International Braz J Urol
Official Journal of the Brazilian Society of Urology
33 (6): 837-853, November - December, 2007

Re: Steerable Antegrade Stenting: A New Trick of the Trade

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Int Braz J Urol, 33: 389-394, 2007

To the Editor:

The authors describe as a novelty the percutaneous kidney punction with the patient placed in supine position to carry out in an antegrade way the ureteral stenting (1). However we described this procedure 20 years ago (2), in a work that was published in many important urological journal such as the Journal of Urology (3), the Journal of Endourology (4) and the Brazilian Journal of Urology (5) among others.

Among the advantages demonstrated by the percutaneous kidney approach with patient in supine position, (which have been referenced in our previous communications) the possibility exists of simultaneously performing combined endoluminal instrumentation, which can even carry out with a rigid transuretral ureterorrenoscopy at the same time as a percutaneous nephroscopy. This fact has been recently highlighted by many authors, notably including Ibarlucea et al. (6) and Scarpa & Scoffone (7).

In contrast to the opinion of the authors of this paper and of Park (8) who made the first editorial comment to this process, we can confirm that with the patient in supine position does not result in the essential sonographic control in order to perform the percutaneous punction of the kidney. We only make use the sonographically guided renal puncture in extreme circumstances. In the majority of instances we carry out the punction under a simple radioscopic control in P-A, without having to change the position of the C arm which is precisely one of the multiple advantages of this procedure.

Liatsikos & Voudoukis (9), who make the second editorial comment attribute the origin of the combined technique (called "Redezvous Technique") to Marci et al. (10), who described it for the ureteral stenting in 2005. Nevertheless, in our work published in the Journal of Endourology in 1990 (4) we already showed a radiological image with a face to face in to the kidney of a percutaneous nephroscope and a rigid transurethral ureterorenoscope, when referenced the advantages of working both, radiologically and edoscopically, simultaneously from both fields.

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Re: Lack of Association between Matrix Metalloproteinase-1 (MMP-1) Promoter Polymorphism and Risk of Renal Cell Carcinoma

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Int Braz J Urol, 33: 622-629, 2007

To the Editor:

Matrix Metalloproteinases (MMPs) are a family of extracellular matrix degradative enzymes physiologically involved in tissue development and remodeling. Now they are being widely studied for their potential role in the progression and metastasis of many tumors (1).

Indeed degradation of extracellular matrix is one of the crucial and early steps in many carcinomas. The role of the huge family of these enzymes and their inhibitors in cancer cells invasion, metastasis (2), proliferation and angiogenesis (3) is probably much more complex than it seems and still needs to be clarified.

On these basis, many authors paid attention to the overexpression of MMPs enzymes in renal cell carcinoma (RCC). Overexpression of MMP2 and MMP9 has been described in association with poor prognosis of patients with RCC (4-6). Overexpression of MMP1, MMP3, MMP7, MMP11, MMP12 and MMP14 has been described in tissue of RCC (7,8). More recently, a strong relation between MMP10 expression and stage and grade of RCC has been demonstrated (9).

These growing evidences of MMPs role in RCC pathogenesis is the strong rationale to plan genetic investigation to assess not only the phenotype but the genotype modification that stand behind RCC development and progression.

The genetic population based studies are mainly aimed at identifying groups at a higher risk of developing a cancer or at a higher risk of having a cancer with a worse prognosis. The case control population based researches are often biased by not controllable factors especially when the sample size is limited. Moreover, the results of genetic studies are complicated by the wide heterogeneity between different ethnic groups. To draw any conclusion from genetic statistics we need wide sample sizes, from different regions to compare the results of different ethnic groups.

The efforts and the costs of such studies are worthy. Indeed the future possibility of identifying a high-risk group for RCC by a simple test for genetic polymorphism will lead to an early diagnosis of cancer in these patients. The people bearing the high-risk alleles will take advantage of a strict clinical surveillance for example with periodic ultrasound scan.

