Original Research Article

ROLE OF ALPHA-BLOCKER, ANTI-CHOLINERGICS AND COMBINATION THERAPY IN TREATMENT OF SYMPTOMS RELATED TO DJ STENT

ABSTRACT

In routine urological procedure ureteric DJ stents are important and basic tool. The history of DJ stenting is too old, Gustav simon in 1800s performed first DJ stenting following open cystostomy. Following his success, Zimskind et al in 1967 placed DJ stent endoscopically [1].Later on it flourished as a important tool in endourology. With the passage of time, multiple changes were made in features & structure of DJ stent to ensure a good urinary drainage with lesser complications. In modern age of urology the uses of DJ stent have been expanded.

Ureteric stents are now used in treatment of various diseases related to urinary tract. For example, to prevent ureteric obstruction postoperatively from mucosal oedema, mucosal erosion/damage following uretrorenoscopy for ureteric stone or other upper tract interventions, following ballon dilatation of ureteric stricture, following endopyelotomy / pyeloplasty, to relieve obstruction in pelvic malignancy etc.[2] DJ stenting is now performed in routine endourological and open surgery for avoidance of ureteric obstruction [3]. Selective alpha blockers / anti- muscarinic are used in alleviating the symptoms due to DJ stent like urgency, frequency of urination and painful micturation

Objectives: To assess the role of α-blockers(tamsulosin) or anticholinergic(tolterodine) alone and in combination, in the management of DJ related symptoms

Material and Methods:

Study Design: Randomized control Trial

Study Setting: JINNAH HOSPITAL LAHORE ,PAKISTAN.

Study Duration: six months – ONE YEAR

Data collection and analysis:

All patients with DJ stent in situ were followed on weekly basis in outpatient department to assess the development of DJ related symptoms. A total of ninety patients, who developed symptoms during their course of follow up were separated in three groups, group A, B & C, each comprising of 30 patients. Group A, patients received 0.4 mg tamsulosin daily. Group B, received 2mg tolterodine twice daily. Group C, received 0.4 mg tamsulosin daily& 2mg tolterodine twice daily. IPSS and VAPS score were compared within and in between groups at enrollment, during each follow up weeks and at the completion of study. The results were compared between Group A, B (monotherapy) and group C (combination therapy).

Key Words: Urethral stent / DJ Stent, Anticholinergic, Alpha blockers.

Introduction:

In routine urological procedure ureteric stents are important and basic tool. There are relatively less side effects reported in early researches but later researches shows that these ureteric stents can cause hematuria, dysuria, lumbar pain, pain suprapubic region, frequency,urgency.In routine urological procedure ureteric stents are important and basic instruments. Stent are now extensively used as a basic tool in endourological surgery. They are generally placed in anticipation to prevent ureteric obstruction postoperatively from mucosal oedema, mucosal erosion/damage following uretrorenoscopy for ureteric stone or other upper tract interventions. Though the use of DJ stent have been increasing day by day, its use is not free of symptoms & complications. There are relatively less side effects reported in early researches but later researches shows that these ureteric stents can cause hematuria, dysuria, pain suprapubic region, frequency, urgency etc. Moreover DJ stent may get broken, migrate or can have encrustation over it. The problem of stent migration was resolved by Finny in 1978 by introducing double coiled stent i.e JJ stent or DJ stent.[4] Researches shows that these ureteric stents can cause symptoms like hematuria, dysuria, pain suprapubic region, frequency,urgency etc. [5] About 83% of patient with DJ stent are symptomatic.[6] Few studies correlated association of DJ stent length and symptoms. More than the required length of DJ stent causes over coiling and bizzare symptoms. So if DJ stenting is required following endoscopic surgery, length of ureter needs to be calculated so that a suitable DJ stent can be used, which decrease distal migration and DJ stent symptoms.[7] Injection of botulinum toxin type A following DJ stent insertion in subtrigonal region has been shown to reduce pain and sedative requirement [8]. A variety of medicines were used

in relieving symptoms related to DJ stent. Selective alpha blockers / antimuscarinic are used in alleviating the symptoms due to DJ stent like urgency, frequency of urination and painful micturation.[9] Combination of tamsulosin and tolterodine is effective to recover both irritative and obstructive complaints.[10] In Damiano study, IPSS total score, irritative subscore, Quality of life and VAP score were not statistically remarkable [11]. This study is designed to evaluate the efficacy of anticholinergic or alpha blocker alone and in combination, in treatment of double J stent related symptoms at the Urology & Renal Transplantation department, JINNAH Hospital,AIMC/Lahore, Pakistan.

OBJECTIVE: To assess the role of α-blockers (tamsulosin) or anticholinergics (tolterodine) alone and in combination, in the management of DJ related symptoms.

Subjects and Methods:

SAMPLE SELECTION:

Inclusion criteria

- Both Male & female cases with average age 16-40 years
- Patients with DJ stent surgery (endoscopic & open surgery) for any indication.

