A prospective randomized double blinded placebo controlled trial to study the effect of diuretics on shock wave lithotripsy treatment of renal and upper ureteric calculi

A prospective randomized double blinded placebo controlled trial to study the effect of diuretics on shock wave lithotripsy treatment of renal and upper ureteric calculi

A dissertation submitted to The Dr. M.G.R. Medical University, Tamil Nadu, in partial fulfillment of the requirements for M.Ch. Branch-IV (Genitourinary surgery) examination to be held in August 2013.

Department of Urology

Christian Medical College and Hospital

Vellore, Tamil Nadu

Certificate

This is to certify that the work incorporated in this dissertation entitled "**A prospective randomized double blind placebo controlled trial to study the effect of diuretics on shock wave lithotripsy treatment of renal and upper ureteric calculi**" is the bonafide work done by Dr. Sagar Sabharwal in partial fulfillment of the rules and regulations of MCh Branch IV (Genitourinary Surgery) examination of the Tamil Nadu Dr. MGR Medical University, Chennai to be held in August 2013.

Guide:

Dr. Antony Devasia

Professor and Head

Department of Urology, Unit 1

Christian Medical College,

Vellore - 632 004

Tamil Nadu, India

Head of Department:

Dr. Nitin Sudhakar Kekre

Professor and Head

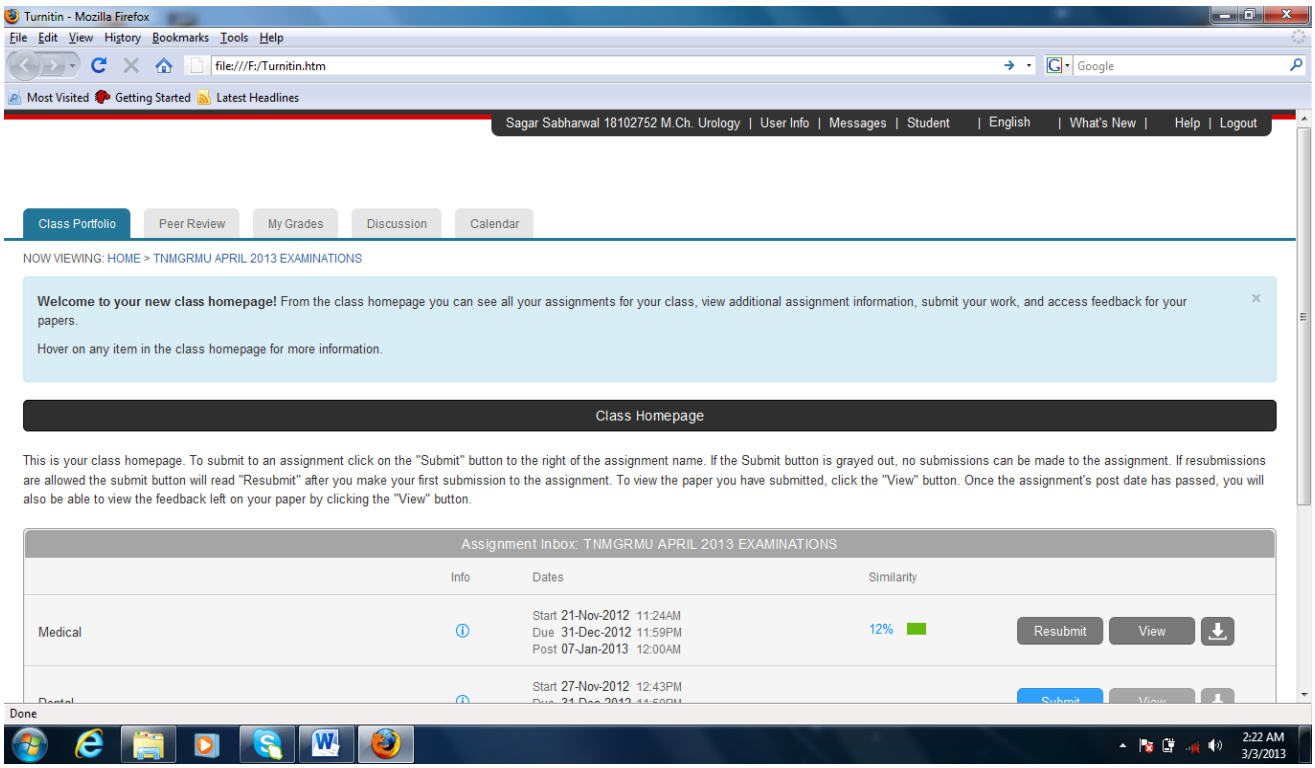
Department of Urology

Christian Medical College

Vellore - 632004

Tamil Nadu, India

Anti plagiarism certificate



Acknowledgements

I would like to express my deep gratitude to,

Professor Antony Devasia, my research supervisor for his patient guidance and enthusiastic encouragement

Professor Nitin Sudhakar Kekre for his useful critiques and constant reminders

Dr Rajiv Paul Mukha and Dr Arun Jacob Philip George for their constuctive suggestions and assistance in keeping my progress on schedule

My parents for their unlimited love and constant support

My wonderful wife for understanding and believing in me and for being by my side all along

Abbreviations

SWL	Shock wave lithotripsy
URS	Ureterorenoscopy
PCNL	Percutaneous nephrolithotomy
RIRS	Retrograde intrarenal surgery
UTI	Urinary tract infections
BMI	Body mass index
IVU	Intravenous urogram
CECT	Contrast enhanced computed tomogram
PID	Percussion, inversion and diuresis
MET	Medical expulsion therapy
IV	Intravenous
CIRF	Clinically insignificant residual fragments

Contents

Introduction

Introduction

The introduction of shock wave lithotripsy (SWL) treatment for renal and ureteric calculi in 1983 rapidly replaced open surgery for smaller stones. Over time the indications and techniques have been constantly redefined in pursuit of a better outcome.

With the arrival of minimally invasive surgical procedures like ureterorenoscopy (URS), percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS) the status of SWL has become all the more threatened. But, the unique stature of SWL as a practically 'no touch' approach in the treatment of urolithiasis scores over these minimally invasive techniques. It is therefore imperative, that a continuous effort is made to identify novel methods that can improve the treatment outcome of SWL.

One such method proposed is to provide diuresis during the shock wave session to enhance the fragmentation and clearance. This is a prospective randomized double blinded placebo controlled trial that aims to analyse the effect of diuretics on SWL treatment of renal and upper ureteric calculi.

Review of literature

Review of literature

History of SWL

SWL represents an offshoot of technology from military development. Dents were noticed on the wings of Lockheed F-104 fighter planes when they reached twice the speed of sound. Dornier – an aircraft business organisation from Germany investigated this and found that the supersonic shock waves generated by the falling rain drops caused local erosion as well as changes in the surrounding molecular structure.

Following this, a comprehensive research began involving Dornier and the Ludwig Maximilians University in Munich leading on to the first human treatment by Chaussy et al in 1980 using Dornier HM1 lithotriptor. The first Dornier HM3 was installed at the Klinikum Großhadern in Munich in 1983, thereafter, leading on to a global spread of lithotripters and a radical change in stone management.(1)

Technique of SWL, physics and theories of stone fragmentation and clearance

Essentials of lithotripsy include a shock wave generator, a system to converge the shock waves on a target, a stone localization system and a coupling medium.

A shock wave is a sonic pulse which consists of a rapid initial rise of peak pressure to about 50-80 MPa followed by a longer lower amplitude negative pressure of 10 MPa with a short life cycle of less than 10 microsecond.(2)

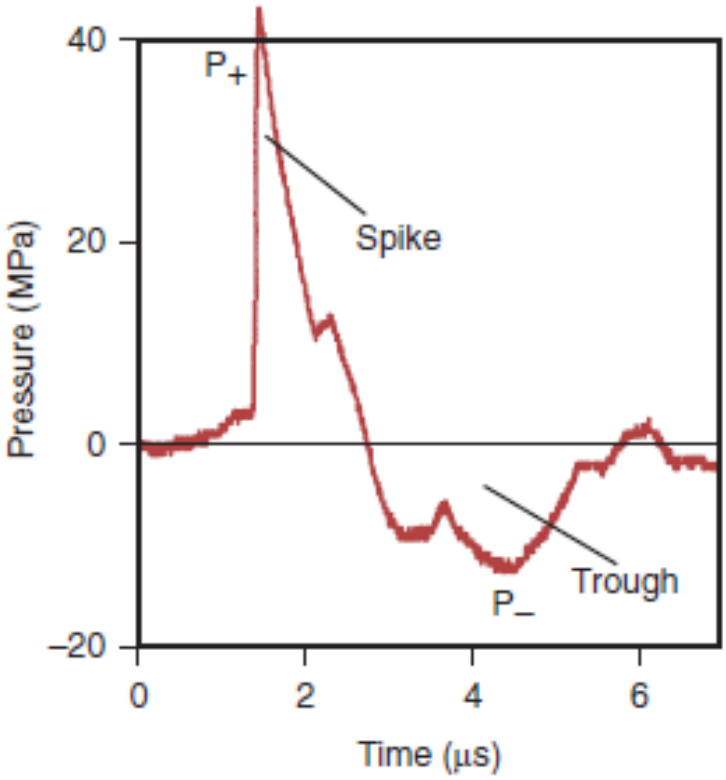


Figure 1: A typical pressure pulse at F2

Stones fragment as a result of stress induced by the shock wave. Cracks are induced which grow and accumulate with repeated shocks, finally leading on to stone disintegration. The mechanisms include tear and shear forces, cavitation, spallation, quasi-static squeezing and dynamic squeezing.(3)

Table 1: Existing theories of stone fragmentation (3)

Hypothesis	**Mechanism**	**Pre requisites**	**Action**	**Comments**
Tear and shear forces	Pressure gradients resulting from impedance changes at the front and distal stone surface with pressure inversion	Shock wave smaller in space extension than the stone	Hammer like action resulting in crater like fragmentation at both ends of the stone	Only relevant for small focal zones
Spallation	Reflected tensile wave at distal surface of the stone with maximum tension at the distal part of stone	Shock wave smaller in space extension than the stone	Breaking the stone from inside	Only relevant for small focal zones
Quasi static squeezing	Pressure gradient between	Shock wave is broader than stone. Shock	Nut cracker like action requiring large focal	Only relevant for large focal zones

	circumferential and longitudinal waves results in squeezing of the stone	wave velocity is lower in water than in stone	diameters	
Cavitation	Negative pressure waves induce a collapsing bubble at the stone surface		Microexplosive erosions at the proximal and distal ends of the stone	More important during stone comminution. Useful for improving the efficacy of shock waves
Dynamic squeezing	Shear waves initiated at the corner of the stone are reinforced by squeezing waves along the calculus	Parallel travelling of longitudinal waves. Shock wave velocity is lower in water than in stone	Nut cracker like action in combination with spalling	

Figure 2: Tear and shear forces and cavitation(4)

