FSH polymorphism and its potential physiological significance: clinical and experimental lectin-based studies.

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FSH is a polymorphic hormone; its heterogeneity arises from differences in the carbohydrate composition and structure of its oligosaccharides which are needed for full expression of biological activity. FSH microheterogeneity has been mainly ascribed to variations in the sialic acid content, without considering possible differences in carbohydrate complexity. We have previously shown that differences in both, sialic acid content and the inner structure of the glycans determine FSH polymorphism and influence the full biological expression of the gonadotropin signal. The endocrine milieu modulates FSH polymorphism; GnRH and sex steroids have been proposed as the main regulators of oligosaccharide structure and composition. Lectin affinity chromatography has proved useful to determine the distribution profile of FSH glycosylation variants with diverse carbohydrate complexity under different physiological and pathological situations. Using this methodology we have observed: a) a sexual dimorphism: in normal men, the three groups of isolated Concanavalin-A (Con A) isoforms are present in circulation from prepuberty until advanced age; in women, only two groups can be isolated, but they differ in their carbohydrate complexity and relative abundance when determined in the follicular phase of menstrual cycles or during menopause; b) changes during pubertal development in the male: the relative abundance of FSH bearing highly-branched oligosaccharides progressively increases whereas that of FSH bearing incompletely processed carbohydrate chains decreases; c) changes in the distribution profile of FSH isoforms after castration or when functional testis are absent and the ability of androgen to reverse the altered profile; d) a unique lectin-based FSH isoform distribution profile in women during lactational amenorrhoea; this was the only physiological condition where a similar distribution profile to that observed in normal men was found. FSH isoforms bearing incompletely processed carbohydrate chains disappeared and the relative abundance of those bearing highly branched carbohydrate chains significantly increased in the follicular phase of recovered menstrual cycles. All the above mentioned variations were independent of hormone sialic acid content.

These observations suggest that a fully functional gonad seems to require the stimulation of FSH isotypes bearing highly-branched oligosaccharides, since they are practically absent in the postmenopausal state and their relative abundance is low during lactational amenorrhoea, at prepuberty, in castrated animals and in anorchid patients. Therefore, these molecules might be differently involved in the regulation of both ovarian follicle and seminiferous epithelium development and maturation. Further studies are needed to determine the molecular mechanisms operating on the regulation of the activity of specific enzymes involved in hormone carbohydrate processing in the gonadotrope. We might conclude that a sophisticated mechanism must be responsible for triggering the appropriate gonadotropin signal at the appropriate stage during reproductive life.