Physiol. Res. 44: 349–351, 1995

Milk-Borne Hormones: Possible Tools of Communication Between Mother and Suckling

O. KOLDOVSKÝ[1], H. ILLNEROVÁ[2], L. MACHO[6], V. ŠTRBÁK[6], R. ŠTĚPÁNKOVÁ[4]

[1]Department of Pediatrics, University of Arizona, Tucson, Arizona, USA, [2]Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic, [6]Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Slovak Republic and [4]Institute of Microbiology, Academy of the Czech Republic, Prague, Czech Republic

Summary

Early studies suggested endocrine type mother-pup interaction: ^{131}I administered to suckling rats appeared via the urine of the suckling and mother's milk in the circulation of litter mates who were not injected with iodine; levels of thyroxin in rat milk were influenced by the status of the thyroid gland of the lactating rat. Administration of TRH (thyrotropin releasing hormone) to lactating mothers led to an appearance of unaltered hormones in the milk and stomach content of sucklings. TSH (thyroid stimulating hormone) or ACTH (adrenocorticotropic hormone) when given orogastrically to suckling rats increased thyroid hormones and corticosterone serum levels in suckling rats. Functional effects of gastrointestinal administration of insulin, bombesin (mammalian analog of gastrin-releasing peptide) and epidermal growth factor (EGF) are reviewed in detail (32 references).

Key words

Mother-pup interaction – Thyroxin – Thyroid-stimulating hormone – Epidermal growth factor – Insulin – Insulin-like growth factors IGF-I and IGF-II – Somatostatin – Melatonin – Protective role of milk-borne factors

Thirty years ago interesting studies were performed suggesting mother-pup interaction in the metabolism of iodine. Sámel *et al.* (1963) and Sámel and Čaputa (1965) showed that ^{131}I administered to suckling rats appears *via* the urine of the suckling and mother's milk in the circulation of littermates who are not injected with iodine. Štrbák *et al.* (1974) and Krulich *et al.* (1977) reported that levels of thyroxin in rat milk were influenced by the status of the thyroid gland of the lactating rat. Thyroid-stimulating hormone (TSH) was demonstrated in rat (Krulich *et al.* 1977) and human milk (Tenore *et al.* 1981).

Sámel (1975) showed that the increased uptake of ^{131}I in 4- to 8-day-old suckling rats stimulated by partial thyroidectomy was inhibited by subcutaneous administration of thyroxine (50 μg) to their mothers. Administration of TRH (thyrotropin releasing hormone) to lactating mothers led to an appearance of unaltered hormones in the milk and stomach content of sucklings. It is very important to note that a decrease of TSH levels in the hypophysis and an increase in serum levels were detected in the suckling (Štrbák *et al.* 1980). TSH or ACTH (adrenocorticotropic hormone) when given orogastrically to suckling rats increased thyroid hormones (Tenore *et al.* 1980, Vaucher *et al.* 1983) and corticosterone serum levels in suckling rats (Vaucher *et al.* 1983). Alexandrová and Macho (1983) reported glucocorticoids in human, bovine and rat milk.

Insulin caused a hypoglycaemic effect after its administration into the stomach (Mosinger *et al.* 1959) or into the intestinal lumen of suckling rats (Hiršová and Koldovský 1969). Orogastrically-administered bombesin (mammalian analog of gastrin-releasing peptide) to suckling rats evoked pancreatic secretion of trypsin (Pollack *et al.* 1989) and inhibited gastric emptying (Jiang *et al.* 1991).

Other studies demonstrated the presence of epidermal growth factor (EGF) in rat milk (Schaudies *et al.* 1990); interestingly, transforming growth factor-α (TGF-α) was not detected (Dvořák and Koldovský 1994). The presence of melatonin in human milk was

recently reported by Illnerová *et al.* (1993). Melatonin in human blood and milk was beyond the limit of detection during the day, whereas the melatonin concentration during the night was 280±34 pmol/l in serum and 99±26 pmol/l in milk. The presence of daily rhythm in milk suggests that melatonin fluctuations in the milk might communicate time-of-day information to breast-fed infants.

Other studies have shown higher gastrointestinal (GI) "survival" of EGF during the suckling period (*in vitro*: Rao *et al.* al. 1986, Britton *et al.* 1988, 1989; *in vivo*: Thornburg *et al.* 1984, 1987, Rao *et al.* 1990b, 1991). Milk contains factors that protect *in vitro* degradation of EGF, insulin-like growth factors IGF-I and IGF-II (Rao *et al.* 1993b) and somatostatin (Rao *et al.* 1990a). Other studies have demonstrated absorption of "intact" EGF from the GI tract suckling rats (Thornburg *et al.* 1984, 1987, Rao *et al.* 1990b, 1991); only fragments of somatostatin appeared in the periphery (Rao *et al.* 1993a).