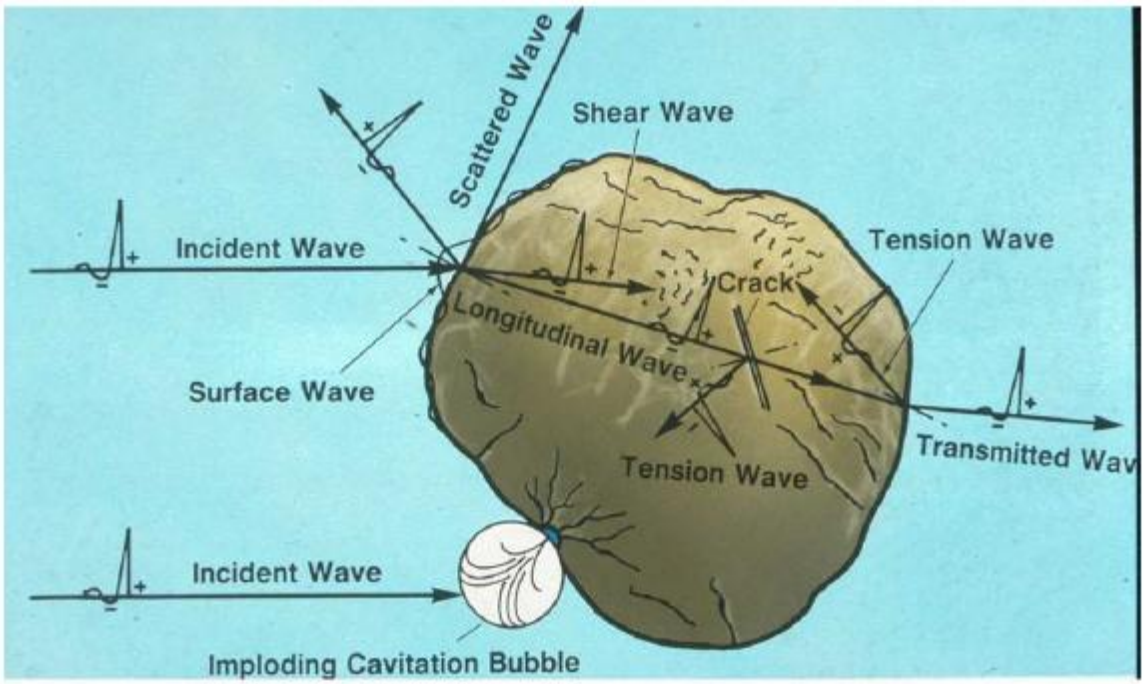


Figure 3: Spalling(3)

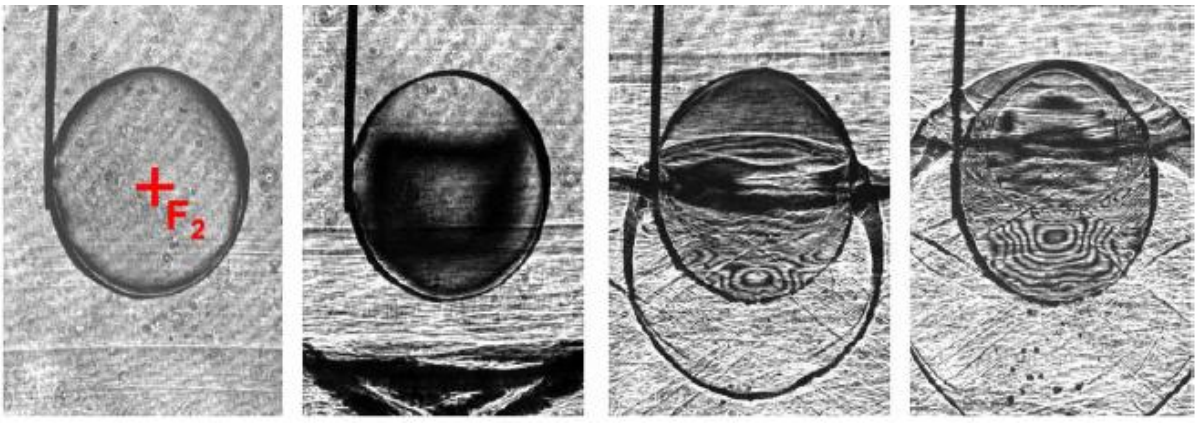
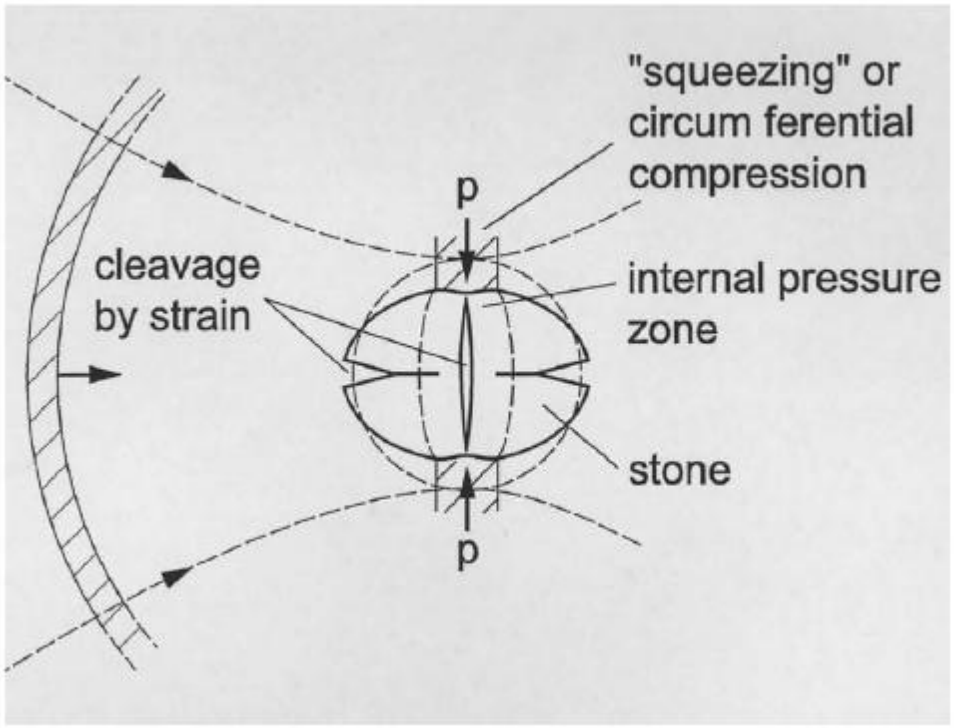


Figure 4: Quasistatic squeezing(4)



Presently, four different types of shock wave generators are used which includes electrohydraulic, electromagnetic, piezoelectric and electroconductive. The Dornier HM3 was the prototype first generation electohydraulic lithotripter, the most powerful till date with unmatched stone free rates of up to 90% in uncomplicated non lower polar calculi.(1,4)

Coupling media for SWL have ranged from an ideal water bath for Dornier HM3 to the present day water filled coupling cushions covered with ultrasound jelly. The efficiency of shock waves is inversely proportional to the area occupied by air pockets which can be minimised by the judicious use of jelly.(1,4)

Successful SWL depends on precise localisation and monitoring of the calculus during treatment. The modern day lithotripters have an option of fluoroscopic as well as ultrasound guided localisation techniques. Most often, the first line is the fluoroscopy which has it's inherent advantages of familiarity to the urologist, localisation of the ureteric calculi as well and the use of contrast agents, if needed.(1)

Indications

For renal and ureteric calculi are as follows;

Renal calculi (5)

Table 2: Recommended treatment for renal calculi (5)

Renal pelvic or upper/middle calyceal calculi	
> 2 cm	1. Endourology (PCNL, flexible URS) 2. SWL 3. Laparoscopy
1 – 2 cm	SWL or endourology
< 1 cm	1. SWL 2. Flexible URS 3. PCNL

Renal lower calyceal calculi			
> 2cm			1. Endourology (PCNL, flexible URS) 2. SWL
1 – 2 cm	Favourable factors for SWL	Yes	1. SWL 2. Endourology
		No	1. Endourology 2. SWL
< 1 cm			1. SWL 2. Flexible URS 3. PCNL

Recommendation	Grade
SWL is the first choice for stones < 2 cm within the renal pelvis and upper/middle calyces. Larger stones should be treated by PCNL	B
For lower calyx, PCNL or flexible URS are recommended even for stones > 1.5 cm because the efficacy of SWL is limited (depending on favourable/unfavourable factors)	B

Ureteric calculi(5)

Table 3: Recommended treatment for ureteric calculi

Stone size and location	First choice	Second choice
Proximal ureter < 10 mm	SWL	URS
Proximal ureter > 10 mm	URS (retrograde or antegrade) or SWL	
Distal ureter < 10 mm	URS or SWL	
Distal ureter > 10 mm	URS	SWL

Recommendation	Grade
Percutaneous antegrade removal of ureteral stones is an alternative when SWL is not indicated or has failed and when the upper urinary tract is not amenable to retrograde URS	A
Patients must be informed about the existing treatment modalities along with their risks/benefits	A

Contraindications

There are many contraindications for SWL;

• pregnancy, due to the potential disruptive outcome on the foetus

• bleeding diatheses; correction for at least 24 hours before and 48 hours after treatment

• untreated urinary tract infections (UTIs)

• skeletal malformations and severe obesity, which hinder targeting of the stone

• arterial aneurysm in the vicinity of the treated stone

• anatomic obstruction distal to the stone(5)

Complications

Table 4: Complications of SWL

Complications			Percentage
Stone fragment related		Steinstrasse	4 – 7
		Residual fragment regrowth	21 – 59
		Colic	2 -4
Infection		Bacteriuria	7.7 – 23
		Sepsis	1 - 2.7
Tissue effect	Renal	Haematoma, symptomatic	< 1
		Haematoma, asymptomatic	4 – 19
	Cardiovascular	Dysrhythmia	11 -59
		Morbid cardiac events	Case reports
	Gastrointestinal	Bowel perforation	Case reports
		Liver, spleen haematoma	Case reports

Relationship between SWL and diabetes/hypertension is unclear. Published data are contradictory and no conclusions can be reached.(5)

Anticipated clinical outcome

A few patients are likely to fail SWL treatment and pretreatment identification of such patients avoids needless shock wave exposure. Alternative treatment modalities should be employed in these situations.