Even if the results of the authors do not allow identifying an increased risk of RCC for the MMP1 promoter polymorphism in Brazil, they are still important. If further data support these results, the geneticists will have to search for more loci in order to identify one or more gene polymorphisms responsible for increased risk of RCC in Brazil. If further data do not support the result of the aforementioned study, the geneticists will have to plan a wider population based study to answer to the question about the MMP1 promoter polymorphism and the risk of RCC in Brazil.

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Re: Phase II Trial of Neoadjuvant Gemcitabine and Cisplatin in Patients with Resectable Bladder Carcinoma

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Int Braz J Urol, 33: 630-638, 2007

To the Editor:

Malignancy is not aware of the artificial boundaries between surgery and oncology. The malignant tumor lives and expands by its own rules and biological possibilities. To approach any malignancy with curative intent, one must be aware of these facts. A multidisciplinary approach reaching beyond the borders of pride and enthusiasm over ones own capacity as a surgeon or oncologist is the proper way to improve treatment options for the patient. Because, at the end of the day, an increase in survival benefit is what the patient is actually seeking for and mainly nothing else.

Neoadjuvant chemotherapy in muscle invasive urothelial urinary bladder carcinoma adds a survival benefit for our patients as we can see in a number of trials published and presented in recent years. The ABC-group in the meta analysis from 2003 showed that clearly with a combined hazard ratio of 0.87 in favor of the neoadjuvant regime and an absolute benefit of 5 % at 5 years, improving survival from 45% to 50% (1). In the second report from the very same group 2005, in which the SWOG-trial (2) also was included, the power of the trial increased and the hazard ratio of 0.86 was even more favorable. The absolute benefit of 5 % at 5 years remained (3).

The two Nordic trials Nordic Cystectomy Trial 1 and 2 constituted a large part of the mentioned ABC meta analysis. Separately the Nordic trials were also merged into a meta analysis of their own, published in 2004 (4). The outcome in some aspects was different compared to the larger ABC-trial, mainly following; the ARR (absolute risk reduction) was 8 % in the trial as a whole and the subgroup analysis showed a distinct advantage in the T3-subgroup (UICC, 1982) with an ARR of 11 %. The hazard ratio for the whole trial was 0.80 in favor of neoadjuvant chemotherapy and for the T3-subgroup 0.69. Five-year overall survival for patients with clinical T3 in the experimental arm was 48% and in the control arm 37%. For the T2-subgroup the hazard ratio was 0.85 (but without statistical significance).

The explanation for this outcome comparing to the larger ABC trials was as follows; “The studies are comparatively large and clinically homogenous since they were done within the same recruitment areas, within a similar biological domain and cystectomy was baseline treatment in both studies.”

The routine use of neodjuvant chemotherapy (platinum-based combination chemotherapy) in urothelial urinary bladder carcinoma is now standard treatment of T2b - T3b -tumors in two major Swedish university hospitals, Karolinska University Hospital and Uppsala University Hospital. Still one needs to address novel approaches that are emerging. One is the use of new and more efficient chemotherapy

regimes and the other is the extent of lymph node dissection.

