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AN OPEN LABEL, NON-RANDOMIZED, CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF HOMEOPATHIC FORMULATION "KIDFLAME TABLET" IN PATIENT WITH KIDNEY STONE.

Nephrology

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ABSTRACT

Background: Urolithiasis is the course or process of formation of a stone in the kidney or anywhere in the urinary tract. The development of the stones is associated with a reduced urine volume or an augmented excretion of stone-forming components such as calcium, cystine, oxalate, xanthine, urate, and phosphate. The primary outcome of this study is to assess efficacy of Kidflame tablet in Urolithiasis and overall compliance to the drug treatment. The secondary outcome is to assess the efficacy of kidflame tablets by symptomatic relief from clinical symptoms of urolithiasis and reduction or expulsion of the stone size by ultrasonography.

Methods: This study was an open label, non-randomized, clinical study to evaluate the efficacy and safety of homeopathic formulation "Kidflame tablets" in patients with kidney stones. The Inclusion criteria was adult-Above 18 years to 60 years, both male and female. All eligible subjects who meet the Inclusion and Exclusion was enrolled into the study and were visited the study site on screening day, Day 0 (Baseline visit), Day 30 and Day 60. The 123 subjects were enrolled in this study. The primary endpoint was mean of the reduction in the size of the stone/expulsion of stone. The primary endpoint was analyzed using the p-trend test .The secondary efficacy of kidflame tablets by symptomatic relief from clinical symptoms of urolithiasis and reduction or expulsion of the stone size by ultrasonography and endpoint reduction in symptoms of Urolithiasis and percentage change in Urolithiasis Symptom Score. The secondary endpoint was analyzed using p-trend test. The p-value for trend was found out to be statistically significant.

Results: A total of 123 samples was included in this study among them, 44 (35.8%) were female and 79 (64.2%) were male patients. The average age was 41.67± 8.67 (range, 23 – 60) years. The change over the time in vital measure was found out not to be statistically significant (p=NS). A summary of adverse events, adverse events that occurred or not worsened during treatment. Most of the patients were reported with pain, however, a smaller number of the patients expressed with worsening pain. The results show that a significant decrease in pain/colic, dysuria, number of stones, size of the stones (mm), position of stones in the kidney. Efficacy results from this study was shown more significant results with kidflame.

Conclusion: Kidflame at dose at least three times daily had more efficacious. The adverse event was not a higher incidence also the serious adverse event was not found. This is needed as this will help in bringing forward the positive effects of this medicine to worldwide physicians so that more patients of kidney stones can be benefitted. The Pelvis of Kidney/ Calyces of the kidney were not worsened during the treatment. The incidence rate of adverse events was low and no patients reported serious adverse events, hence demonstrating the favorable tolerability profile of Kidflame. Data from this study demonstrated the favorable safety profile of Kidflame.

KEYWORDS

BACKGROUND:

Urolithiasis is the course or process of formation of a stone in the kidney or anywhere in the urinary tract. The development of the stones is associated with a reduced urine volume or an augmented excretion of stone-forming components such as calcium, cysteine, oxalate, xanthine, art, and phosphate. Urolithiasis has been a threat to mankind, since a long time and continues to be on the increase worldwide in addition to an imperious issue due to its incidence, recurrence, and malicious consequences. (1) In India, about 5–7 million patients are diagnosed with the kidney stone disease and not less than 1/1000 of Indian population require hospitalization due to the problem of urolithiasis. (2) About 70 to 80% of the calculi are made up of mainly calcium oxalate (CaOx) mixed with varying amounts of calcium phosphate. (3) The major objective while treating renal stones is to achieve extreme clearance of stone, while possibly triggering the lowermost amount of morbidity to the patient.

Various minimally invasive modalities are designated for this, which include shock wave lithotripsy, percutaneous nephrolithotomy, and retrograde intra renal surgery; nevertheless, the recurrence rates are estimated at 50% over a 10-year and 75% over 20-year period, with some people suffering 10 or more episodes over the course of a lifetime besides showing equally worse side effects. (4)

