Effects of prenatal ginger rhizome extract treatment on pregnancy outcome and postnatal development of Sprague Dawley rats

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Abstract

The effect of prenatal exposure to ginger on pregnancy outcome and postnatal development of Sprague Dawley rats was studied. Pregnant rats were administered with dry powder extracts of ginger orally at doses of 500 or 1000 mg/kg/day from gestation day 5 to 15.

The daily food and water intake was significantly reduced during the exposure period in both groups of ginger fed rats. The weight gain during the exposure period and the total weight gain in pregnancy were also significantly low in both groups of ginger fed rats compared to the control. There was a significant embryonic loss in ginger fed rats. The growth and physical maturation parameters of the offspring exposed to ginger were unaffected. The results of this study suggests that maternal administration of ginger during mid pregnancy results in reduced maternal weight gain and increased embryonic loss without affecting the postnatal growth and physical maturation of the surviving offspring.

Key words: Ginger, pregnancy, postnatal development, prenatal development.

Introduction

Ginger (*Zingiber officinale Roscoe*) has been used in the treatment of a wide range of ailments. These include rheumatic disorders, cough, baldness, toothache and gastrointestinal disorders such as indigestion, vomiting, diarrhoea, colics and ulcers (1,2). Studies are available to show its efficacy as an antiulcer (3), anti inflammatory (4), antiplatelet (5), anti hyperlipidaemic (6), antiemetic and anxiolytic (7) agent.

One of the uses of ginger is in the treatment of nausea and vomiting during pregnancy in humans. In one study, it has been found that ginger was used in over 50% of pregnancies (8). Several controlled clinical trials have shown the efficacy of ginger in the treatment of nausea and vomiting during pregnancy (9,10,11). The constituents in ginger have mutagenic as well as antimutagenic properties (12). A group that investigated the teratogenic potential of ginger extract found no embryotoxic or teratogenic effects (13). Another group showed embryotoxicity associated with prenatal exposure of rats to ginger tea (14). However, in a double blinded, randomized, cross-over clinical trial, no teratogenic abnormalities were observed in infants born to mothers treated with ginger for severe vomiting during pregnancy (10).

To date there is a dearth of literature available on the effect of prenatal ginger

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treatment on postnatal development of the offspring. Therefore the present study was undertaken to investigate the effects of prenatal ginger treatment on the postnatal growth and physical maturation of the rat.

Material and Methods

Ethical clearance for this study was obtained from the ethics committee, Faculty of Medicine, University of Peradeniya, Sri Lanka. Sexually mature, experimentally naive, nulliparous female Sprague Dawley rats were timely mated with sexually mature male rats on a one to one basis. The mating was confirmed on the following morning by the presence of sperms in the vaginal smears. The day on which the vaginal smears were positive was considered as day 0 of gestation. Successfully mated rats were assigned to 3 groups, namely, the control group (C), ginger treatment group 1 (GT1) and ginger treatment group 2 (GT2). All the animals were given free access to water and solid diet and were exposed to natural day and night cycles at a room temperature of 25 to 27° C.

Fresh mature rhizomes of ginger uprooted from the home garden were air-dried and powdered using an electric grinder. A yield of 16.5g of dry powder was obtained from 100 g of fresh ginger rhizome.

From day 5 to day 15 of gestation, rats in GT1 and GT2 were fed with 500mg/kg/day and 1000mg/kg/day of dry powder extracts of ginger, respectively. Powder was dissolved in 2ml of distilled water and administered using a gavage needle.

Starting from the gestational day 19, the dams were examined twice daily, for the presence of litter. After delivery, the litter size (including live births and still births), the weight and the body length were measured. Live birth index (LBI) was calculated for each litter (LBI = number of live births/litter size). In addition, the weight was measured on postnatal days (PND) 10, 20, 30, 50, 70, 90, 120 and the body length was measured on PND 5 and 10. The day of the opening of eyes (from PND 10 to 15), the eruption of incisors (from PND 5 to 10), the opening of vaginal orifice in females (from PND 30 to 50) and the separation of prepuce in males (from PND 30 to 50) were recorded as milestones of physical maturation. On PND 21, dams were killed and the uteri were harvested. The number of implantation sites was counted by placing the uteri in 10% ammonium sulphide as described by Wilkinson [13] and the number of resorptions was calculated.

The data were reported as mean ± standard deviation. Comparisons between the groups were carried out with Kruskal Wallis test followed by Wilcoxon Rank-sum test.

Results

The control, GT1 and GT2 consisted of 6, 4 and 5 rats, respectively. During the exposure period from day 5 to 15, the food and the water intake was significantly reduced ($p<0.05$) in both ginger treated groups compared to the control (Table 1).

The weight gain was significantly lower ($p<0.05$) in both treatment groups during the exposure period (Table 2). There was no statistically significant difference in weight gain between the control and the test groups during pre and post exposure periods. The total weight gain was significantly lower ($p<0.01$) in both ginger treated groups compared to the control.