In the present trial of Herchenhorn et al., gemcitabine was combined with cisplatin, which is a relatively new constellation. By utilizing gemcitabine, the tolerability increases and enables patients of higher age to be treated in future trials and treatment regimes. One of the major caveats in above-mentioned trials was the relatively low age of the study populations, which also has been commented on previously (5). Still in the present trial (Herchenhorn et al.), the ages were ranging from 18-70 with a median age of 63 and it would be of interest to also follow a population of higher age. The question of extent of lymphadenectomy is still debated, although some prestigious investigators have utilized their non-randomized retrospective single centre experiences to advocate this regimen emphatically. When it comes to staging it is for sure the best tool we have for establishing nodal status and nodal extent of the present malignancy. Still we find ourselves in a biological dilemma. On one hand we have patients with macrometastatic dissemination to a number of lymph nodes heralding a generalized disease. Certainly a generalized disease cannot be treated by local surgical resection. On the other hand we have patients with micrometastatic disease and some proponents of extended dissection dearly wish that surgical skills would remove that very disease. Investigations into the immunobiology of nodal dissemination in urothelial urinary bladder cancer has in the same time shown the existence of a strong defense mechanism directed against the assaulting tumor dissemination (6). Thus there is a slight risk that an overzealous removal of nodal deposits can lead to the surgeon depriving the patient of an existent immunological response! Randomized trials entailing the use of neaodjuvant cisplatin combination therapy carries so far the only conclusive evidence for improving the survival chances in our patients. It is of that reason of great interest to follow new attempts, like the present trial, to improve the neoadjuvant regimen in terms of tolerability and lower toxicity.

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Re: Erectile Dysfunction in Patients with Chronic Renal Failure

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Int Braz J Urol, 33: 673-678, 2007

To the Editor:

Although it is a major factor affecting quality of life in end stage renal disease (ESRD), sexual dysfunction receives very limited attention in follow up of dialysis patients (1). Successful dialysis improves most symptoms of ESRD, yet many patients continue to experience many forms of sexual dysfunction during the dialysis treatment (2). Sexuality was the fifth most important life stressor cited by 135 dialysis patients in a study of quality-of-life issues (3). More than half of patients suffering from ESRD and receiving dialysis treatment describe sexual dysfunction, most commonly a loss of interest in sexual activity (1,4). Despite the importance of these issues, only 25 % of patients discuss sexual function with their physicians (3). Moreover, it has been noted that lack of knowledge about sexuality, conservative attitudes toward sexuality, and anxiety when discussing sexual concerns are widespread among health care providers (5).

Sexual dysfunction addresses alterations related to drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm and satisfaction with orgasm (6); all are affected by ESRD. A questionnaire given to dialysis patients revealed that 65 % were dissatisfied with sex since starting dialysis, 40% have stopped having sex, 27 % have no desire for sex, and 23 % reported they could not achieve orgasm (2). There is no known single cause for these changes, but there are several physical and psychological factors that are thought to contribute to them. Stress, depression and anxiety due to kidney disease and treatment may affect patients' sexual desire and ability to enjoy sex (4). Other factors that may influence a patient's interest in sex include medications, diet, anemia, lack of sleep, inadequate dialysis, uremia and changes in hormone balance (1,3,7).

Complaints of reduction in libido, impotence and marked reduction in the frequency of sexual relations have been reported in more than 50% of male ESRD patients (7). Proposed factors that may cause sexual dysfunction in male dialysis patients are uremia, decreased penile blood supply, hormonal disturbances, low hematocrit level, drugs such as beta-blockers, fatigue, psychological problems such as depression and anxiety, and difficulties with partner (1,2,8).

In comparison to males, sexual dysfunction is more common in healthy females as well as females on dialysis (1). A study comparing sexual function before and after renal insufficiency found that the percentage of females who completely abstained from sexual intercourse increased from 9 to 40%. Among the females on dialysis who continued to have sexual activities, the anorgasmic percentage increased from 9 to 31% (8,9). In another study, 100% of the women on hemodialysis, 67% of those on peritoneal dialysis, and 31% of those with kidney transplants reported a lack of desire for sexual activity and lack of sexual fantasy (10). Numerous hypotheses have been put forward as to the origin of

the sexual dysfunction in female dialysis patients including: uremia, hyperprolactinemia, gonadal dysfunction, depression, changes in appearance, hyperparathyroidism and zinc-deficiency (7-10). Moreover, the capacity of hemodialysis in reversing sexual dysfunctions do not appear to be significant at 6-months (11) and 18 month follow ups (12).

The study conducted by Messina et al. adds further understanding of erectile dysfunction that reaches up to 60 % in their patients undergoing hemodialysis.