- Stone burden is one of the most important factors and includes both stone size and number. SWL is usually not preferred for stone size > 20mm.
- Stone position: infundibulopelvic angle and infundibular width/length and calyx pelvic height have a bearing on the clearance of lower calyceal calculi.
- Stone composition: very hard stones like cystine, brushite, calcium oxalate monohydrate and very soft stones like matrix calculi have poor fragmentation.
- Anatomical abnormalities: like horseshoe kidneys, malrotated or duplex systems, calyceal diverticulae and post operative strictures have lower clearance rates.
- Obesity with a body mass index (BMI) of > 25-30.(1,6,7,8)

Optimal clinical practise and how to enhance success rate

- Pre treatment imaging: intravenous urogram (IVU) or non contrast/ contrast enhanced CT scan is required for appropriate delineation of the calculus and the collecting system.
- Pre SWL stenting: is only indicated in special situations like single functioning kidney, a very large stone bulk or when follow up is likely to be less stringent. This may actually reduce clearance rates.
- Antibiotic prophylaxis: antibiotics are indicated in case of positive culture, suspicion of infection stones, history of instrumentation or UTI's and presence of foreign bodies like stents/ nephrostomies.
- Shock wave rate: rather than a high shock wave frequency of 100-120 per minute, lower rates are presently recommended. This leads to better fragmentation and less tissue damage.
- Power ramping: SWL sessions should be stepped up from low to high energy levels so as to trigger vasoconstriction and thus causing lesser kidney damage.
- Mechanical percussion, inversion and diuresis (PID) therapy: is recommended for lower calyceal calculi.
- Adjuvant drug therapy: medical expulsion therapy (MET) using α blockers or calcium channel blockers reduces pain and time to stone expulsion as well as brings about higher stone free rates.(1,5,9,10,11,12,13,14,15)

Role of diuresis

Diuresis has been proposed as a factor which might enhance both fragmentation and clearance of renal and ureteric calculi. Fragmentation is facilitated by a fluid film interface between the stone and ureteric wall. Also, the initial shockwaves break the outer shell of the calculus and further disintegration of the core is enhanced by the seepage of fluid below the cracks, creating an interface. Thus, the effect of the collapsing cavitation bubble is enhanced. It is also proposed that diuretics reduce therequirement of total number of shocks and sessions.(16,17,18,19)

Material and methods

Material and methods

Design and location

This hospital based prospective randomized double blinded placebo controlled trial was conducted at the Department of Urology, Christian Medical College, Vellore.

Duration

Between June 2011 and December 2012.

Patients

Patients with renal and upper ureteric calculi who satisfied the following inclusion and exclusion criteria were included;

Inclusion criteria

Age: adults > 18 years

Non obstructive radio opaque renal and upper ureteric calculi up to 1.5 cm (obstruction – no contrast seen beyond the calculus up to the 1 hour film on intravenous urogram)

Sterile or treated urine culture

Normal renal function (creatinine up to 1.4 mg%)

Exclusion criteria

Anatomical abnormality

Distal obstruction

Morbid obesity (body mass index > 40)

Pregnancy

Coagulopathy

History of any previous intervention on the same side

Significant cardiac history

Methodology

Patients underwent SWL as an out-patient procedure. They were allocated by block randomization to either SWL or SWL along with diuretics (placebo or 40 mg furosemide iv at the start of SWL). 'Dornier Compact Delta 2' electromagnetic lithotripter was used. As per protocol they received shocks at a rate of 80/min starting at 7kv with dose escalation up to 16kv until the stone fragmented or up to a maximum of 1500/2000 shocks per session (for renal and upper ureteric calculi respectively) up to a maximum of 3 sessions for stones up to 1 cm and 4 for stones between 1-1.5cm. Imaging was repeated at 4 days & repeat sessions were instituted if required i.e failure of fragmentation, fragments larger than 5mm or lead fragment larger than 4mm.

To minimise interindividual variation in fluid intake and eliminate bias, all patients were given a target intake value (volume in ml = weight in kg x 50), made to strictly adhere to it and followed up with frequency-volume charts.

Data was collected regarding procedure related events like

Number of shock and sessions required

Duration of treatment

Frequency-volume charts to monitor intake-output

Figure 5: Dornier Compact Delta 2 lithotriptor used at our institution

Complications like pain, haematuria, fever, steinstrasse and need for ancillary procedure like percutaneous nephrostomy or DJ stenting.

Method of randomization:

Stratified block randomization was done. The patients were divided into 2 strata;

Stratum 1: calculi upto 1 cm

Stratum 2: calculus size from 1.1 to 1.5 cm

In each Stratum, block randomization was done using SAS software with the blocks of 2, 4 and 6. That is, 25%, 50% and 25% of 2, 4 and 6 blocks was done respectively. This was done by the Department of Biostatistics, Christian Medical College, Vellore.

Method of allocation concealment:

The Department of Biostatistics prepared sealed opaque envelops and sent these to the Pharmacy department**.**

Masking

The subjects and the investigators were blinded for the allocation.

Primary Outcome:

SWL failure (fragmentation): no fragmentation after 3/4 sessions

Success rate (clearance): Stone free after 3/4 sessions

For renal calculi, clinically insignificant residual fragments (CIRF) were included as successful outcome in calculating the success rate. However, any residual fragments for ureteric calculi were considered as a failure for the calculation of success rate.

Secondary Outcome:

Number of shocks and sessions

Target sample size and rationale:

Based on the review, the clearance rates have been reported to be 70 to 80%. It was assumed that the clearance rate would be around 70% in the placebo arm or in the conventional treatment. We proposed to suggest diuretics only if there was an improvement of 20% with alpha = 5% and power = 80%. The number of subjects, thus needed was 48 in each arm.

Table 5: Sample size calculation

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation					
Proportion of clearance in the placebo arm	0.8	0.8	0.8	0.7	**0.7**
Proportion of clearance in the Furosemide arm	0.9	0.95	0.95	0.85	**0.9**
Estimated risk difference	-0.1	-0.15	-0.15	-0.15	**-0.2**
Power (1- beta) %	80	80	70	80	**80**
Alpha error (%)	5	5	5	5	**5**
1 or 2 sided	2	1	1	1	**1**
Required sample size for each arm	199	59	45	95	**48**

Statistical analysis

Descriptive statistics such as mean, median, standard deviation and range were calculated for each study variable. The distribution of study and outcome variables was tabulated according to the outcome variable fragmentation and clearance (yes/no). Chi-square test was done to study the difference between two proportions and Wilcoxson Mann Whitney two sample test to compare the two groups.

For statistical analysis n-Master version 2 software was used.

Results

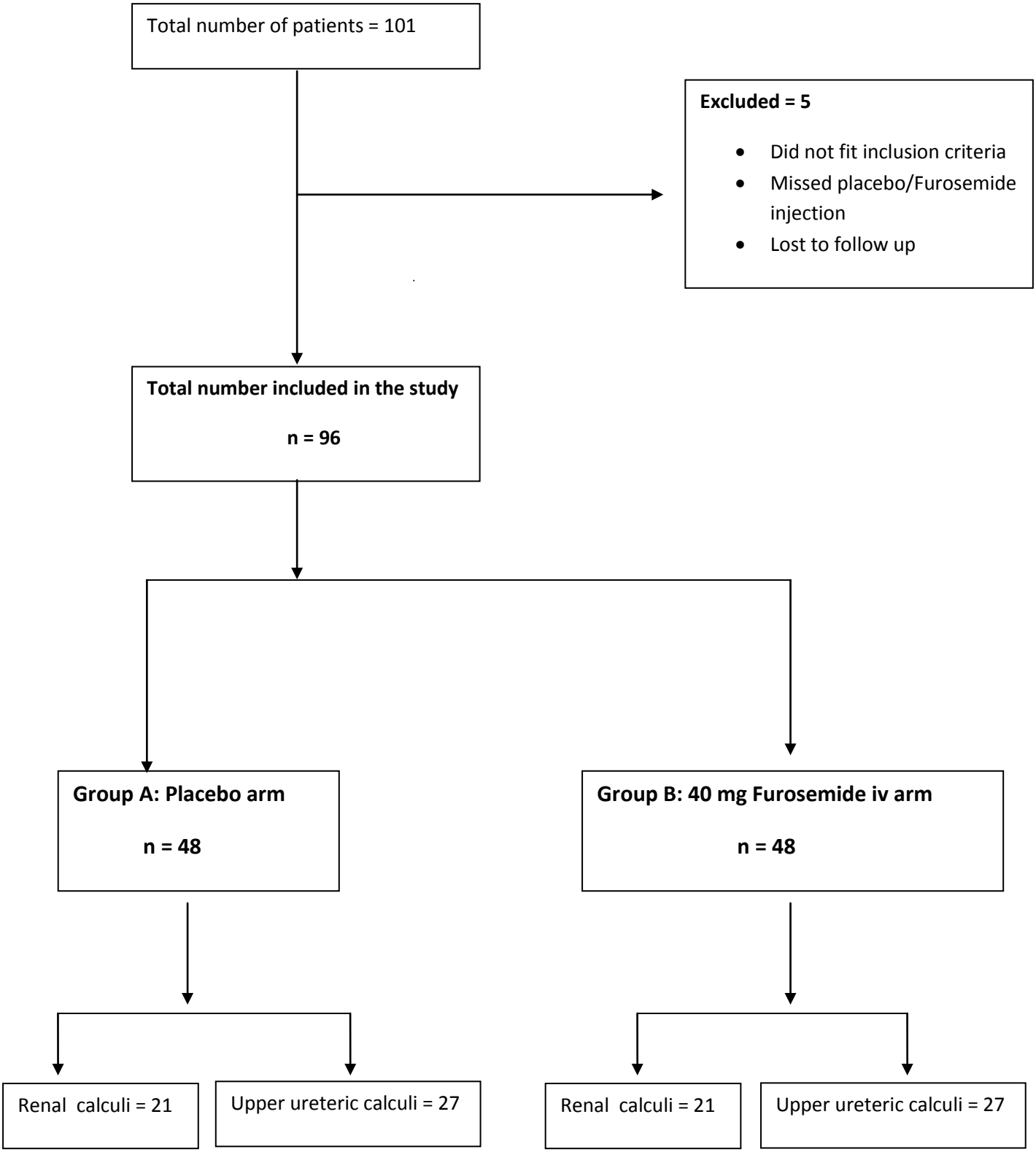
Results

During the study period from June 2011 to December 2012, a total of 96 patients were included. These comprised both renal and upper ureteric calculi as per inclusion criteria. They were randomised into two groups;

Group A: Placebo arm

Group B: 40 mg Furosemide iv arm

Figure 6: CONSORT flow diagram



The mean age in group A was 39.45 years and group B was 38.56 years.