The importance of the intake of milk-borne EGF was demonstrated in studies showing that the EGF content of the GI tract of suckling rats was depleted during fasting (Schaudies *et al.* 1989, Grimes *et al.* 1992), and increased after resuckling or refeeding with rat milk substitute (RMS) to which EGF had been added (Grimes *et al.* 1992); administration of RMS that was not supplemented had no effect. Addition of EGF to RMS fed to suckling rats for four days normalized the protein/DNA ratio in their colon compared to suckling rats fed RMS only (Pollack *et al.* 1987).

Finally, recent studies suggested a protective role of presently unknown factor(s) in rat milk. Artificially-fed suckling rats that received gliadin (a substance known to provoke gluten-sensitive enteropathy in children and adults) intragastrically immediately after birth exhibited various pathological changes in the small intestine whereas similarly-treated mother-fed suckling rats appeared to be normal. Although various other factors might be involved, it is noteworthy that artificially-fed suckling rats without administration of gliadin had normal enterocyte structure (Štěpánková *et al.* 1989, 1990).

References

ALEXANDROVÁ M., MACHO L. : Glucocorticoids in human, cow and rat milk. *Endocrinol. Exp.* **17:** 183–189, 1983.

BRITTON J. R., GEORGE-NASCIMENTO C., KOLDOVSKÝ O. : Luminal hydrolysis of recombinant human epidermal growth factor in the rat gastrointestinal tract: segmental and developmental differences. *Life Sci.* **43:** 1339–1347, 1988.

BRITTON J. R., GEORGE-NASCIMENTO C., UDALL J. N., KOLDOVSKÝ O. : Minimal hydrolysis of epidermal growth factor by gastric fluid of preterm infants. *Gut* **30:** 327–332, 1989.

DVOŘÁK B., KOLDOVSKÝ O. : The presence of transforming growth factor α in the suckling rat small intestine and pancreas and the absence in rat milk. *Pediatr. Res.* **35:** 348–353, 1994.

GRIMES J., SCHAUDIES P., DAVIS D., WILLIAMS C., CURRY B. J., WALKER M. D., KOLDOVSKÝ O. : Effect of short-term fasting/refeeding on epidermal growth factor content in the gastrointestinal tract of suckling rats. *Proc. Soc. Exp. Biol. Med.* **199:** 75–80, 1992.

HIRŠOVÁ D., KOLDOVSKÝ O. : On the question of the absorption of insulin from the gastrointestinal tract during postnatal development. *Physiol. Bohemoslov.* **18:** 281–284, 1969.

ILLNEROVÁ H., BUREŠOVÁ M., PRESL J. : Melatonin rhythm in human milk. *J. Clin. Endocrinol. Metab.* **77:** 838–841, 1993.

JIANG Q., KOLDOVSKÝ O., BEDRICK A., POLLACK P., PORRECA F. : Bombesin differentially affects gastric emptying in suckling, weanling and adult rats. *J. Pharmacol. Exp. Ther.* **257:** 603–607, 1991.

KRULICH L., KOLDOVSKÝ O., JUMAWAN J., LAU H., HOROWITZ C. : TSH in serum and milk of normal, thyroidectomized and hyperthyroid lactating rats. *Proc. Soc. Exp. Biol. Med.* **155:** 599–601, 1977.

MOSINGER B., PLACER Z., KOLDOVSKÝ O. : Passage of insulin through the wall of the gastrointestinal tract of the infant rat. *Nature* **184:** 1245–1246, 1959.

POLLACK P. F., GODA T., COLONY P. C., EDMOND J., THORNBURG W., KORC M., KOLDOVSKÝ O. : Effects of enterally fed epidermal growth factor on the small and large intestine of the suckling rat. *Regul. Pept.* **17:** 121–132, 1987.

POLLACK P. F., ADAMSON C., KOLDOVSKÝ O. : Effects of enterally- and parenterally-administered bombesin on intestinal luminal tryptic activity and protein in the suckling rat. *Experientia* **45:** 385–388, 1989.

RAO R. K., KOLDOVSKÝ O., DAVIS T. P. : Inhibition of intestinal degradation of somatostatin by rat milk. *Am. J. Physiol.* **258:** G426–G431, 1990a.

RAO R. K., KOLDOVSKÝ O., DAVIS T. P. : Fate of intraduodenally administered somatostatin in rats in vivo. *Peptides* **14:** 1199–1203, 1993a.