Since improving the quality of life is a major goal in medicine, we should pay more attention to the sexual functioning of our patients that might help increasing our patient's enjoyment and satisfaction with life with minimal or no additional costs.

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Re: Erectile Dysfunction in Patients with Chronic Renal Failure

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Int Braz J Urol, 33: 673-678, 2007

To the Editor:

Erectile dysfunction is an important cause of quality of life limitation (1). Messina et al. evaluate erectile dysfunction (ED) in chronic renal failure (CRF). Their cross-study showed the prevalence of ED among 58 patients in hemodialysis program.

The prevalence of their study was 31.4% and 68.6% between patients younger and older than 50 years, respectively. Age, diabetes mellitus & hemodialysis characteristic were associated with higher incidence of ED (2), while they found that neither hypertension (even it is common) nor the duration of dialysis are associated with ED. They brilliantly suggest to all physician and all health professional to pay more attention to their patients' sexual problems.

With high respect to Messina and his colleagues, we want to give some comment on their study:

1) Assessment of ED is done by International Index of Erectile Function-5 (IIEF-5) (3,4).

2) Their study was done only on male patients. Indeed, women who suffered from CRF may have ED. Therefore, for assessment of ED in women patients, Index of Female Sexual Function (IFSF) should be asked (5).

3) ED is a multifactor disease or as we say, symptom. Therefore, hypercholesterolemia, hyperlipidemia, hyper or hypo thyroidism, low blood zinc, low testosterone, high prolactin and even high parathyroid hormone are associated with ED (4,5). Messina et al did not mention the measurement of such tests (2).

4) Obesity in CRF patients can cause ED (1).

5) There is no doubt that psychological problems are the important causes of ED. So all patients should be asked Beck Depression Inventory (BDI) to investigate their depression symptoms.

6) Bellinghieri et al. found ultrastructural changes of corpora cavernosa in uremic male patients. These changes are more evident in male patients with longer time on dialysis.

7) In our clinic, our evaluation of male patients for ED consists of taking and even drug history (e.g. antihypertensive, H2 blocker receptors, etc.), physical exam, measuring BUN, creatinine, FBS, cholesterol, triglyceride, HDL, LDL, testosterone, prolactin, thyroid and parathyroid function tests; and besides those, cavernosal injection of vasoactive agents, color Doppler sonography, cavernosography and cavernosometry and Rigiscan as needed.

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Int Braz J Urol, 33: 673-678, 2007

To the Editor:

The association of chronic renal failure (CRF) to erectile dysfunction (ED) is a well known fact, but the prevalence of ED obtained in this population is variable. The lack of an standardised instrument for ED assessment before generalisation of the international index of erectile function (IIEF) and the heterogeneity of CRF patients regarding the presence of commorbidities are two facts that have probably contributed to this variability. However, a high prevalence of ED has generally been reported in CRF patients. In this sense, Messina and collaborators report in this issue that the prevalence of ED in a

study population of brazilian men suffering from CRF and undergoing hemodialysis was 60.3%. This means that a large number of patients undergoing hemodialysis also complaint from ED. When ED is added to the deterioration in quality of life caused by the renal failure as the need to stay several hours per day, three times a week, connected to the hemodialysis machine, the decline of the quality of life becomes harder. The prevalence reported in this study is not far from that reported by other authors in CRF patients in Brazil (1) which was 57.9%. In addition, age is a variable associated with ED in both studies. The present study, also confirms that diabetes is a main factor associated to ED in patients undergoing hemodialysis. In fact, almost all diabetic patients with CRF presented ED. Since diabetes is independently associated to ED, this could indicate that the presence of two risk factors prompts the patient to develop ED. Diabetes is related to a reduction of nitric oxide (NO)-mediated activity (2) while CRF has also been suggested to decrease NO availability (3,4). Thus, the presence of the two conditions should hardly impact the NO/cGMP pathway, a key pathway in the erection process. Due to the high proportion of hypertensive patients in this study, authors cannot evaluate the association of hypertension with ED in patients undergoing hemodyalisis. However, interesting information could have been obtained by analysing the relationship between ED and the specific antihypertensive medication. A novel finding of the study by Messina and collaborators is that ED correlated with parameters of hemodialysis adequacy (Kt/V) suggesting that ED could be prevented by achieving good standards of dialysis. The lower risk for ED when urea is effectively cleared from plasma is consistent with the fact that uraemia results in reduced bioavailability of NO (5) and the serum levels of endogenous inhibitors of NO synthase are increased in uraemic patients (6). In conclusion, the high prevalence of ED among the patients with CRF compels practitioners to ask for erectile function of these patients, in order to try to improve their quality of life. A better understanding of the specific pathophysiological mechanisms leading to ED in CRF patients could help to find the adequate treatment option.