METHODS

This study was an open label, non-randomized, clinical study to evaluate the efficacy and safety of homeopathic formulation "Kidflame tablets" in patients with kidney stones. The Inclusion criteria were adult-Above 18 years to below 60 years, both male and female. Patients recently diagnosed with renal stone and the symptoms such as pain in back radiating from back to groin, nausea and vomiting, frequent Urination and burning Micturition were included in the study. While those with the confirmation of stone by USG KUB region-measurable stone and non-complicated Kidney Stone(s) size over 3 mm to 18 mm were also included in the study. The exclusion criteria was complex stone anticipating multiple access site, stones that are not clearly able to be measured on USG-KUB, severe Hydronephrosis/pylenephrosis, Cystitis, patients with known history of DM and HTN, H/o renal, hepatic or blood disorder or severe cardiac insufficiency, subjects with ongoing fever and pregnant women, lactating women and women of childbearing potential not following adequate contraceptive measure, women who were found positive for urine pregnancy test was not included in the study. All eligible subjects who meet the Inclusion and Exclusion criteria was enrolled into the study and were allowed to visit the study site on screening, Day 0 (Baseline visit), Day 30 and Day 60. The 123 subjects were enrolled in this study. Subjects in the study had received the active Investigational Product and advised to take one tablet three times a day after food. The physical examination and demographics were recorded at screening time physical examination and monitoring was also continued on Day 30 and Day 60. Vitals were recorded on all the visits. USG KUB at baseline and at final visit the Urolithiasis Symptom Score were taken on all visits (Intensity of pain/ colic, haematuria, dysuria, was being graded from 0-3. Calculi (single or multiple), size of calculi (s), position of calculi (kidney, ureter, bladder-above downwards) was assessed in each case). Adverse events were monitored up to 60 days and were recorded on Day 30 and Day 60. A buffer period of ±3 days was being allowed for every visit and beyond which it was considered as a protocol deviation. All the subjects who meet the eligibility criteria and have received at least one dose of study medication and had post baseline

efficacy data was included in the efficacy analysis and safety analysis. Patient data from all the centers were pooled together and analyzed.

Study rational: The management of renal calculus the various minimally invasive modalities are designated for this, which include shock wave lithotripsy, percutaneous nephrolithotomy, and retrograde intra renal surgery; nevertheless, the recurrence rates are estimated at 50% over a 10-year and 75% over 20-year period, with some people suffering 10 or more episodes over the course of a lifetime besides showing equally worse side effects. 4 As a substitute, other novel treatment options such as Homoeopathy can be considered as a replacement for the invasive treatment strategies. There have been few pre-clinical studies conducted in various parts of the world which have assessed the effects of various homeopathic preparations containing Berberis vulgaris, Cantharis vesicatoria, Dioscorea villosa, Petroselinum sativum, Stigmata maydis, Thuja Occidentals, Uva ursi and Vesicaria communes against the treatment of urolithiasis to positive results. Homeopathic clinicians are using these medicines for treatment of urolithiasis from years. However, there is a paucity of the clinical studies which have assessed their effects in the treatment of urolithiasis.

Statistical analysis:
Demographic data such as age, gender was analyzed using descriptive statistics. Out of 123 subjects 120 subjects have complete data. Categorical data were represented in the frequency form and continuous data were presented as the Mean ± SD or median (IQR). The vital measures and changes in stone size from baseline to end of treatment was analyzed using Non- parametric test Wilcoxon sign rank test. The primary outcome of the study is efficacy of the Kidflame tablet in Urolithiasis and overall compliance to the drug treatment and endpoint was the percentage of the reduction in the size of the stone/expulsion of stone. The primary endpoint was analyzed using the up-trend test.The secondary efficacy of kidflame tablets by symptomatic relief from clinical symptoms of urolithiasis and reduction or expulsion of the stone size by ultrasonography and endpoint reduction in symptoms of Urolithiasis and percentage change in Urolithiasis Symptom Score. The secondary endpoint was analyzed using p-trend test. A p-value≤0. 05 in a two-tailed test was considered statistically significant. Statistical analyses were performed using SPSS (the statistical package for social sciences) IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

RESULTS

A total of 123 samples was included in this study among them, 44 (35.8%) were female and 79 (64.2%) were male patients. The average age was 41.67± 8.67 (range, 23 – 60) years. The change over the time in vital measure in the table and figure [1]. The median Systolic BP (mmHg) at baseline was 120 (111 -125) and at 30 days was 120 (110 - 120). The p-value was 0.132, which was found not to be statistically significant. Whereas, at baseline to 60th day shows not statistically significant (p-value= 0.757) results after treatment. Hence, treatment effect was not shown significantly change at 30th and 60th day as compare to baseline. Hence the Systolic BP not significant changes over the time.

