The relationship between fat and progesterone, estradiol, and chorionic gonadotropin levels in Quebec cow's milk

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Abstract

Purpose The majority of milk in industrialized countries is obtained from pregnant cows, which contains increased levels of estrogen and progesterone compared to non-pregnant cows. The aim of this study was to quantify the amount of hormones present in milk with different fat content because previous studies on humans have shown potential effects of increased milk consumption on serum and urine hormone levels as well as on sperm parameters. However, it is unclear whether consumption of milk at the currently recommended levels would lead to systemic effects.

Methods Samples of cow's milk of varying fat concentrations (0, 1, 2, 3.25, 10, and 35%) were analyzed via competitive ELISA assays.

Results Progesterone concentrations were significantly correlated to increasing fat content of milk ($r = 0.8251$, $p = 0.04$).

Conclusions Research on conditions in which additional progesterone may have an effect on human health should consider inclusion of limitation of milk intake and its effects. Further studies are needed to determine the concentration of progesterone in milk of different fat content in other regions and countries and to quantify the potential pathophysiologic role.

Keywords Cow milk · Progesterone · Milk consumption · Sex hormones

Introduction

Milk in industrialized countries is obtained from pregnant cows to increase production [1]. This occurs in most countries with the exception of India, Thailand, and China [1]. Several European studies have been performed in differing countries demonstrated increased sex hormones in commercially available milk, helping to confirm the pregnant status of commercial cows [2, 3]. Progesterone and estrone sulfate are the bovine hormones of pregnancy [1]. Progesterone is lipid-soluble and has increasing concentrations in butter and cream when compared to skim milk [4]. Men who consumed a bolus of 600 mL/m² of body surface area of cow's milk had higher levels of estrone, estradiol, and progesterone in serum and urine [5]. These men also had decreased serum levels of pituitary gonadotropins and testosterone within hours after consuming the milk [5]. All adults and children in this study were noted to have significantly increased urine concentrations of estrone, estradiol, estriol, and pregnanediol after increased intake of cow's milk [5]. Another study noted an inverse correlation between full-fat dairy intake throughout the day and sperm morphology ($p = 0.004$) and motility ($p = 0.05$) [6]. Although it remains to be demonstrated why estradiol levels increased with milk consumption, since estradiol levels are anticipated to be low in cow's milk, estradiol is not one of the bovine pregnancy hormones. Elevations of estradiol in humans after drinking cows' milk would be expected to be derived from enzymatic conversion of estrone or progesterone.

The American dietary guidelines recommend 710 ml of dairy per day for adults [7], a quantity potentially placing individuals at risk for some of the mentioned effects. Another study estimated that levels of estrone in whole milk represents 0.01 to 0.1% of the daily production of estrone in humans and thus falls below the US Food and Drug

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Administration recommendations to consume less than 1 % of endogenous hormone production [8]. Given the inconsistent findings in the literature and the paucity of studies on this topic, we felt that further research on this potentially important topic was necessary.

Methods

Samples of cow's milk containing varying percentages of fat were analyzed: 0 % (skim), 1, 2, and 3.25 % (full-fat), 10 % (cream), and 35 % (whipping cream) fat. The milk was purchased from the independent grocers' association commonly known as IGA grocer in Montreal, Canada, in January 2017. The two samples of milk from each fat content were analyzed. Three different brands of milk were purchased at random. Competitive ELISA assays were run in duplicate at a Montreal-based fertility clinic with intra-assay and inter-assay coefficients of variation < 6 % for progesterone, estradiol, and chorionic gonadotropin assays. Results were averaged at each fat concentration and compared with Pearson's correlation coefficients.

Results

Levels of chorionic gonadotropin and estradiol were undetectable in all samples, irrespective of fat content of the milk, with lower limits of the assay of 0.1 IU/L and 72 pmol/L, respectively. However, progesterone concentrations were significantly correlated to increasing fat content of the milk (Fig. 1a).

When defining baseline progesterone levels as those present in 0 % milk, there was a significant correlation between fat content and percent change from baseline of progesterone levels as a function of increasing fat content of milk (Fig. 1b).

Progesterone differences between brands of milk at the same fat level differed by 0.1 to 1.3 nmol/L. This translated to a difference of 2.0 to 7.7 %. In all cases except for two, these differences were less than 6 % and were in the intra-assay variability range. The two levels above this range were 0.2 and 1.8 % higher, respectively.

Discussion

When comparing the lowest fat concentrations of milk, there is 90 % more progesterone in 1 % milk compared to 0 % milk. Although milk from outside of Quebec was not studied, it is likely that this finding would be consistent among milk obtained from areas outside of this region, pending that the cow's milk was also obtained from cows that were kept consistently pregnant. However, this research should be repeated in other

Fig. 1 **a** Correlations of progesterone levels (nmol/L) and increasing fat content of cow's milk. **b** Correlations of percent change as compared to skim milk (0 % fat) and progesterone levels with increasing fat content of cow's milk

regions of Canada and other countries around the world to confirm this finding.

With respect to the undetectable levels of chorionic gonadotropin seen, this is not a bovine pregnancy hormone [1] and therefore was not expected to be present. This study confirmed this finding. As discussed, the bovine pregnancy hormones are estrone and progesterone [1]. Given the bovine hormones of pregnancy do not include appreciable estradiol levels, it is interesting to note that previous studies have shown increased effects on estradiol concentrations in urine and serum [5], related to milk consumption. Most likely, this represents endogenous enzymatic conversion of estrone and progesterone to estradiol. If this is the case, consumption of cow's milk in large quantities may have increased risk in estradiol-sensitive disease processes.

There are various medical conditions in which additional progesterone may be detrimental and others in which it may be helpful. Milk steroids may have an effect on sperm parameters [6]. In addition, progesterone has been implicated in hormone-responsive malignancies, including breast cancer, as well as uterine fibroids. First pass hepatic metabolism may limit some of these effects, but current data suggests that it can be overcome with milk consumption slightly above the recommended level [5, 6]. It is unclear whether progesterone levels in the ranges we described would cause a clinically relevant effect on physiological or disease processes. Conversion to estradiol, if occurring, should also be considered.

Conclusion

It could be prudent for women with breast cancer, uterine fibroids, or males with poor sperm to preferentially consume skim milk and possibly restrict levels of milk intake. By contrast, women with recurrent pregnancy loss may benefit from milk-origin progesterone supplementation in the luteal phase. Importantly, studies comparing progesterone supplementation to placebo in women with recurrent pregnancy loss should likely control for or limit milk intake. Further studies of this nature are indicated to assess the concentration of progesterone in differing fat content of milk in other areas in Canada as well as other countries to re-confirm this finding and ultimately to quantify the pathophysiologic role, if present.

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