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Re: Intracaval and Intracardiac Extension of Wilms' Tumor. The Influence of Preoperative Chemotherapy on Surgical Morbidity

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Int Braz J Urol, 33: 683-689, 2007

To the Editor:

Wilms tumor (WT) or nephroblastoma is the most common tumor of renal origin found in children. It accounts for 6% of all pediatric tumors and is the second most frequent intrabdominal solid organ tumor found in children. Initial survival rates in the early part of the last century were only 30%, but now long-term survival is approaching 85% with many low stage tumors significantly higher (1-3). Despite the success there are several challenging clinical scenario's that face treating physicians. One problem, which is the subject of the article by Cristofani and colleagues, addresses the best method to treat a child with a Wilms tumor that extends into the inferior vena cava or up to the right atrium.

Wilms tumors may extend through the renal vein into the inferior vena cava and up to the atrium. In large published series, caval extension was reported between 2% and 5% and atrial extension in 0.2% to 1.2% of children with Wilms Tumor (4-6). There are two primary treatment strategies to treating a child with Wilms tumor. The first utilizes upfront nephrectomy followed by chemotherapy, the second employs pre-nephrectomy chemotherapy (7). To date no randomized studies have been conducted to guide definitive therapy in a patient with caval or atrial extension. Nevertheless, several publications including the series presented in this edition of the International Braz J Urol help guide therapy. The central treatment problem is defining who should undergo primary nephrectomy and removal of the vascular extension of tumor and who would benefit from pre-nephrectomy chemotherapy. The potential benefits for preoperative chemotherapy include possibility of resolution of thrombus, partial/complete response of thrombus, decreasing the need for cardiopulmonary bypass surgery and bleeding. The potential drawbacks include tumor emboli, tumor progression, a marginal reduction in complications and the recognized increased difficulty of removing a tumor from the venal cava or atria following chemotherapy.

In addition to Cristofani's paper, three large series provide insight to managing a child with vascular extension (4,6,8). The International Society of Pediatric Oncology (SIOP) 93-01 GPOH study and the United Kingdom Children's Cancer Study Group UKW3 utilized preoperative chemotherapy as the primary mode of therapy. In the SIOP study, 33 of 1151 patients had vascular extension. In nine, there was extension into the atrium. Twenty-nine underwent preoperative chemotherapy. Twenty (69%) responded to chemotherapy including one of those with extension into the atria. Nine required cardiopulmonary bypass to remove the tumor. There were no surgical deaths. In the UKW3 trial 59 patients had vascular extension with 10 extending into the atria. Fifty-two underwent preoperative chemotherapy with 35 (67%) responding. Unfortunately 5/52 (10%) died at operation due to uncontrolled bleeding. The National Wilms Tumor Study Group #4 trial reported

outcomes on 134 with vena cava or vascular extension. Unlike the two previous trials where pre-nephrectomy chemotherapy was the treatment of choice the initial treatment was left up to the individual treating physicians. In this report 69 received preoperative chemotherapy. Seventy-one percent had some response to therapy. In five cases a tumor embolism and progression was noted with three patients developing acute respiratory distress syndrome. When all the complications of therapy were considered, including those that occurred during the interval of preoperative chemotherapy the incidence of complications among those receiving preoperative therapy was not statistically different from the incidence among those who underwent primary resection. Although the overall complications were similar the majority of children responded to chemotherapy. The compelling response rate of the thrombus to chemotherapy has lead the Children's Oncology Group (formerly the NWTS) to recommend that preoperative chemotherapy be given to all patients with tumor extension above the hepatic cava.