Exclusion criteria

Coagulopathy, Current Pelvic trauma/fracture, Urogenital carcinomas, Prostatic enlargement or Chronic prostatitis, Bladder neuropathy, Stone in bladder, Bilateral DJ,DJ in reimplantated ureters, Untreated UTI, Pregnant females, Diagnosed retroperitoneal fibrosis, Patients with residual stone after surgery, Patients with

contraindications for using alpha-blocker or anticholinergics e.g. glaucoma, myasthenia gravis,female diagnosed as stress/urge incontinence

A Randomized control trial was conducted at Department of Urology, jinnah hospital hospital from june 2015 to May 2016.

Indications for DJ Stents includes:. Following URS/ intracorporeal pneumatic lithoclast for ureteric stone**,** following pyeloplasty/pyelolithotomy requiring DJ stent placement**,** To relieve renal obstruction in pelvic malignancies**,** following Endopyelotomy**,** following balloon dilatation of ureteric strictures

Total 90 patients those fulfilling inclusion criteria age 16- 64 years of either gender with double j stenting for various urological problems following endoscopic/open procedures were recruited through non-probability sampling for the research after informed consent. The subjects were asked to fulfill the proforma. Follow up was done through OPD and patients were asked for DJ stent related symptoms on weekly follow up till DJ was removed. Subjects were allocated in three groups; group A,B&C, each group of 30 patients. Group A, patients were given 0.4 mg tamsulosin one daily Group B, patients were given 2 mg tolterodine twice daily. Group C were given combination of 0.4 mg tamsulosin& 2mg tolterodine. Patients in all groups were kept on follow up on weekly basis for relief of their symptoms. Responders in all groups took their corresponding responding drugs till the DJ stent were removed.DJ stent was removed in all the cases after the desired objective of stenting was achieved (after of average 4 weeks). Meanwhile the non-responders of all groups were labeled as failure of therapy and they were managed accordingly. Stent removal was done after the desired objective of DJ stent insertion was obtained. Effectiveness among three therapy i.e. alpha-blocker, anti-cholinergic alone and in

combination was assessed by comparing the relief of symptoms in all the groups. All patients with DJ stent in situ were followed on weekly basis in outpatient department to assess the development of DJ related symptoms. A total of ninety patients, who developed symptoms during their course of follow up were separated in three groups, group A, B & C, each comprising of 30 patients. Group A, patients received 0.4 mg tamsulosin daily. Group B, received 2mg tolterodine twice daily. Group C,received 0.4 mg tamsulosin daily& 2mgtolterodine twice daily. All patients received analgesics on demand. Patients in all groups were kept on follow up on weekly basis for the relief of symptoms. If the number of patients group A , B & C remains below 30, more patients were added to complete the requisite number i.e. thirty (in each groups). Responders in all groups will kept on take their responding medicine and were followed till completion of study. During the course of follow up if any patient developed symptoms related to infection (like fever, pyuria) urine complete examination and urine culture sensitivity were done and he were excluded from study and accordingly managed. Double J stents were removed after the objective of stent placement were obtained. For all the symptomatic patients, weekly relief of symptoms were defined in terms of; No response (no/minimal relief of symptoms, patient unhappy), partial response (moderate relief of symptoms, patients satisfied) and complete response (more than 90% relief of symptoms, patient happy).The LUTs were classified with irritative (urgency, frequency, nocturia) and obstructive symptoms(weak stream, intermittency, straining, incomplete voiding) and were scored as IPSS score. The intensity of painful micturition/flank pain were scored with visual analogue pain score (VAPS).IPSS and VAPS score were compared within and in between groups at enrollment, during each follow up weeks and at the completion of study. The results were compared between Group A, B (monotherapy) and group

C (combination therapy). Data were entered and analyzed in SPSS ver: 21.0. Mean and SD was calculated for numerical variable like age and IPSS score. Frequency and percentages were calculated for nominal variable like gender, relief of symptoms. Anova test compared the mean variation in between the groups. A P<0.05 was taken as statistical important.

RESULTS:

Table no: 1 IPSS baseline and final score descriptive statistics

IPSS Score		N	Mean	Standard Deviation	Minimum	Maximum	ANOVA	
							F	Sig.
Baseline	Group A (TAMSULOSIN 0.4 MG H.S)	30	16.1000	5.73164	5.00	27.00	1.931	.151

	Group B (TOLTERODINE 2MG BID)	30	18.6000	4.42251	8.00	27.00		
	Group C (COMBINATION THERAPY)	30	17.4333	4.53099	9.00	27.00		
	Total	90	17.3778	4.98217	5.00	27.00		
Final Score	Group A (TAMSULOSIN 0.4 MG H.S)	30	8.3000	3.38506	.00	14.00	35.662	.000
	Group B (TOLTERODINE 2MG BID)	30	4.8333	3.33305	.00	12.00		
	Group C (COMBINATION THERAPY)	30	1.5333	2.51524	.00	9.00		
	Total	90	4.8889	4.13927	.00	14.00		

