolactinemia produced morphological signs of reduction of cellular activity in lacrimal glands during the proestrus phase and pregnancy as a consequence of increased cell death by apoptosis. It is hypothesized that this effect might be related to the hyperprolactinemia-induced decrease in the hormonal production of estrogen and progesterone.