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A possible negative effect of co-administered amlodipine and atorvastatin on semen volume and spermatozoa in men

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To the editor,

We read with great interest the recent study of Kumar et al (2008) published in this journal, concerning the role of glibenclamide or gliclazide and repaglinide in decreasing sperm quality. The authors, in this well designed and performed study, highlighted the role of intrasperm calcium concentration in regulating motility and viability of ejaculated spermatozoa. In recent years, other reports concerning the impact of some drugs, such as miconazole, clotrimazole or loperamide, on viability of human spermatozoa have been reported (Gulati et al 2006). However, the impact of drugs on sperm quality and male fertility may be underestimated. We focused our attention on the co-administration of statins (or HMG-CoA reductase inhibitors) and calcium-channel antagonists. The co-administration of atorvastatin and amlodipine has been reported as well-tolerated treatment for coexisting hypertension and dyslipidaemia (Messerli et al 2006) and without demonstrating significant adverse pharmacodynamic interactions or effects (Preston et al 2007). No studies regarding the effect of the co-administration of atorvastatin and amlodipine on male fertility have been reported. On the other hand, the absence of influence of statins on testicular reproductive function has already been demonstrated by several authors (Bernini et al 1998; Dostal et al 2001). We have recently reviewed our outpatients urological database to evaluate the impact of the co-administration of atorvastatin and amlodipine on male fertility. From a total study population of 689 patients with coexisting hypertension and dyslipidaemia attending our department for all urological diseases (with the exception of infertility), we selected all those patients who had been treated with either atorvastatin or amlodipine or atorvastatin and amlodipine co-administration, with an age lower than 55 years. We finally enrolled 287 patients; 12 patients were excluded for lack of clinical information. Thus, data from 275 were analysed. Ninety-one out of 275 had been treated with atorvastatin, 87 with amlodipine and 97 co-administered atorvastatin and amlodipine. All patients (mean age 48.5 years) had been undergoing pharmacological treatments for at least 12 months. From each patient we obtained at least two consecutive semen parameter analyses (with a mean interval time of 13.3 months). Fisher's exact test or Chi-square test (χ^2) were used to assess statistical significance with $P < 0.05$ accepted as significant. The two groups of patients did not show any significant difference in terms of smoking or other drug use. The two groups of patients who had undergone atorvastatin or amlodipine treatment did not have significant changes in two consecutive semen characteristics analyses. On the other hand, the group of patients who had undergone co-administration with atorvastatin and amlodipine demonstrated significant differences in semen parameters in the two consecutive semen analyses. In particular, the semen volume was significantly different (3.4 mL vs 1.1 mL) between the two determinations ($P < 0.001$). The number of spermatozoa was also different (87 million vs 65 million) ($P < 0.001$). However, sperm morphology and motility, as well as other semen parameters, were not modified. This report highlights that co-administered atorvastatin and amlodipine treatment could have an important impact on sperm quality, even if it does not seem to significantly decrease male fertility.

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References

Bernini, G. P., Brogi, G., Argenio, G. F., Moretti, A., Salvetti, A. (1998) Effects of long-term pravastatin treatment on spermatogenesis and on adrenal and testicular steroidogenesis in male hypercholesterolemic patients. *J. Endocrinol. Invest.* **21**: 310–317

Dostal, L. A., Juneau, P., Rothwell, C. E. (2001) Repeated analysis of semen parameters in beagle dogs during a 2-year study with the HMG-CoA reductase inhibitor, atorvastatin. *Toxicol. Sci.* **61**: 128–134

Gulati, A., Tiwary, A. K., Jain, S., Moudgil, P., Gupta, A. (2006) Intrasperm Ca2+ modulation and human ejaculated sperm viability: influence of miconazole, clotrimazole and loperamide. *J. Pharm. Pharmacol.* **58**: 1145–1151

Kumar, N., Jain, S., Gupta, A., Tiwary, A. K. (2008) Spermicidal activity of sulfonylureas and meglitinide analogues: role of intrasperm Ca2+ elevation. *J. Pharm. Pharmacol.* **60**: 323–330

Messerli, F. H., Bakris, G. L., Ferrera, D., Houston, M. C., Petrella, R. J., Flack, J. M., Sun, W., Lee, E., Neutel, J. M., AVALON Investigators (2006) Efficacy and safety of coadministered amlodipine and atorvastatin in patients with hypertension and dyslipidemia: results of the AVALON trial. *J. Clin. Hypertens.* (Greenwich) **8**: 571–581

Preston, R. A., Harvey, P., Herfert, O., Dykstra, G., Jukema, J. W., Sun, F., Gillen, D. (2007) A randomized, placebo-controlled trial to evaluate the efficacy, safety, and pharmacodynamic interaction of coadministered amlodipine and atorvastatin in 1660 patients with concomitant hypertension and dyslipidemia: the respond trial. *J. Clin. Pharmacol*. **47**: 1555–1569