Table 6: Age of patients

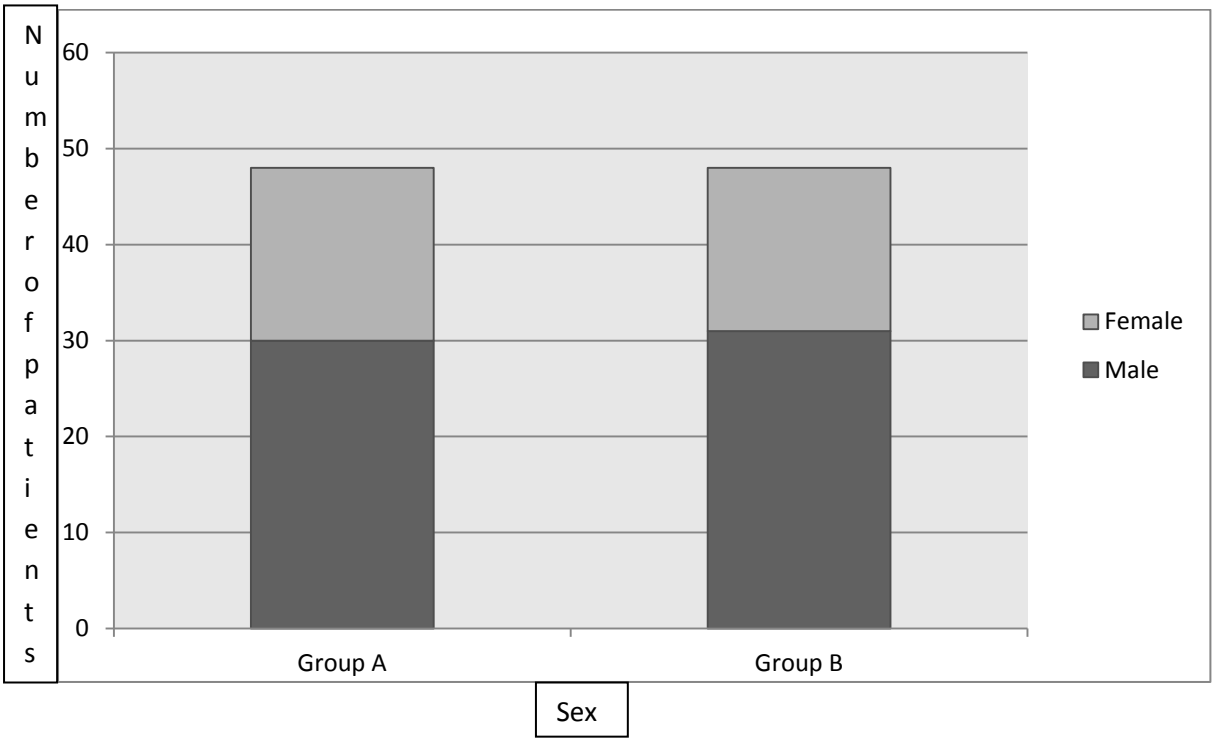
Mean age in years (range)	**Group A**	**Group B**
	39.458 (20 – 61)	38.562 (18 – 56)

The female to male ratio was almost similar in both groups. There were 30 men and 18 women in group A, whereas in group B it was 31 men and 17 women.

Table 7: Sex ratio

Sex	**Group A (n = 48)**	**Group B (n = 48)**
Male (percentage)	30 (62.50)	31 (64.58)
Female (percentage)	18 (37.50)	17 (35.42)

Figure 7: Sex ratio



The mean weight of the patients in group A was 61.16 kg and in group B was 61.39 kg.

Table 8: Weight of patients

Mean weight in kilograms (range)	**Group A**	**Group B**
	61.166 (35 – 80)	61.395 (42 – 90)

The mean calculus size in group A was 9.26 mm and group B was 9.41 mm.

Table 9: Calculus size

Mean calculus size in millimetres (range)	**Group A**	**Group B**
	9.260 (4 – 15)	9.416 (5 – 15)

The details were as follows;

Figure 8: Calculus size in group B

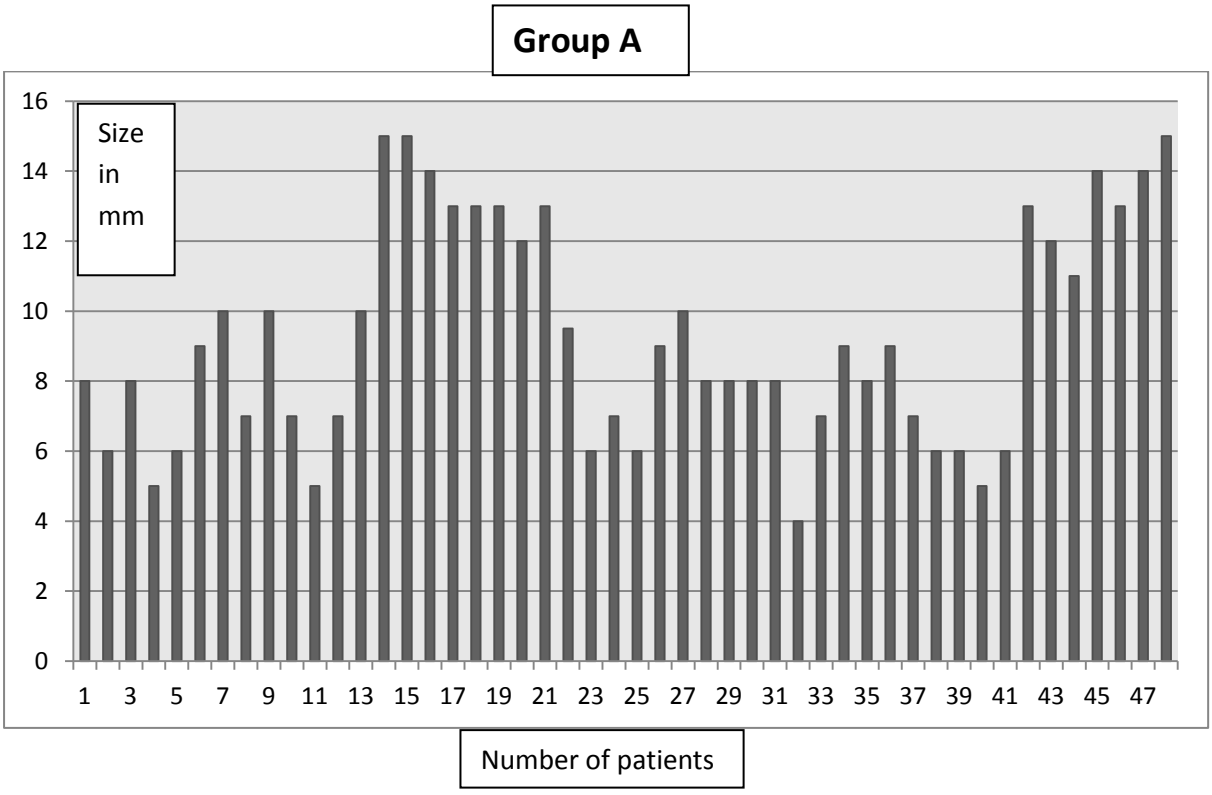
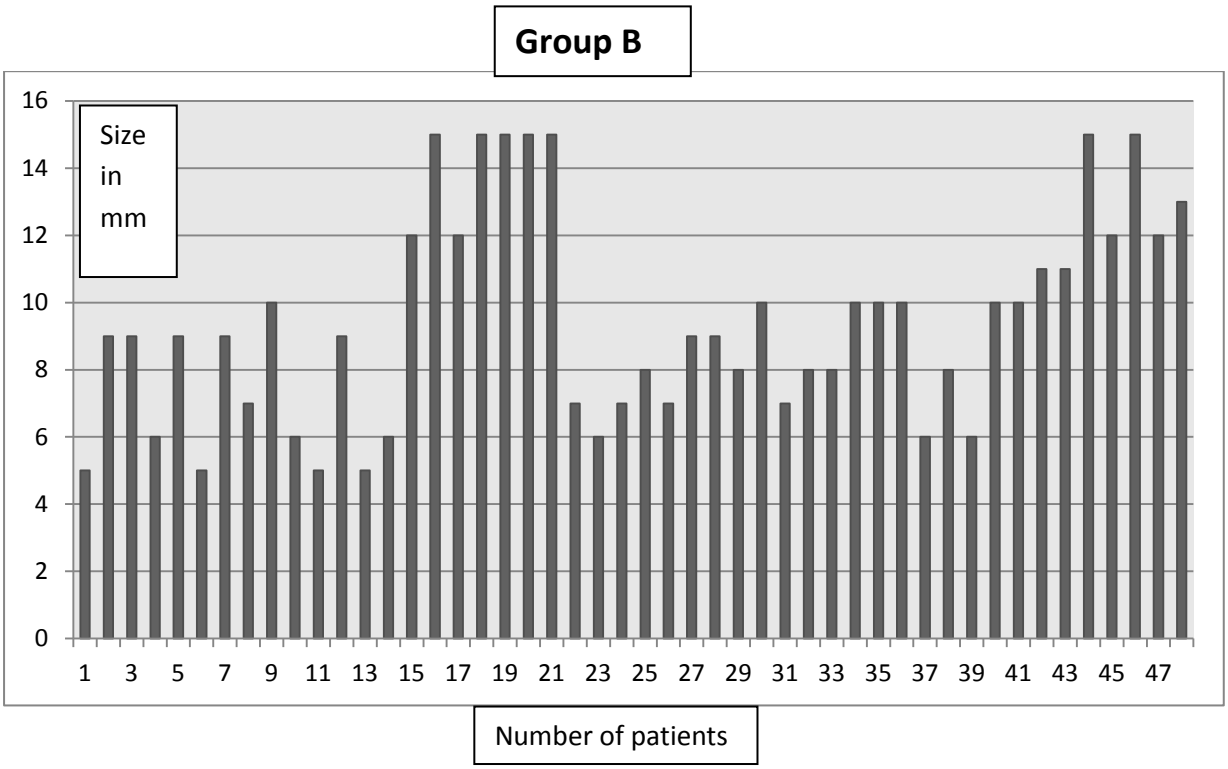


Figure 9: Calculus size in group B



The detail of the site of the calculi was as follows;

Table 10: C aculus site

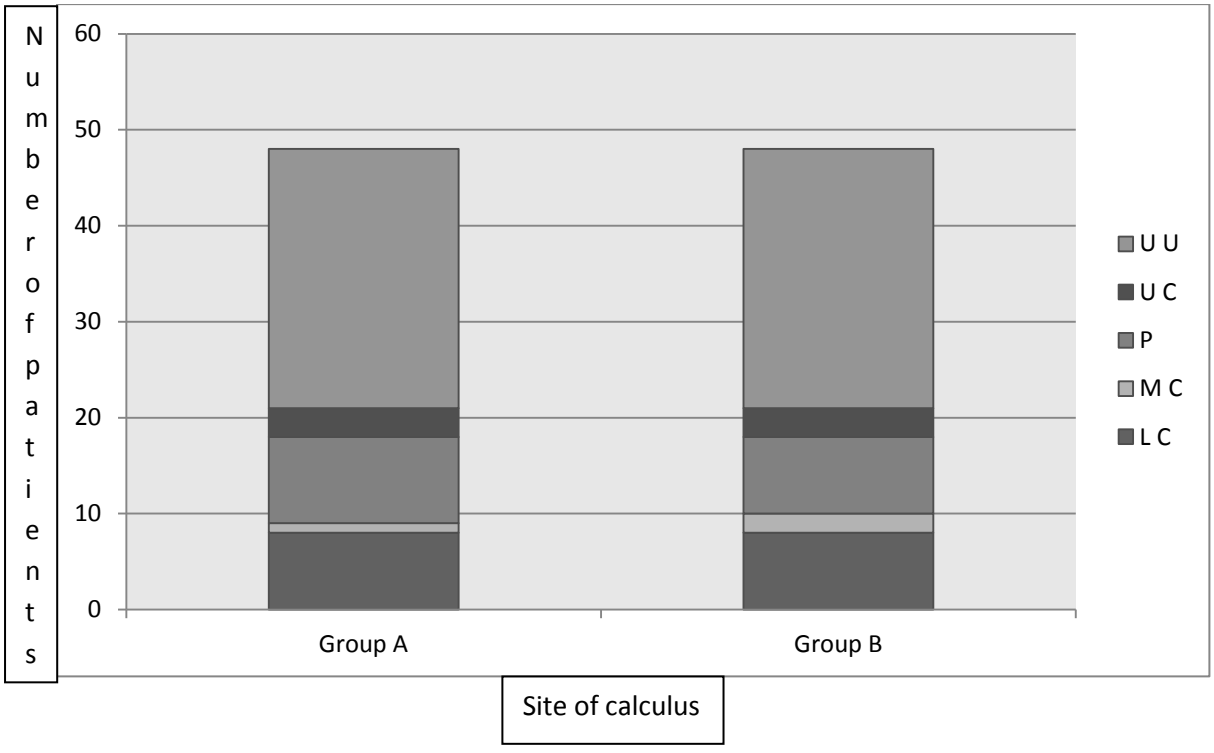
Site of the calculus	**Group A**		**Site of the calculus**	**Group B**	
	n	**%**		**n**	**%**
L LC	4	8.33	**L LC**	2	4.17
L P	5	10.42	**L MC**	2	4.17
L UC	1	2.08	**L P**	4	8.33
L UU	8	16.67	**L UC**	2	4.17
R LC	4	8.33	**L UU**	14	29.17
R MC	1	2.08	**R LC**	6	12.50
R P	4	8.33	**R P**	4	8.33
R UC	2	4.17	**R UC**	1	2.08
R UU	19	39.58	**R UU**	13	27.08

