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Effects of cisapride on anorectal and vesicourethral function in spinal cord injured patients

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The effect of cisapride on constipation in para and tetraplegia is well known. We have investigated the effects of this prokinetic drug on anorectal activity and on the function of the lower urinary tract. One result of the anorectal study showed a significant increase in activity and a reduction in compliance of the ampulla. The urodynamic study demonstrated earlier and higher amplitude reflex contractions in hyperactive bladders; hypoactive bladders significantly reduced their compliance. No functional alterations of striated urethral sphincter were observed.

Keywords: spinal cord injury; anorectal activity; vesicourethral function; cisapride.

Introduction

Severe effects on intestinal activity and on vesicourethral function follow spinal cord injury. Besides the direct consequence on anorectal activity due to a neurological lesion, inhibition of the aminergic nervous system was also suggested. Cisapride enhances gastroduodenal coordination and reduces colonic transit time by increasing gastric contractility and propulsive action at the ileo colonic level.[1]

Materials and methods

Fifteen patients with complete traumatic spinal cord injury were evaluated by a complete urodynamic and anorectal study both before and after treatment with cisapride, 10 mg × 3 daily for 3 days, over a period of 18 months. There were 13 males and 2 females. The level of cord injury was C4 to L1. Time since injury was 3 months to 4 years.

The anorectal study was conducted at four different times; at the first a compliant rectal balloon was distended at a rate of 40 ml/H_2O per minute. The rectal balloon comprised a urinal condom fixed on the top of a 20 ch Foley catheter, whose compliance was separately studied and considered to be insignificant. During this time rectal sensibility, compliance and distensibility during filling were studied; the facilitatory anorectal reflex was also evaluated. Electromyographic activity of the anal sphincter during filling of the ampulla was studied, as well as reflex anal contraction and inhibition or increase in electric activity. Gastrointestinal function is attempted in para and tetraplegia in different ways. Motor paralysis causes a great reduction in gastrointestinal transit time and a decrease of metabolic activity. The modification in hormonal secretion makes an additional contribution to the alterations of the gastrointestinal function. Intestinal mobility is harmonised by the myoenteric plexus and modulated by autonomic nervous terminations.[2]

Severe constipation and prolonged colonic transit time can be found in most patients with spinal cord injuries. In the past 10 years, several papers have been published on the action of cisapride, a new prokinetic drug, on constipation in para and tetraplegic patients.[3,4] Most are concerned with the action of cisapride on colonic motility and transit time; in a few there is also a report on the effects on vesicourethral function, as a reduction of post micturition residual and modifications of cystometric parameters.[1] Hansen and Soler[5] asked if the treatment of chronic constipation by such a prokinetic drug could modify vesicourethral function. The aim of our study was to

investigate the effects of cisapride on the lower urinary tract, involving a full urodynamic study.

Cisapride is a substituted synthetic benzamide which enhances the release of Ach in Auerbach's plexus in the gastrointestinal tract. An evaluation of reflex and voluntary sphincter contraction was also made. On the third occasion an anal pressure prophile was performed; anal closure pressure was recorded at 4, 3, 2, 1 cm from anal edge. During this time maximal closure pressure, voluntary sphincter contraction and inhibitory rectoanal reflex were also evaluated.[6]

The urodynamic study consisted of a urethral pressure profile and urethrocystometry during bladder filling at a rate of 40 ml/H_2O per minute; electromyographic activity of the striated urethral sphincter was simultaneously recorded. Patients were divided into two groups according to the degree of the neurological lesion; subjects with UMN lesions were in group one and those with the LMN type in group two. As far as hyperactive bladders are concerned, we considered the filling volume at first reflex contraction and the pressure reached during it. Compliance (pressure measured at 400 ml of filling) was investigated in hypoactive bladders.

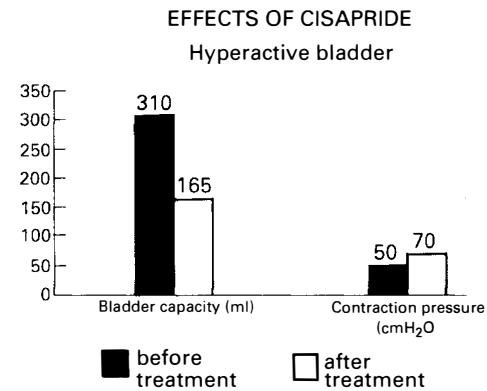

Figure 1 Bladder volume and pressure at the first reflex contraction, before and after treatment with cisapride in hyperactive bladders (UMN lesions).

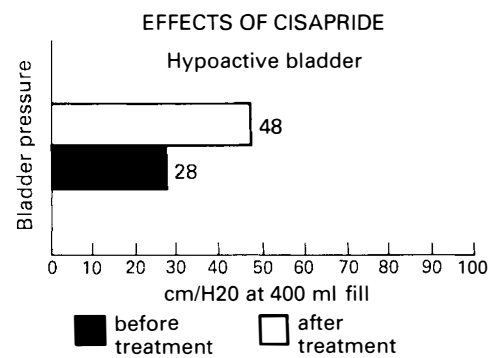

Figure 2 Bladder pressure at 400 ml filling (compliance at 400 ml filling) before and after treatment with cisapride.

Results

As regards the results of the anorectal study, a reduction of the ampulla sensitive threshold and early contractions were found in some patients with a supranuclear lesion. In all of the patients a significant reduction of ampulla compliance was evident. Easier elicitability of the anorectal facilitatory reflex was noticed in patients with a supranuclear lesion, while no modifications of rectoanal inhibitory reflex were evident.

As regards the results of the urodynamic study after cisapride had been taken, a significant change in detrusor activity was noticed in all of the patients studied. In hyperactive bladders earlier and higher amplitude reflex contractions were evident (Fig 1). Hypoactive bladders had a significantly reduced compliance (values at 400 ml filling). No definite modifications were observed as regards maximal urethral closure pressure, nor on functional alterations in the striated sphincter.

Conclusions and discussion

The work by Hansen and Soler stimulated us to do this study; it dealt with the comparison of the parasympathomimetic effect on neuropathic bladders following treatment with cisapride. In particular they observed a reduction of the post micturition residual bladder capacity. These authors emphasised the necessity of a follow up study of the patients in relation to the possibility of overcoming functional modifications in the upper urinary tract following therapy with cisapride.[3]

The results of our study permit us to stress the important and potentially dangerous changes on the lower urinary tract's activity following treatment with cisapride in SCI patients. In those with hyperactive or hypoactive neuropahtic bladders, cisapride increased the risk of renal failure as well as impaired continence; and our study demonstrated the modifications in detrusor activity according to the type of neuropathic bladder, and to the level of the lesion. The results were the same in all patients with the same neurological level. We stress that a drug which is active on the autonomic nervous system should be carefully evaluated by SCI specialists for any possible side effects on the vesicourethral apparatus before it is used clinically.

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