RAO R. K., KOLDOVSKÝ O., GRIMES J., WILLIAMS C., DAVIS T. P. : Regional differences in gastrointestinal processing and absorption of epidermal growth factor in suckling rats. *Am. J. Physiol.* **261:** G790–G798, 1991.

RAO R. K., KOLDOVSKÝ O., KORC M., POLLACK P. F., WRIGHT S., DAVIS T. P. : Processing and transfer of epidermal growth factor in developing rat jejunum and ileum. *Peptides* **11:** 1093–1102, 1990b.

RAO R. K., LAM K., PHILIPPS A. F., WILLIAMS C., LAKE M., KOLDOVSKÝ O. : Presence of multiple forms of peptidase inhibitors in rat milk. *J. Pediatr. Gastroenterol. Nutr.* **17:** 414–420, 1993b.

RAO R. K., THORNBURG W., KORC M., MATRISIAN L., MAGUN B. E., KOLDOVSKÝ O. : Processing of epidermal growth factor by suckling and adult rat intestinal cells. *Am. J. Physiol.* **250:** G850–G855, 1986.

SÁMEL M. : Effect of thyroxine administration to the mother on postnatal radioidine uptake by the thyroid of partially thyroidectomized rats. *Physiol. Bohemoslov.* **24:** 489–492, 1975.

SÁMEL M., ČAPUTA A. : The role of the mother in 131I metabolism of suckling and weaning rats. *Can. J. Physiol. Pharmacol.* **43:** 431–436, 1965.

SÁMEL M., ČAPUTA A., ŠTRUHÁROVÁ L. : Extra-uterine recirculation of iodine-^{131} from young to mother in rats. *Nature* **198:** 489, 1963.

SCHAUDIES R. P., GRIMES J., DAVIS D., RAO R. K., KOLDOVSKÝ O. : EGF content in the gastrointestinal tract of rats: effect of age and fasting/feeding. *Am. J. Physiol.* **256:** G856–G861, 1989.

SCHAUDIES R. P., GRIMES J,. WRAY H. L., KOLDOVSKÝ O. : Identification and partial characterization of multiple forms of biologically active EGF in rat milk. *Am. J. Physiol.* **259:** G1056–G1061, 1990.

ŠTĚPÁNKOVÁ R., TLASKALOVÁ-HOGENOVÁ H., FRIČ P., TREBICHAVSKÝ I. : Enteropathy induced in young rats by feeding with gliadin – similarity with coeliac disease. *Folia Biol. (Prague)* **35**: 19–26, 1989.

ŠTĚPÁNKOVÁ R., DVOŘÁK B., ŠTERZL J., TREBICHAVSKÝ I. : Effects of essential fatty acid deficiency in milk diets on the development of germ-free and conventional rats. *Physiol. Bohemoslov.* **39**: 135–146, 1990.

ŠTRBÁK V., MACHO L., KNOPP J., ŠTRUHÁROVÁ L. : Thyroxine content in mother milk and regulation of thyroid function of suckling rats. *Endocrinol. Exp.* **8:** 59–69, 1974.

ŠTRBÁK V., ALEXANDROVÁ M., MACHO L., PONEC J. : Transport of ^{3}H-TRH from plasma to rat milk: accumulation and slow degradation in milk and presence of unaltered hormone in gastric content of pups. *Biol. Neonate* **37:** 313–321, 1980.

TENORE A., OBERKOTTER L., KOLDOVSKÝ O., PARKS J., VANDENBERG C. : Thyrotropin in human breast milk. *Horm. Res.* **14:** 193–200, 1981.

TENORE A., PARKS J., GASPARO M., KOLDOVSKÝ O. : Thyroidal response to peroral TSH in suckling and weaned rats. *Am. J. Physiol.* **238**: E428–E430, 1980.

THORNBURG W., MATRISIAN L., MAGUN B., KOLDOVSKÝ O. : Gastrointestinal absorption of epidermal growth factor in suckling rats. *Am. J. Physiol.* **246:** G80–G85, 1984.

THORNBURG W., RAO R. K., MATRISIAN L. M., MAGUN B. E., KOLDOVSKÝ O. : Effect of maturation on gastrointestinal absorption of epidermal growth factor in rats. *Am. J. Physiol.* **253:** G68–G71, 1987.

VAUCHER Y., TENORE A., GRIMES J., KRULICH L., KOLDOVSKÝ O. : Absorption of TSH and ACTH in biologically active form from the gastrointestinal tract of suckling rats. *Endocrinol. Exp.* **17:** 327–333, 1983.

Reprint Requests

O. Koldovský, Department of Pediatrics, University of Arizona College of Medicine, Tucson, Arizona, USA.