L = left, R = right, LC = lower calyx, P = pelvis, MC = middle calyx, UC = upper calyx, UU = upper ureter

This shows that the groups were evenly matched according to the site of calculi as well.

Site of the calculus	Group A		Group B	
	n	%	n	%
Lower calyx	8	16.66	8	16.66
Middle calyx	1	2.08	2	4.16
Pelvis	9	18.75	8	16.66
Upper calyx	3	6.25	3	6.25
Upper ureter	27	56.25	27	56.25

Figure 10: Calculus site



LC = lower calyx, P = pelvis, MC = middle calyx, UC = upper calyx, UU = upper ureter

The mean serum creatinine in group A was 1.12 mg% and in group was 1.04 mg%.

Table 11: Serum creatinine

Mean serum creatinine in mg% (range)	**Group A**	**Group B**
	1.122 (0.4 – 1.4)	1.047 (0.75 – 1.4)

The mean total number of shocks required for group A was 3849.79 and group B was 3661.46**.**

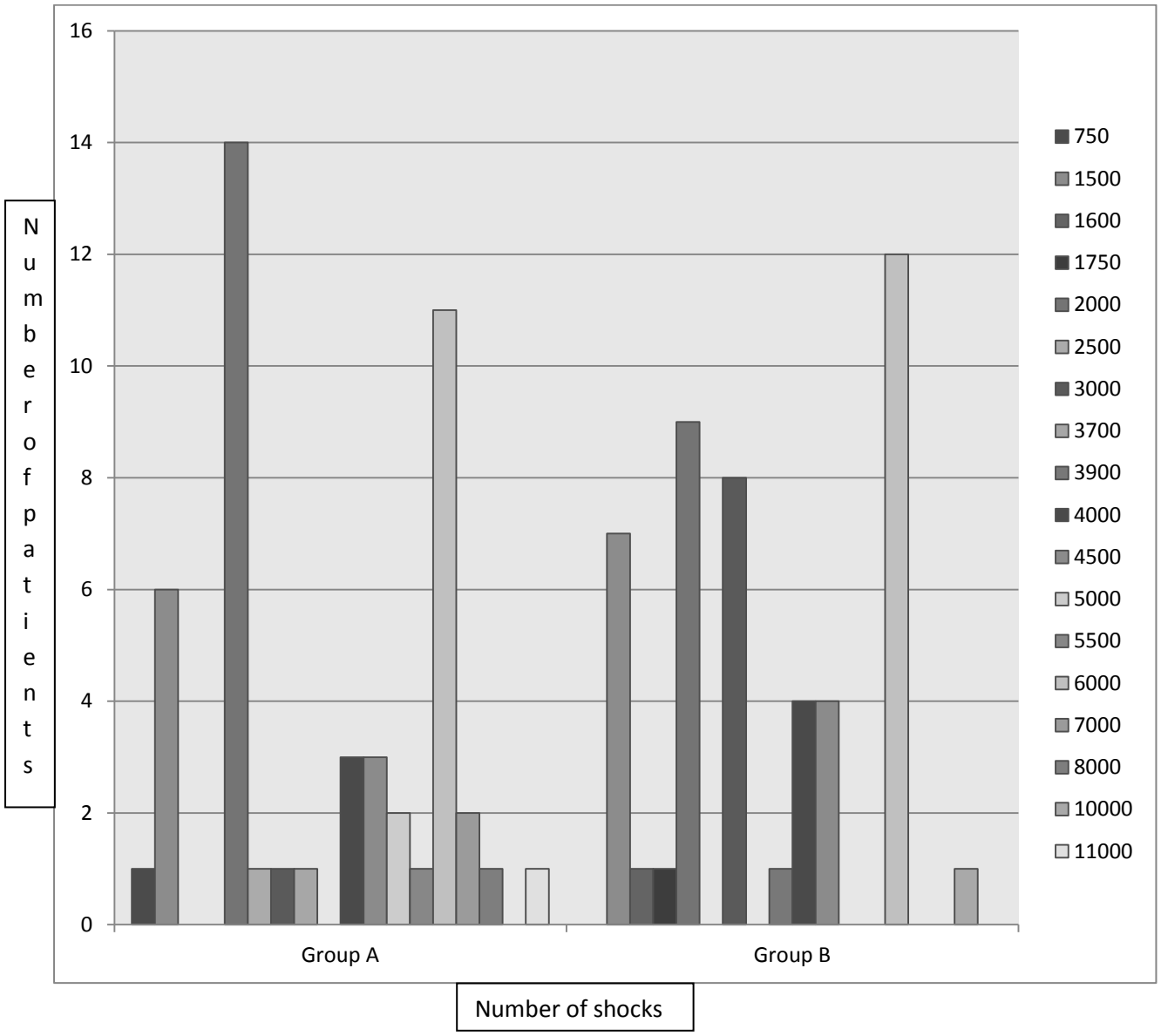
Table 12: Number of shocks

Mean total number of shocks (range)	**Group A**	**Group B**
	3849.79 (750 – 11000)	3661.46 (1500 – 10000)

The details of the number of shocks were as follows;

Total number of shocks	**Group A**		**Total number of shocks**	**Group B**	
	n	**%**		**n**	**%**
750	1	2.08	**1500**	7	14.58
1500	6	12.50	**1600**	1	2.08
2000	14	29.17	**1750**	1	2.08
2500	1	2.08	**2000**	9	18.75
3000	1	2.08	**3000**	8	16.67
3700	1	2.08	**3900**	1	2.08
4000	3	6.25	**4000**	4	8.33
4500	3	6.25	**4500**	4	8.33
5000	2	4.17	**6000**	12	25.00
5500	1	2.08	**10000**	1	2.08
6000	11	22.92			
7000	2	4.17			
8000	1	2.08			
11000	1	2.08			

Figure 11: Number of shocks



The mean total number of sessions for group A was 2.25 and group B was 2.12.

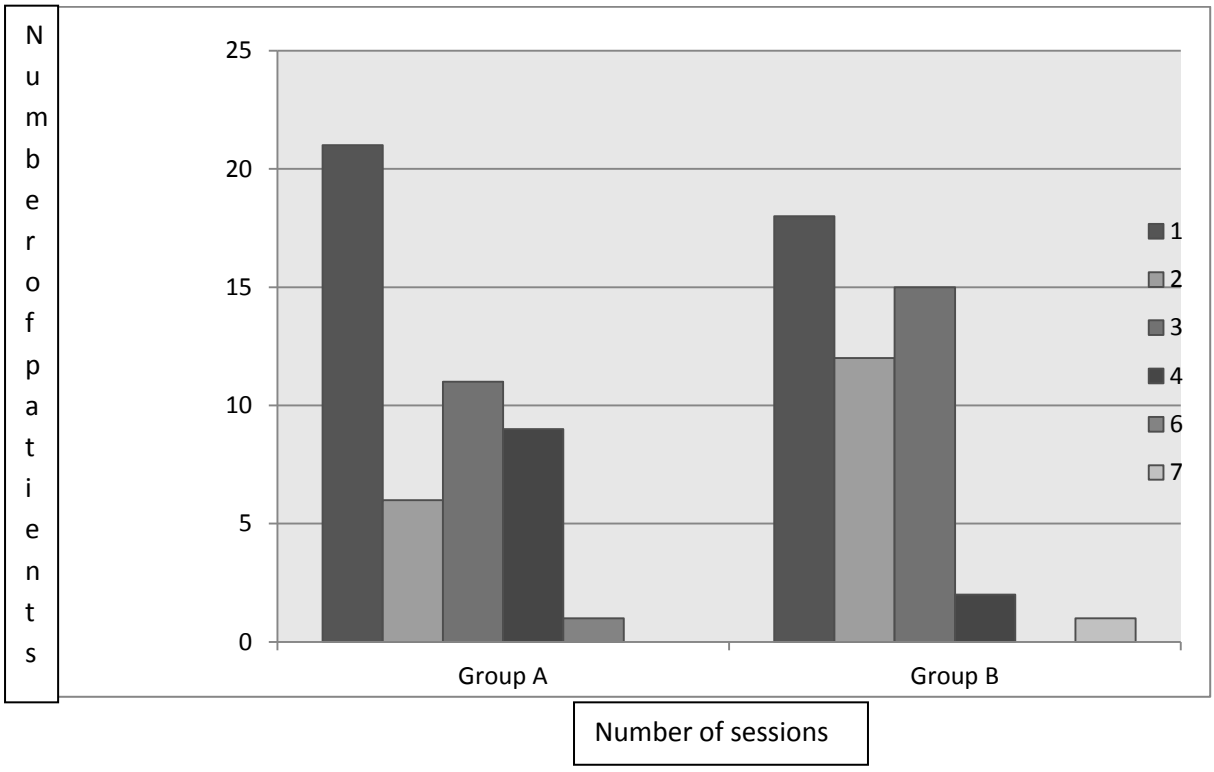
Table 13: Number of sessions

Mean total number of sessions (range)	**Group A**	**Group B**
	2.25 (1 – 6)	2.12 (1 – 7)

The details of the number of sessions were as follows;

Number of sessions	Group A		Number of sessions	Group B	
	n	%		N	%
1	21	43.75	**1**	18	37.50
2	6	12.50	**2**	12	25.00
3	11	22.92	**3**	15	31.25
4	9	18.75	**4**	2	4.17
6	1	2.08	**7**	1	2.08

Figure 12: Number of sessions



The fragmentation of calculi in both the groups was as follows;