Table no: 2 VAPS baseline and final score descriptive statistics

VAPS		**N**	**Mean**	**SD**	**Minimum**	**Maximum**	**ANOVA**	
							F	**Sig.**
Baseline	Group A (TAMSULOSIN 0.4 MG H.S)	30	5.8667	4.37653	.00	15.00	1.547	.219
	Group B (TOLTERODINE 2MG BID)	30	6.3000	5.28596	.00	15.00		

	Group C (COMBINATION THERAPY)	30	4.2000	4.94382	.00	15.00		
	Total	90	5.4556	4.91309	.00	15.00		
Final	Group A (TAMSULOSIN 0.4 MG H.S)	30	1.1667	2.29066	.00	8.00	1.835	.166
	Group B (TOLTERODINE 2MG BID)	30	1.6667	2.39732	.00	5.00		
	Group C (COMBINATION THERAPY)	30	.6333	1.44993	.00	4.00		
	Total	90	1.1556	2.10890	.00	8.00		

Table no 3: Response among group Crosstabulation

Group	RESPONSE		Total	Chi-Square P value
	No Response	Response		
Group A (TAMSULOSIN 0.4 MG H.S)	22	8	30	X 2 = 31.985 P= .000
	71.0%	13.6%	33.3%	
Group B (TOLTERODINE 2MG BID)	7	23	30	
	22.6%	39.0%	33.3%	
Group C (COMBINATION THERAPY)	2	28	30	
	6.5%	47.5%	33.3%	

Results: The average age of all included ninety patients was 28.14 years SD 7.57, with minimum age of 16 years & maximum age of 40 years. Mean IPSS score at baseline in Group A was 16.10 SD 5.73, In Group B mean score was 18.60 SD 4.42,

and in Group C mean was 17.433 SD 4.530.(P>.05). Mean IPSS score at 14 days in Group A was 11.033 SD 3.96, In Group B mean score was 7.033 SD 3.37, and in Group C mean score was 3.433 SD 2.812.(P<.000). Mean IPSS final score in Group A was 8.300 SD 3.38, In Group B mean score was 4.833 SD 3.33, and in Group C mean score was 1.533 SD 2.515.(P<.000).

IPSS and VAPS baseline, and final score were compared among three groups using paired sample t test. Mean IPSS baseline and final was 12.48 SD 6.33. (p <.000) and Mean VAPS baseline and final was 4.300 SD 4.45. (p <.000). (Table no:1,2).

On the basis of response totreatment, and improvement in IPSS score patients were categorized into responders and non-responders. In Group A 13.6% responded to treatment, in group B 39.0% responded to treatment and in Group C 47.5% responded to treatment. Chi-square test was used to assess statistical significance (X = 31.985, P < .000) (Table no 3).

Discussion:

DJ stents are widely used in endourology. For example, in anticipation to prevent obstruction of ureters, to avoid damage to the kidney because of obstruction or in anticipation to prevent the blockage because of stone burden after lithotripsy2. Ureteric stents are mostly used after difficult ureteroscopy or to prevent steinstrasse

following lithotripsy.[12] DJ stents are used in management of various renal tract pathology, but patients with DJ stents have been identified to complain of a series of stent associated symptoms. Lumbar pain, urinary frequency, urgency are main DJ related symptoms.[13] These symptoms are transitory and patients get symptomless after stent removal. The exact pathophysiology of stent related symptoms is mysterious. Thomas et al gave his opinion regarding these symptoms, and he postulated that in patients with indwelling DJ stent there is increased intrarenal pressure(upper coil) and irritation of trigone(lower coil) during urination which is the cause of stent related symptoms [14]. Joshi & his co-worker in their study mentioned that because of DJ stent related symptoms, 80% of patient have a decreased quality of life.[15] In order to resolve these stent related symptoms many studies have been done and different new ideas were brought in practise. Zimskind et al tried to change the material of stent in order to reduce symptoms. Lee et al studied tamsulosin and tolterodine in treatment of DJ symptoms with a placebo group.[16] sNo significant differences were showed by each group in the IPSS or VAPS. In their report it was found that stent position/ location was more important in development of DJ symptoms. IPSS score had remarkable change in the combination therapy group & VAP score was unremarkable. Following are the limitations of Lee et al study. On the preoperative day, few patients did not full filled the questionnaire. As a result, we could not make use of this questionnaire. Due to small groups study, valuable information couldn't be gathered. Hence, large scale, randomized, prospective study is required to get more precise information.

Conclusion

The conclusion of my study is that combination of tamsulosin and tolterodine was superior in relieving obstructive subscore, irritativesubscore and VAP score than the montherapy. Among monotherapy ,tolterodine and tamsulosin groups, tolterodine was better in relieving total IPSS and VAP score. Hence, combination of tamsulosin and tolterodine must be prescribed in the patients with DJ related symptoms.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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