A novel application of $^1$H magnetic resonance spectroscopy: non-invasive identification of spermatogenesis in men with non-obstructive azoospermia

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BACKGROUND: About 10% of infertile men have no sperm in their ejaculate due to poor or absent spermatogenesis, also known as non-obstructive azoospermia (NOA). Testis $^1$H magnetic resonance spectroscopy ($^1$H-MRS) is a non-invasive imaging tool that can potentially identify and localize spermatogenesis in the testis. This study sought to identify metabolic signatures associated with various histological states of spermatogenesis in infertile men.

METHODS: Quantitative high resolution magic angle spinning spectroscopy was performed on snap frozen testicular tissue from 27 men with three classic histological patterns: (i) normal spermatogenesis (men with prior paternity undergoing vasectomy reversal), (ii) maturation arrest (early or late, MA) or (iii) Sertoli-cell only (SCO). Concentrations of 19 tissue metabolites were acquired from each biopsy specimen. One-way ANOVA analysis was used to determine inter-group differences in metabolite concentrations among the three histologic groups.

RESULTS: Phosphocholine (PC) and taurine tissue concentrations were significantly different between normal and SCO tissue. Mean PC concentrations were three times higher in normal testes compared with SCO (5.4 ± 1.4 versus 1.5 ± 0.3 mmol/kg; P = 0.01). No differences in metabolite concentrations were observed between normal and MA testes or between SCO and MA testes. Further histologic stratification of MA testes into subsets of those with (early) and without (late) spermatids or mature sperm, identified differences in PC concentrations. A predictive model for sperm presence with $^1$H-MRS was developed based upon PC tissue concentrations.

CONCLUSIONS: PC concentrations are significantly higher in testes with spermatogenesis. This suggests that a unique metabolic signature for spermatogenesis is possible using $^1$H-MRS which could aid in the non-invasive diagnosis of sperm in men with NOA.

Key words: MR spectroscopy / azoospermia / male infertility / spermatogenesis

Introduction

It is estimated that 10–15% of couples are infertile, and of those, nearly half will involve male factors (Thonneau et al., 1991). Further, 6–10% of infertile men have no ejaculated sperm due to testicular failure, a condition termed non-obstructive azoospermia (NOA; Costabile and Spevak, 2001). Some NOA men have small numbers of sperm in the testicle which can be extracted using sperm retrieval techniques and used with in vitro fertilization and intracytoplasmic sperm injection (ICSI) for biological pregnancies (Palermo et al., 1992; Donoso et al., 2007).

Unfortunately, determining which NOA men have retrievable sperm in the testicle is a clinical challenge. Potential predictors of successful sperm retrieval that have been examined include infertility diagnosis, history of ejaculated sperm, serum hormones, testis volume and testis biopsy histology (Schlegel et al., 1997; Seo and Ko, 2001; Raman and Schlegel, 2003). Although all are poor predictors, the testicular biopsy best predicts the presence or absence of spermatogenesis.