Table 14: Fragmentation

Fragmentation	**Group A**		**Group B**	
	N	**%**	**n**	**%**
Complete	39	81.25	43	89.58
Failed	9	18.75	5	10.42

Figure 13: Fragmentation

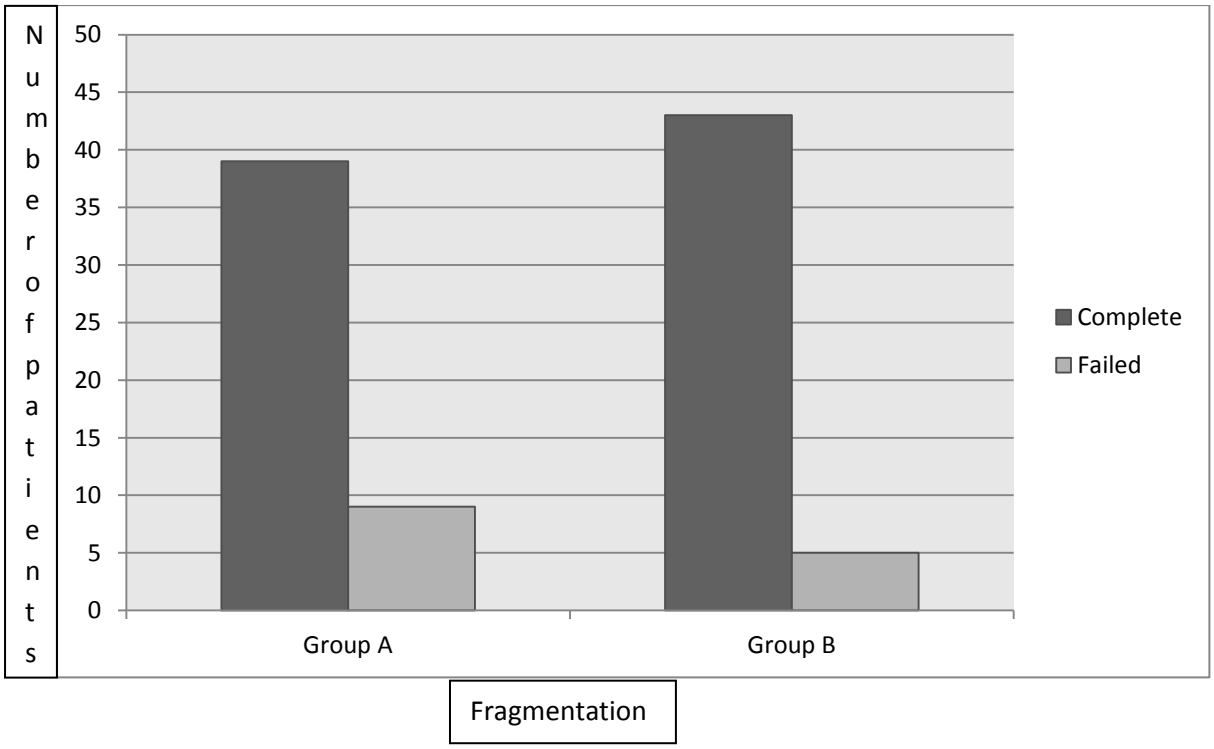
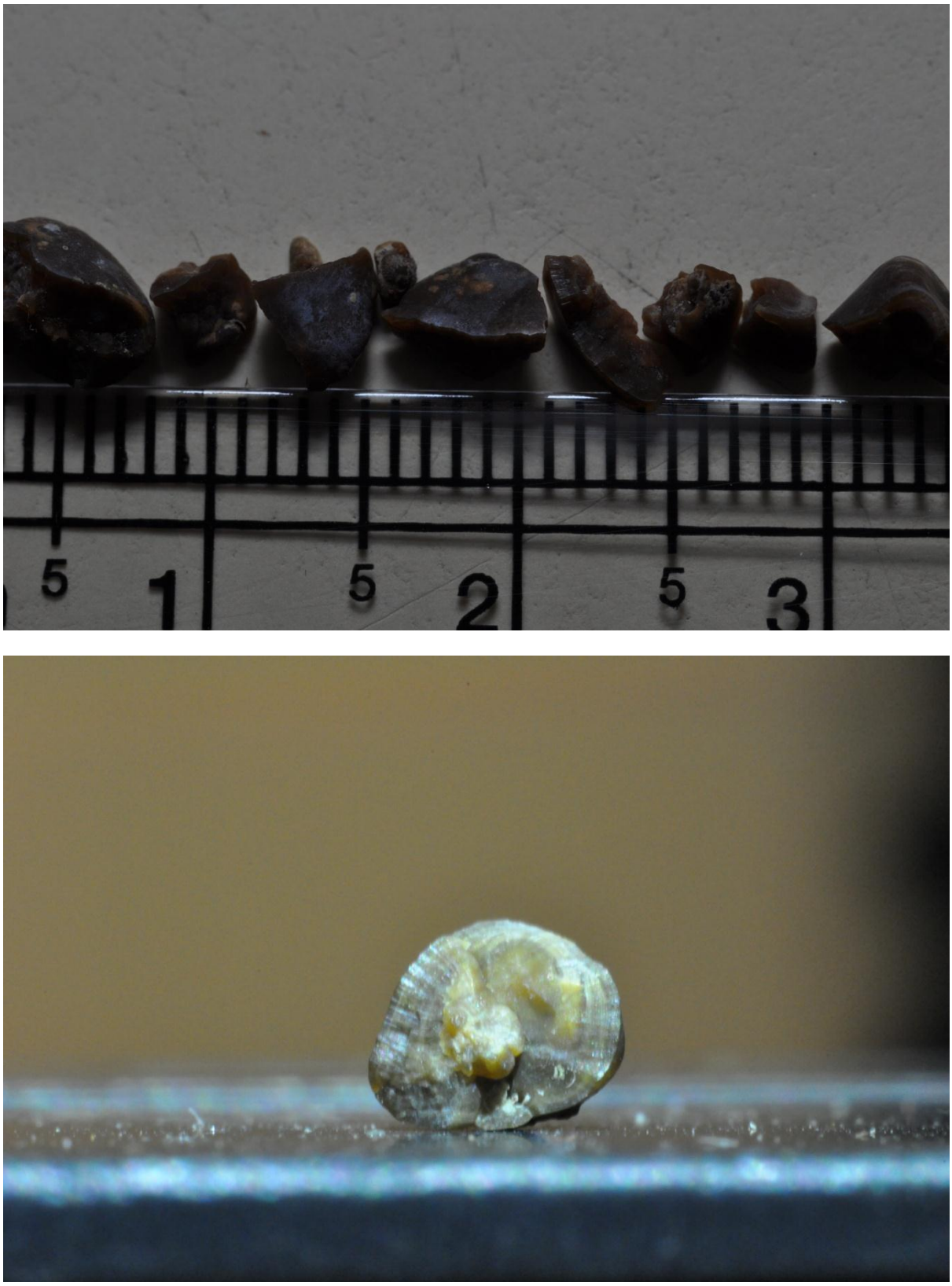


Figure 14: Fragmented and cleared calculi

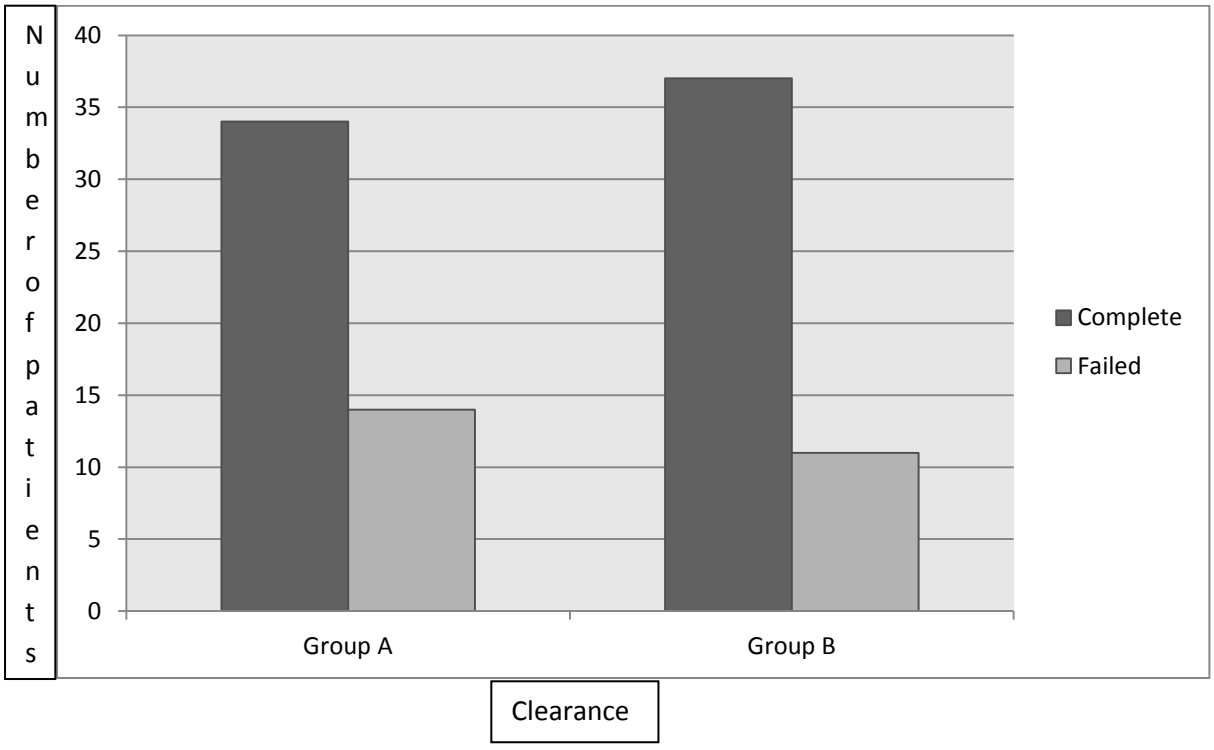


The clearance of calculi in both the groups was as follows;

Table 15: Clearance

Clearance	**Group A**		**Group B**	
	N	**%**	**n**	**%**
Complete	34	70.83	37	77.08
Failed	14	29.17	11	22.92

Figure 15: Clearance



The mean duration of treatment in group A was 11.43 days and group B was 11.91 days.

Table 16: Duration of treatment

Mean duration of treatment in days (range)	**Group A**	**Group B**
	11.43 (3 – 30)	11.91 (4 – 45)

When the primary outcomes were analysed, it was seen that complete fragmentation was achieved in 89.58% of the patients in the Furosemide arm as compared to 81.25% in the placebo arm. Clearance of the fragments was achieved in 77.08% of the patients in the Furosemide arm as compared to 70.83% in the placebo arm. On analysis, there was no statistically significant difference between the groups for both fragmentation and clearance, though the rates were higher in the Furosemide arm.