Cristofani and colleagues present 16 patients over twenty-two years with vascular extension. The clinical outcomes of these patients are outstanding, one of the highest reported in the literature. This paper is helpful because both treatment strategies were used and evaluated. This study joins others in the literature showing an excellent response (72%) to chemotherapy. In one of the cases tumor extension to the atria resolved and cardiopulmonary bypass was not need.

The most important comment that the authors make is that these children need to be treated by a multidisciplinary team. These are difficult high-risk patients. Preoperative chemotherapy is warranted but tumor embolism may occur and these children need to be watched very carefully. Finally, although the tumor may shrink, morbidity and mortality are significant as noted in the SIOP, UKW3 and NWTS4 reports. These cases require an experienced team of physicians to guide therapy to ensure maximum outcomes with minimal morbidity.

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Re: Pubovaginal Sling with a Low-Cost Polypropylene Mesh

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Int Braz J Urol, 33: 690-694, 2007

To the Editor:

The authors are commended on a nice review of their experience with the distal urethral polypropylene sling, which may provide a low-cost alternative to some of the new midurethral polypropylene sling techniques. This technique, which is often referred to as DUPS by the original authors, was first described by Rodriguez & Raz in 2003 (1). Subsequent reports of the UCLA experience with DUPS have ensued, with a recent long-term, report with follow up in excess of five years.

The study design is retrospective with mean follow up of 42 months (range 14-61). The success of the procedures is notable with adequate minimum follow up for current standards. The conclusions reached by these authors are very similar to those made in the original Rodriquez & Raz paper (1). Although no particularly new facts are presented in this manuscript, it is encouraging to see confirmation of the experience of the original group. Long term follow up by the original group has also proven satisfactory (2), and it would be ideal to have further follow-up of the present cohort to validate this data.

Finally, in this era of cost-consciousness, it behooves us all to consider technical and material options that may preserve successful outcomes, while providing economic advantages. The authors are congratulated on a fine confirmatory report.

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Re: Interleukin-11 Attenuates Ifosfamide-Induced Hemorrhagic Cystitis

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Int Braz J Urol, 33: 704-710, 2007

To the Editor:

The study was conducted to investigate the anti-inflammatory effect of rhIL-11 used in prophylaxis of ifosfamide-induced hemorrhagic cystitis in an animal model. There has been no publication on the use of rhIL-11 in prophylaxis of hemorrhagic cystitis in the literature previously.

The study design and methods used in this experiment were chosen and are presented correctly. Although the studied groups (each consisted of 6 mice) were rather small, the statistical methods used in this publication are adequate to the number of animals used.

I do not completely agree with the statement, that there are no adequate methods that prevent hemorrhagic cystitis induced by oxazaphophosphorine agents (such as cyclophosphamide or ifosphamide). Several studies indicate the use of hyperhydratation (which shortens the exposition time to urotoxins) and mesna (which binds acroleine, responsible for bladder mucosa damage) considerably reduces the incidents of early-onset toxic hemorrhagic cystitis even in patients receiving high-dose chemotherapy (1). Early-onset hemorrhagic cystitis is not a major clinical issue nowadays. Its rate presented in many studies is lower than the 33% quoted by the authors basing on one publication (2-6). However, prevention of late-onset hemorrhagic cystitis related to the reactivation of viruses (mainly human polyoma BK virus), in patients after allogeneic stem-cell transplantation, still remains an unsolved problem (3,7,8-10). One may speculate that the initial bladder mucosa damage caused by cytostatics used in conditioning regimens may play a role in the occurrence of virus induced hemorrhagic cystitis (10). It has been documented in many publications that not oxazaphophosphorine drugs, but rather busulfan is currently the main agent identified as a risk factor for hemorrhagic cystitis (5,6,9,11). No specific prophylactic measures protecting the bladder from busulfan toxicity exist so far. This is the reason why investigation of methods that may prevent from cytostatic-induced urothelium damage remains a challenge.