The duration of pregnancy, litter size, number of implantation sites and the live birth index were not altered by ginger treatment. There was a statistically significant higher ($p<0.05$) number of embryo resorptions observed in both test groups (Table 3). No external congenital anomalies were found either in the ginger fed groups or in the control.

Table 1: Daily food (g/kg/day) and water intake (ml/kg/day) of female Sprague Dawley rats during pre exposure, exposure and post exposure pregnancy. Data are presented as mean ± SD.

		Control	GT1	GT2
Pre exposure	Food	68.5 ±6.98	68.87 ± 6.4	69.7 ± 3.18
	Water	105.07 ± 7.69	96.84 ± 8.92	101.81 ± 12.18
Exposure	Food	61.4 ± 6.32	45.25 ± 0.62*	47.51 ± 3.08*
	Water	82.75 ± 7.35	68.32 ± 5.01*	59.15 ± 8.49*
Post exposure	Food	72.8 ± 5.19	65.53 ± 2.76	65.94 ± 6.95
	Water	100.48 ± 10.28	108.85 ± 14.51	98.75 ± 12.17

(* $p<0.05$ versus control group)

Table 2. Weight gain (g) of female Sprague Dawley rats during pregnancy. Data are presented as mean ± SD.

	Control	GT1	GT2
Pre exposure	34.5 ± 7.12	31 ± 3.55	30.2 ± 8.55
Exposure	31 ± 8.2	19.5 ± 3.1*	18.8 ± 6.05*
Post exposure	48.33 ± 7.94	34 ± 11.8	37.4 ± 13.74
Total weight gain	113.83 ± 11.58	84.5 ± 11.09 **	86.4 ± 8.01 **

(* $p<0.05$ versus control group; ** $p<0.01$ versus control group)

Table 3. Outcome of pregnancy following prenatal exposure to ginger. Data are presented as mean ± SD.

	Control	GT1	GT2
Pregnancy duration (days)	21.33 ± 0.81	21.75 ± 0.5	21.2 ± 1.30
Number of pups per litter	11 ± 1.09	9.75 ± 2.21	9.2 ± 1.64
Number of implantation sites per litter	12.33 ± 1.36	13.5 ± 1.29	13.2 ± 1.3
Number of resorptions per litter	1.33 ± 0.81	3.75 ± 1.25*	3.8 ± 1.3*
Live Birth Index	97 ± 7.34	97.22 ± 5.55	95.55 ± 9.93

(* $p<0.05$ versus control group)

There were no treatment related effects on postnatal body weight (Figure 1) and length (data not shown) of the male and the female rats.

As shown in Table 4, the milestones of physical maturation were unaffected by treatment with ginger. Attainment of puberty as indicated by the separation of the prepuce in males and the acquisition of vaginal patency in females were comparable in the control and test groups.

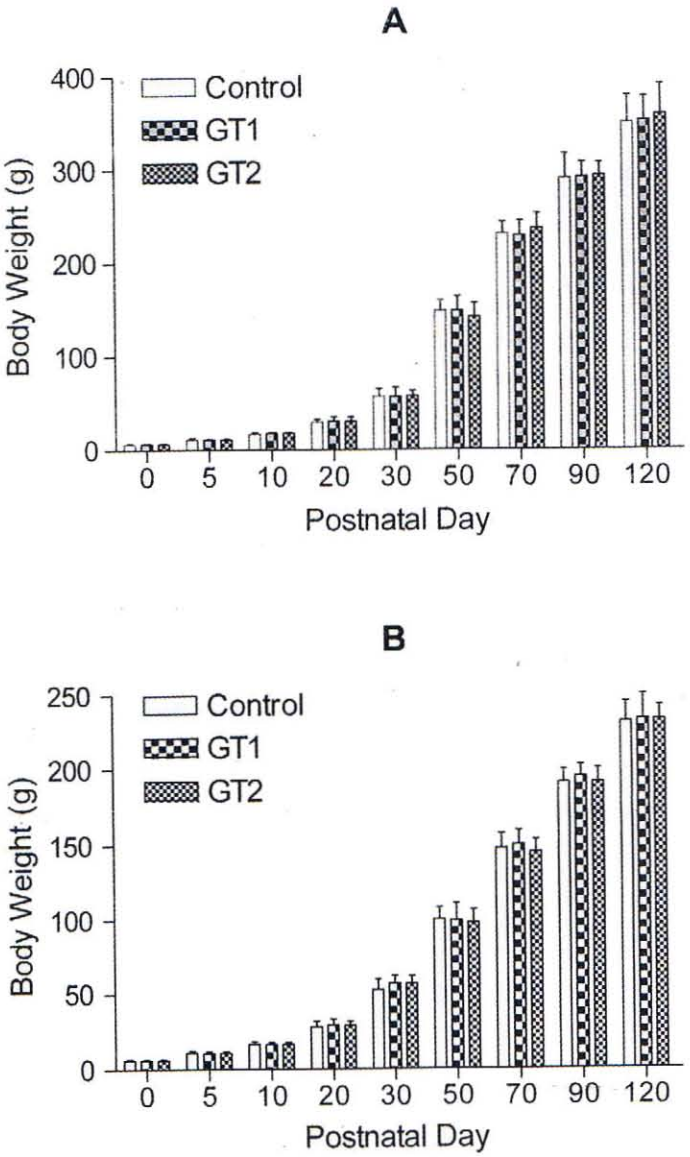

Figure 1. Mean body weights of male (A) and female (B) offspring between postnatal day 1 and 120 after prenatal exposure to ginger.