Table 17: Statistical analysis of fragmentation and clearance of calculi

Fragmentation	**Group A**		**Group B**		**Effect size**	**95% C I**	**p value**
	n	**%**	**n**	**%**	**%**		
Complete	39	81.25	43	89.58	-8.33	(-22.35, 5.69)	0.25
Failed	9	18.75	5	10.42			
Total	48	100.00	48	100.00			

Clearance	**Group A**		**Group B**		**Effect size**	**95% C I**	**p value**
	n	**%**	**n**	**%**	**%**		
Complete	34	70.83	37	77.08	-6.25	(-23.76, 11.26)	0.49
Failed	14	29.17	11	22.92			
Total	48	100.00	48	100.00			

Similarly, the difference in the total number of shocks required, which was a secondary outcome, was not statistically significant between the two groups, though the mean total number of shocks required was higher in the placebo arm.

Table 18: Statistical analysis of number of shocks

Total number of shocks	**Group A**					**p value***
	Mean	**SD**	**Median**	**Q1**	**Q3**	
	3894.79	2254.41	3850	2000	6000	
	Group b					0.68
	Mean	**SD**	**Median**	**Q1**	**Q3**	
	3661.46	1946.53	3000	2000	6000	

* Non Parametric Wilcoxon two sample test

When the total number of sessions required were analysed, it was seen that a higher number of patients required ≥ 3 sessions in the placebo arm as compared to the Furosemide arm.

Table 19: Number of sessions

Number of sessions	**Group A**		**Number of sessions**	**Group B**	
	n	**%**		**n**	**%**
1	21	43.75	**1**	18	37.50
2	6	12.50	**2**	12	25.00
3	11	22.92	**3**	15	31.25
4	9	18.75	**4**	2	4.17
6	1	2.08	**7**	1	2.08

Discussion

Discussion

SWL has established itself as a frontline treatment modality for renal and ureteric calculi, since its inception in the early 1980's. However, the constant rise in technology and the challenge offered by newer techniques like URS, PCNL and RIRS highlights the need to evolve novel strategies to improve treatment outcomes and thus, continue to play an important role as a treatment option.

Various attempts have been made in the past to enhance the effectiveness of SWL, which have become a part of the standard treatment protocol today. These include lower shock wave rate, power ramping, percussion, inversion and diuresis (PID) for lower calyceal calculi and medical expulsion therapy (MET) using α-blockers.

This study aimed at assessing the effect of diuretics on SWL. Set in the Christian Medical College Vellore, a tertiary care teaching hospital in Tamil Nadu, we analysed a group of patients with renal and upper ureteric calculi who underwent SWL treatment for the same and the effect of diuretics (placebo versus 40 mg furosemide iv) on stone fragmentation and clearance.

We found that, though the fragmentation of calculi was higher in the Furosemide arm as compared to placebo arm, it was not statistically significant. Similarly, there was no statistical difference detected in the clearance of the fragments.

The total number of shocks and sessions required was lesser in the Furosemide arm in comparison to the placebo arm, though this too did not reach statistical significance.

Our study was in concordance with the study by Azm TA et al who reported an overall fragmentation rate of 87% for ureteric calculi in the control group versus 96.2% in the furosemide arm. Stone clearance rates were reported as 87% versus 92.3% respectively. However, when further analysed according to the site of the calculus, the two groups were comparable for upper and mid ureteric calculi. Significant difference was achieved between the two groups only for the distal ureteric calculi (93.8% versus 70.6% for fragmentation and 87.5% versus 70.6% for clearance in the furosemide and control groups respectively). Lower number of shocks and sessions were required in the Furosemide group (5300 versus 6295 average shocks and 1.5 versus 1.92 average number of sessions for Furosemide versus control group respectively).

Zomorrodi A et al reported a much higher difference in both stone fragmentation and clearance for ureteric calculi using 40 mg Furosemide before the start of SWL. Fragmentation was achieved in 93.1% versus 81% in the Furosemide and control groups respectively. Clearance was reported as 88.4% versus 68.2% for the above groups.

For lower calyceal calculi Tahir MM et al reported a clearance rate of 73.3% using 20 mg Furosemide versus 60% in the control arm.

Though the results of our study were similar to those reported in the literature, the differences achieved in the placebo versus Furosemide arm were not high enough to achieve statistical significance. However, this is the first randomised double blinded placebo controlled trial to

demonstrate higher, though marginal fragmentation and clearance rates in addition to the requirement of a lower mean number of shocks and sessions for SWL using diuretics.

Conclusions

Conclusions

The use of diuretics along with SWL treatment of renal and upper ureteric calculi results in higher fragmentation and clearance rates along with a requirement of lower number of shocks and sessions, though not statistically significant.

Bibliography

Bibliography

1. Bach C, Buchholz N. Shock Wave Lithotripsy for Renal and Ureteric Stones. Eur Urol Suppl. 2011;10:423-32.
2. Ogden JA, Toth-kischkat A, Schultheiss R. Principles of shock wave therapy. Clin Orthop Rel Res. 2001;387:8-17.
3. Rassweiler JJ, Knoll T, Köhrmann K-U, et al. Shock wave technology and application: an update. Eur Urol 2011;59:784–96
4. Rassweiler JJ, Tailly GG, Chaussy C. Progress in lithotripter technology. EAU Update Series. 2005;3:17-36.
5. Türk C, Knoll T, Petrik A, Sarica K, Straub M, Seitz C. Guidelines on urolithiasis. European Association of Urology; 2012.
6. Chongruksut W, Lojanapiwat B, Ayudhya VCN, Tawichasri C, Patumanond J,Paichitvichean S. Prognostic factors for success in treating kidney stones by extracorporeal shock wave lithotripsy. J Med Assoc Thai. 2011;94(3):331-36.
7. Ceban E. The treatmet of reno-ureteral calculi by extracorporeal shockwave lithotripsy. J Med Life. 2012;5(2):133–138.
8. Tuckey J, Devasia A, Murthy L, Ramsden P, Thomas D. Is there a simpler method for predicting lower pole stone clearance after shockwave lithotripsy than measuring infundibulopelvic angle? J Endourol. 2000;14:475-78.
9. Haleblian G, Kijvikai K, Rosette J, Preminger G. Ureteral stenting and urinary stone management: A systematic review. J Urol. 2008;179:424-30.

10. Rajain S, Kumar S, Gopalakrishnan G, Chacko NK, Devasia A, Kekre NS. Outcome of shockwave lithotripsy as monotherapy for large solitary renal stones (>2cm in size) without stenting. Indian J Urol. 2010;26:359-63.
11. Madbouly K, Moneim el-tiraifi A, Seida M, El-faqih SR, Atassi R, Talic RF. Slow versus fast shock wave lithotripsy rate for urolithiasis: a prospective randomized study. J Urol.2005;173:127-30.
12. Lingeman JE, McAteer JA, Gnessin E, Evan AP. Shock wave lithotripsy: advances in technology and technique. Nat Rev Urol. 2009;6(12):660–70.
13. Bach C, Karaolides T, Buchholz N. Extracorporeal shock wave lithotripsy: What is new? Arab J Urol . 2012;10:289–95.
14. Chiong E, Hwee STP, Kay LM, Liang S, Kamaraj R, Esuvaranathan K. Randomized controlled study of mechanical percussion, diuresis, and inversion therapy to assist passage of lower pole renal calculi after shock wave lithotripsy. Urol. 2005;65(6):1070-74.
15. Bhagat SK, Chacko NK, Kekre NS, Gopalakrishnan G, Antonisamy B, Devasia A. Is there a role for tamsulosin in shock wave lithotripsy for renal and ureteral calculi? J Urol. 2007;177:2185-88.
16. Azm TA, Higazy H. Effect of diuresis on extracorporeal shockwave lithotripsy treatment of ureteric calculi. Scand J Urol Nephrol. 2002;36:209–12.
17. Zomorrodi A, Golivandan J, Samady J. Effect of diuretics on ureteral stone therapy with extracorporeal shockwave lithotripsy. Saudi J Kidney Dis Transpl. 2008;19(3):397-400.

18. Tahir MM, Khan MU, Ghauri S. Extracorporeal shockwave lithotripsy; Impact of diuresis on the clearance of lower pole renal calculi. Professional Med J. 2008;15(2):193-99.
19. Doddamani D, Sinha T, Karan SC, Sethi G, Prasad A, Singh DV. Forced diuresis during extracorporeal shockwave lithotripsy to enhance clearance: A prospective randomised controlled study. Indian J Urol. 2008;24:s28-29.

UROLOGY

S no	H no	name	age	sex	weight	fluid req	cal site	cal size
2	187957f	dipak sen	45	m	67	3350	R MC	8
5	197482f	narayan	35	m	60	3000	R P	6
6	180601b	devaraj	55	m	75	3750	R LC	8
9	253941f	kiran prasa	40	m	65	3250	R UC	5
10	688375d	rivervulet	36	f	72	3600	L LC	6
12	027993d	jamuna dev	50	f	56	2800	L LC	9
13	022828f	dilip kumar	56	m	70	3500	L UC	10
14	268628f	khuku rani	30	f	56	2800	L P	7
17	301155f	subashish	38	m	75	3750	R LC	10
20	324528f	nitu mani	31	m	54	2700	L LC	7
21	325125f	saraswathi	31	f	35	1750	R LC	5
26	824521b	ratna kisho	30	m	65	3250	L LC	7
29	161376f	nagaraj	35	m	62	3100	R LC	10
3	704083a	archana	27	f	49	2450	R P	15
4	573002d	elamathi	22	f	60	3000	R P	15
5	500468d	saraswathi	42	f	74	3700	R P	14
8	317815f	sunil ram	26	m	54	2700	L P	13
11	343536f	john	32	m	73	3650	L P	13
12	345378f	chandana	42	f	60	3000	L P	13
14	339504f	rekha	39	f	50	2500	R UC	12
17	721339d	tirumalai	61	m	72	3600	L P	13
1	953313d	subir mand	36	m	67	3350	L UU	9.5
2	962974d	ranganatha	45	m	56	2800	R UU	6
5	763709c	narayan gh	51	m	56	2800	R UU	7
7	045791f	rahima bee	60	f	56	2800	L UU	6
8	806744c	chawngtha	52	m	55	2750	L UU	9
11	113542f	manoj	34	m	59	2950	R UU	10
14	151921f	jayanthi	47	f	76	3800	R UU	8
15	167788f	ammu v	24	f	57	2850	L UU	8
18	254027d	arumugam	46	m	64	3200	R UU	8
20	205683f	kanak lata	47	f	50	2500	L UU	8
22	229648f	suresh bab	47	m	73	3650	R UU	4
23	509214d	dilip	45	m	60	3000	R UU	7
26	842635c	sakthivelu	34	m	66	3300	R UU	9
28	282139f	varghese	49	m	65	3250	R UU	8
29	097944d	ravisankar	50	m	80	4000	R UU	9
32	287130f	vijayakuma	21	f	39	1950	L UU	7
35	329803c	chapla	34	f	60	3000	R UU	6
36	535777d	kamala	49	f	60	3000	R UU	6
39	326561f	rajak ali	30	m	52	3100	L UU	5
40	370992f	sourav sing	28	m	60	3000	R UU	6
2	977485d	nirmala	50	f	60	3000	R UU	13
5	100052f	manoj kum	26	m	50	2500	R UU	12
7	160736f	leeza pradh	20	f	54	2700	R UU	11
8	155090f	subal chan	43	m	65	2150	R UU	14
11	097944d	ravisankar	50	m	70	3500	R UU	13
14	326217f	sarbeshwa	29	m	60	3000	L UU	14
15	339039f	daniel	44	m	62	3100	R UU	15
1	195809f	kabir uddin	28	m	65	3250	R LC	5
3	214339f	mukti	28	f	52	2600	L P	9
4	225691f	sanjay	33	m	60	3000	R LC	9