In this context, the results presented by the authors are encouraging and justify the use of rhIL-11 in clinical trial in human hemorrhagic cystitis.

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Re: Interleukin-11 Attenuates Ifosfamide-Induced Hemorrhagic Cystitis

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Int Braz J Urol, 33: 704-710, 2007

To the Editor:

Ifosfamide (IFS) is a widely used antineoplastic agent, and the occurrence of ifosfamide-induced hemorrhagic cystitis (HC) continues to be a significant problem in spite of adequate uroprotection. Acrolein, the toxic metabolite of IFS, is the main molecule responsible for this side-effect and mesna (2-mercaptoethane sulfonate) is the most commonly used preventative agent. Mesna binds acrolein and prevent its direct contact with uroepithelium. Current knowledge provides information about the pathophysiologic mechanism of HC. Several transcription factors and cytokines, free radicals and non-radical reactive molecules, as well as Poly (ADP-ribose) polymerase (PARP) activation are now known to take part in its pathogenesis., Whether or not it follows chemotherapy (CP), HC is an inflammatory process. Thus, many cytokines such as tumor necrosis factor (TNF), the interleukin (IL) family, transcription factors such as nuclear factor-κB (NF-κB) and activator protein-1 (AP-1) also play a role in its pathogenesis. When these molecular factors are taken into account, pathogenesis of CP-induced bladder toxicity can be summarized in three steps: (1) acrolein rapidly enters the uroepithelial cells; (2) it then activates intracellular reactive oxygen species and nitric oxide production (directly or through NF-κB and AP-1) leading to peroxynitrite production; (3) finally, the increased peroxynitrite level damages lipids (lipid peroxidation), proteins (protein oxidation) and DNA (strand breaks) leading to activation of PARP, a DNA repair enzyme. DNA damage causes PARP overactivation, resulting in the depletion of oxidized nicotinamide–adenine dinucleotide and ATP, and consequently in necrotic cell death. For more effective prevention against HC, all pathophysiologic mechanisms must be taken into consideration.

Mild forms of HC usually resolve with supportive treatment. However, severe HC may require additional therapies, including hyperbaric oxygen treatment, amifostine, antiviral therapy such as vidarabine or cidofovir, factor VII, bladder irrigation with intravesicular instillation of ε-aminocaproic acid, methyl prednisolone or formalin, cystoscopy and cauterization, and even cystectomy. In addition to acrolein, viral infections such as adenovirus and BK virus (1) have been implicated in the etiology of HC. Therefore therapies directed against viral infections may also be useful in the treatment of HC when appropriate. Further studies are needed to determine the appropriate use of antiviral therapy in virus-associated HC.

Despite the preventative use of mesna, HC is observed in 33% of the patients treated with IFS. This observation stresses the need for novel therapies as additional prevention for acrolein induced HC. Mota et al (2) investigated the role of recombinant human interleukein-11 (rhIL-11) in preventing experimental IFS-induced HC in Swiss

mice and have published their results in this issue of the journal. The observations of Mota et al[2] demonstrate that rhIL-11 partially prevents IFS-induced HC, presumably due to its anti-inflammatory properties and ability to down-regulate many pro-inflammatory cytokines. Thus, rhIL-11 may be a very useful adjunct in prevention of HC induced by IFS. These data support that rhIL-11 be used in clinical trials to investigate its role in prevention of HC in humans.

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