Table 4. Attainment of milestones of physical maturation (days) of offspring. Data are presented as mean ± SD.

		Control	Ginger 1	Ginger 2
Male	Upper incisors	10.0 ± 1.6	9.6 ± 1.9	9.6 ± 1.7
	Lower incisors	10.8 ± 1.2	10.4 ± 1.3	10.7 ± 1.4
	Preputial separation	46.4 ± 2.7	47.5 ± 2.4	47.9 ± 2.4
	Opening of eyelids	14.6 ± 0.6	14.8 ± 0.5	14.9 ± 0.6
Female	Upper incisors	10.1 ± 0.8	9.3 ± 1.7	9.8 ± 1.6
	Lower incisors	11.3 ± 1.3	11.0 ± 1.5	11.3 ± 1.6
	Vaginal opening	38.4 ± 2.9	37.9 ± 2.6	39 ± 3.1
	Opening of eyelids	14.6 ± 0.5	14.5 ± 0.5	14.8 ± 0.5

Discussion

The present study was performed to investigate the effects of prenatal exposure of ginger, on the outcome of pregnancy and postnatal development of Sprague Dawley rats. We used comparatively higher doses of ginger during this experiment in the form of dry powder extract. The doses were selected on the basis of a pilot study to establish a maximum tolerable dose. The highest dose we used in the pilot study (1500 mg/kg/day) was not tolerated well by the rats and was difficult to feed due to the increased thickness of the extract after dissolving in 2ml of water. Therefore we used the doses of 500 and 1000 mg/kg/day. The period of exposure (day 5 to 15 of gestation) was chosen on the basis that it is the time of organogenesis in the rats and that mostly, ginger is taken for nausea and vomiting during early half of pregnancy.

The maternal weight gain of the two ginger treated groups was significantly low compared to the control during the period of exposure. This may be due to the reduced water and food intake due to a direct toxic effect or irritant effect of ginger on gastric mucosa in the ginger treated groups. There was no difference between the two test groups in terms of food and water intake and weight gain, indicating the absence of any dose related effect. During the post exposure period there was no difference in food and water intake, and the weight gain. The total weight gain during pregnancy was low in both test groups. These findings are not in line with the previous study by Weidner and Sigwart (13). In their study, they did not find any effect of prenatal ginger treatment on food and water intake and weight gain. In another study, Wilkinson (14) reported a reduction in fluid intake of pregnant rats exposed to ginger tea, at doses of 20 or 50g/l, without any effect on weight gain. One possible reason for these differences may be the type of ginger preparations used and the doses administered in the two studies.

There were no gross external congenital anomalies in the offspring. However, there was a significant post implantation pregnancy loss indicated by the increased

number of visible resorptions in the ginger treated groups, regardless of the normal litter size and the number of implantation sites. There was no dose related increase in the visible resorptions as both test groups had similar number of resorptions. Our results are in agreement with the observations by Wilkinson (14) who observed doubling of embryo resorptions without affecting the average litter size and also there were no overt teratogenic abnormalities observed in the litter. It has been shown that the constituents of ginger have both mutagenic and antimutagenic properties (12). The active ingredients, [6]–gingerol and shoagol in ginger have been shown to have mutagenic properties (15). Therefore, it is possible that the embryo loss may have been due to an early lethal mutation caused by these mutagenic agents in ginger. Another possible reason for the embryo loss may be the reduced food and water intake by rats in the test groups.

Despite its widespread use in pregnancy, no reports are available to date to describe the effect of prenatal ginger treatment on the postnatal development. In the present study, the litter size, live birth index and birth weight were not affected by the prenatal treatment with ginger. Therefore it is clear that although there was a significant reduction in the maternal weight gain, it has not affected the growth and development of fetuses.

The body weight and the length of the offspring were similar in the control and the test groups indicating normal post-natal growth unaffected by the prenatal ginger treatment. The attainment of the developmental milestones were also unaffected by the treatment with ginger as the eruption of incisors, opening of the eyes, opening of the vagina in females and the separation of prepuce in males were comparable between control and test groups. Thus the results of the present study confirm that there are no long term effects on growth and physical maturation following prenatal exposure to ginger.

Although it is difficult to draw conclusions on human conditions based on the results of animal studies, caution has to be taken when using ginger during pregnancy as two studies including the present study have shown increased embryo resorptions associated with prenatal ginger treatment.

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