7	866790d	gomathi	21	f	43	2150	L	LC	6
8	315664d	poonam	27	f	43	2150	L	P	9
11	729429a	janardhan	51	m	61	3050	R	LC	5
15	251465f	krishna	50	f	75	3750	R	P	9
16	489873c	chandra	54	f	50	2500	R	LC	7
18	288307f	parboti	50	f	49	2450	R	LC	10
19	907358c	valarmathi	44	f	54	2700	R	LC	6
22	290383f	lakshmi pra	32	f	50	2500	L	MC	5
24	345804f	paulraj	52	m	70	3500	L	UC	9
27	954438c	rajkumar	27	m	75	3750	L	UC	5
28	329803c	chapala	34	f	60	3000	L	MC	6
2	224357f	basu sen	40	m	48	2400	R	P	12
6	681403d	abhishek	18	m	75	3750	R	P	15
7	258967f	rina chanda	47	f	42	2100	L	LC	12
9	292199f	sudhakar	45	m	70	3500	L	P	15
10	341214f	sakawan	34	f	75	3750	R	UC	15
13	353800f	ramprasad	34	m	62	3100	R	P	15
16	940808d	suguna	52	f	55	2750	L	P	15
3	968044d	jayachandr	47	m	90	4500	L	UU	7
4	028558f	balaji m	30	m	85	4250	R	UU	6
6	030903f	abraham	55	m	76	3800	R	UU	7
9	057830f	venkatesar	27	m	56	2800	R	UU	8
10	083563f	tahera	33	f	70	3500	R	UU	7
12	896421d	ragothama	56	m	60	3000	R	UU	9
13	104475f	nand kisho	46	m	69	3450	L	UU	9
16	170188f	paneer selv	31	m	76	3550	L	UU	8
17	575447a	raman	54	m	60	3000	R	UU	10
19	913298C	ILLAYARA.	30	m	55	2750	L	UU	7
21	223352f	gautam	27	m	61	3050	L	UU	8
24	249454f	jaydeep	50	m	70	3500	L	UU	8
25	087605f	anusuya	46	m	50	2500	L	UU	10
27	272689f	mojaffar	25	m	53	2650	L	UU	10
30	178108c	dinesh kum	56	m	65	3250	L	UU	10
31	308064f	sourav gho	23	m	44	2200	L	UU	6
33	332278f	partha dey	34	m	62	3100	R	UU	8
34	303951f	govinda	25	m	50	2500	R	UU	6
37	369085d	swapan	43	m	63	3150	R	UU	10
38	345585f	sanatan	48	m	62	3100	R	UU	10
1	392570d	dakshna m	35	m	67	3350	L	UU	11
3	729112d	manik das	41	m	73	3650	L	UU	11
6	117784f	sarita pradl	35	f	66	3300	L	UU	15
9	174888f	tili kumari	35	f	45	2750	R	UU	12
10	986242b	jeslet	36	f	65	3250	L	UU	15
12	290975f	dayarani	42	f	59	2950	R	UU	12
13	264866f	jagannath	40	m	61	3050	R	UU	13

creat	urine cs	shocks	sessions	fragmenta	clearance	FV chart d	duration	Stratum
1.2	conta	6000	4	Complete	Complete	3200/2450	11	1
1.33	ng	1500	1	Complete	Complete	2000/1100	14	1
1.32	Klebsiella	1500	1	Complete	Complete	3400/2300	5	1
1.32	ng	3000	2	Failed	Failed	2950/2100	10	1
1.1	conta	1500	1	Complete	Complete	3250/2500	16	1
1.34	conta	6000	4	Complete	Failed	3000/2500	20	1
1.29	conta	6000	4	Failed	Failed	3300/2000	14	1
0.89	conta	6000	4	Failed	Failed	3000/2050	16	1
1.25	Ecoli 500	5000	3	Complete	Complete	3600/2500	14	1
1.26	conta	1500	1	Complete	Complete	3000/2750	7	1
0.83	conta	1500	1	Complete	Complete	2000/1100	6	1
1.07	ng	7000	4	Complete	Complete	3400/2150	30	1
1.07	ng	4500	3	Failed	Failed	3000/1700	15	1
1.18	conta	4500	3	Complete	Complete	1750/1200	7	2
1.08	conta	7000	4	Complete	Complete	2500/1950	30	2
0.84	conta	1500	1	Complete	Complete	4000/2100	1	2
1.03	ng	6000	4	Complete	Complete	2575/2430	29	2
1.37	ng	4500	3	Complete	Failed	3950/3000	10	2
1.08	conta	5000	3	Complete	Complete	3500/2100	14	2
1.13	ng	11000	6	Failed	Failed	2100/1700	20	2
1.4	ng	6000	4	Failed	Failed	3000/1900	14	2
1	ng	3700	2	Complete	Complete	3500/2000	7	1
1.4	NG	2000	1	Complete	Complete	3000/1750	9	1
1.1	ng	2500	2	Complete	Complete	2900/2150	10	1
0.9	4500 Ecoli	2000	1	Complete	Complete	3000/1700	5	1
0.9	conta	6000	3	Complete	Failed	2700/2850	11	1
1.03	conta	5500	3	Complete	Complete	3100/2400	9	1
0.93	conta	6000	3	Complete	Failed	3200/2100	19	1
0.93	conta	2000	1	Complete	Complete	2250/1150	1	1
1.4	ng	6000	3	Complete	Complete	2800/1500	18	1
0.87	conta	6000	3	Complete	Complete	2450/1500	5	1
1.24	NG	2000	1	Complete	Complete	2750/1350	6	1
1.38	NG	2000	1	Complete	Complete	2950/2000	5	1
1.28	ng	2000	1	Complete	Complete	3300/1850	7	1
1.2	ng	6000	3	Failed	Failed	3250/2100	15	1
1.37	ng	2000	1	Complete	Complete	3400/2400	1	1
0.92	conta	4000	2	Complete	Complete	2000/1150	10	1
0.81	conta	2000	1	Complete	Failed	3000/1750	4	1
1.03	conta	2000	1	Complete	Complete	3500/2300	5	1
1.27	conta	2000	1	Complete	Complete	2600/1750	6	1
0.4	e.co.i 2100	4000	2	Complete	Complete	2600/1900	10	1
1.2	ng	4000	2	Failed	Failed	2850/1900	7	2
1.3	conta	2000	1	Complete	Complete	2700/1950	8	2
0.91	conta	750	1	Complete	Complete	2400/2000	6	2
1.05	ng	2000	1	Complete	Complete	1900/1600	12	2
1.37	ng	2000	1	Complete	Complete	3400/2400	14	2
1.06	conta	2000	1	Complete	Complete	3250/2650	6	2
1.23	600 kleb	8000	4	Failed	Failed	3500/2600	30	2
1.1	conta	3000	2	Complete	Complete	3550/2650	5	1
0.8	conta	3000	2	Complete	Complete	2850/1100	13	1
1.04	ng	1500	1	Complete	Complete	4000/1700	8	1

1.06	conta	1500	1	Complete	Complete	1800/2000	10	1
0.79	conta	1500	1	Complete	Complete	1800/1250	6	1
1.04	Ecoli 4000	4500	3	Complete	Complete	2650/1850	14	1
0.84	conta	6000	3	Failed	Failed	3000/2250	7	1
0.87	conta	1500	1	Complete	Complete	2150/1500	14	1
1.01	ng	4500	3	Complete	Complete	2200/1650	13	1
0.9	strept 5000	3000	2	Complete	Complete	2600/2000	10	1
0.84	NG	6000	4	Complete	Complete	2500/1800	12	1
1.1	conta	3000	2	Complete	Complete	3000/2100	14	1
0.98	conta	1500	1	Complete	Complete	3100/1200	4	1
0.81	conta	3000	2	Complete	Complete	2950/1900	11	1
1.29	conta	3000	2	Complete	Complete	3000/1900	9	2
1.12	conta	3000	2	Complete	Complete	3500/1800	5	2
0.85	conta	6000	4	Complete	Complete	1800/1100	18	2
1.09	conta	10000	7	Failed	Failed	3200/2700	45	2
1.06	E.coli 1000	3000	2	Complete	Failed	3700/2150	17	2
1.05	conta	3900	3	Complete	Complete	3500/2700	18	2
0.87	conta	4500	3	Failed	Failed	3000/2100	18	2
1.2	1800 ecoli	2000	1	Complete	Complete	4000/3100	5	1
1.4	conta	2000	1	Complete	Failed	3850/1850	10	1
0.9	conta	2000	2	Complete	Complete	3800/2400	7	1
0.9	ng	4000	1	Complete	Complete	2350/1500	12	1
0.9	conta	4000	2	Complete	Failed	3400/1725	14	1
1.19	conta	6000	3	Complete	Failed	3400/2750	21	1
0.9	ng	2000	1	Complete	Complete	3650/2890	5	1
1.27	ng	1500	1	Complete	Complete	3250/2100	10	1
1.09	conta	6000	3	Complete	Complete	3200/2850	31	1
1.04	Mixture	6000	3	Complete	Complete	2500/1300	18	1
1.26	ng	1750	1	Complete	Complete	2000/1875	6	1
1.26	conta	1500	1	Complete	Complete	3300/1050	11	1
1.02	conta	2000	1	Complete	Complete	1900/1100	7	1
1.1	conta	2000	1	Complete	Complete	2600/2000	4	1
1.2	conta	6000	3	Failed	Failed	3100/2000	14	1
1.03	conta	2000	1	Complete	Complete	3000/2800	6	1
1.06	conta	6000	3	Complete	Complete	3100/1900	18	1
1.09	conta	6000	3	Complete	Complete	2000/1650	14	1
1.2	ng	6000	3	Failed	Failed	3250/2400	10	1
1.26	conta	6000	3	Complete	Failed	3200/2100	14	1
1.3	conta	1600	1	Complete	Complete	3500/1350	6	2
1.2	conta	2000	1	Complete	Complete	3650/3000	8	2
0.75	enterococc	4000	2	Complete	Complete	3300/1450	8	2
1.06	insig	4500	3	Complete	Complete	2800/2100	15	2
1.13	proteus	2000	1	Complete	Complete	3300/1200	10	2
0.8	conta	4000	2	Complete	Failed	2500/1500	7	2
1.25	ng	6000	3	Complete	Complete	2900/2000	10	2

Type	Treatment
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Renal	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Urete	A
Renal	B
Renal	B
Renal	B

Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Renal	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B
Urete	B