Diastolic BP (mmHg) was not shown statistically significant changes 30th day as compared to baseline. The p-value was found to be 0.784, which was considered as not statistically significant. While the median (IQR) was 120 (110 - 120) at 30th and at baseline was 80 (70 -80), hence this shows that no significant changes over time. Whereas, Diastolic BP (mmHg) was also not significantly change at 60th day as compared to baseline. The p-value was found to be 0.707. The median (IQR) was 70 (70 -80) at 60th and at baseline was 80 (70 -80), hence this shows that there were no significant changes over time.

The baseline median (IQR) was 80 (74 -84) and at 30th day 80 (74 - 84) of the Heart Rate (bpm). Hence, the results were shown not significantly changes. There were the p-value was found to be 0.307, which was not statistically significant. While at 60th day the median (IQR) was found to be 74 (80 -82) and at baseline 80 (74 -84). Since, the results were shows that there were shows not significant changes at the 60th day to compare to baseline. The results was shown that no statistically significant changes over time in Heart Rate.

Respiratory rate (beats/mins) was shown not significantly changes, baseline comparable to 30th day. There were found not to be statistically significant (p-value=0.668). The median (IQR) was 14 (14 -16) at baseline and 12 (14 -16) at 30th. This result was shown that no significant changes. Whereas, the p-value was at 60th days was not found to be statistically significant as compare to baseline (p-value=0.633). Hence the results were showing that not significant changes at 60th day median 12 (14 -16) as compared to baseline. Hence, the results were shown that not significant changes at baseline to 30th day and 60th day for Respiratory rate.

The median (IQR) was 68 (68 -72.76) at baseline of the Body temperature (degree Celsius) and 30th day 36.2 (35.05 - 37). This result was shown not significant changes at 30th as compared to baseline. The p-value was not found to be statistically significant (p-value=0.914). Whereas, at 60th days was also not shows statistically significant changes as compared to baseline. The p-value was found to be 0.372, which was not found to be not statistically significant. Hence, the results were shows that the body temperature was not significantly changes.

Body weight (kg) shows are not significant changes over the baseline to 30th day at 60th day. The median (IQR) at baseline was 68 (56.75 -72.76) and at 30th, 68 (56.75 -72.57) not statistically significant changes. The p-value was found to be 0.317, which were shown not statistically significant. At 60th day the p-value was not found to be statistically significant (p-value=0.317). This was shown that not significant changes over the time as compare to baseline. Hence, the results was shown that not significant changes over the time in body weight.

Results were not statistically significant, but not clinically meaningful mean decrease or increase in vital measure observed in the after treatment. In addition to the key results reported below, further results (including efficacy, safety and tolerability results) are reported.

Efficacy
The primary endpoint of the study was the percentage reduction in stone size table [2]. The Urolithiasis Symptoms Score (USS) Chart Score for in size of the stones (mm) was shown in table [2]. Those patients had a zero mm size of the stone at baseline was 0 (0%) and at 57 (56.4%) it significantly increase. Hence, it was shown that the treatment efficacy more (p=<0.001). Whereas, those patients were large size of the stone was the majority of the percentage decrease at the 60th day 11 (10.8%) as compared to at baseline 4 (4%). Which was shown more significant trend over the time. The size of the stones (mm) was significantly decreased (p=<0.001). Similarly, those patients had 3mm,3-6mm and 6-9mm size of the stone, these patients decreased over the time. The p-value for trend was shown that the trend over the time was found to be statistically significant (p=<0.001).

The Urolithiasis Symptoms Score (USS) Chart Score in Pain/Colic over the time in table [2]. The Score was in No pain/ colic at baseline, 55 (53.9%), at 30th day 74 (72.5%) and 60th day 95 (94.1%). This was showing a significant increase trend in pain/ colic (p=<0.001). Whereas, the mild pain/ colic at baseline was 27 (26.5%), at 30th day was 23 (22.5%) and at 60th day 6 (5.9%) in pain/ colic. This showed significant decrease in the pain/ colic (p=<0.001). The moderate pain/colic at baseline was 9 (8.8%), at 30th day 2 (2%) and at 60th day 0 (0%). Which was shows decreasing trend in pain/colic (p=<0.001). At baseline 11 (10.8%) patients had severe pain/colic, whereas 3 (2.9%) at 30th day and 0 (0%) at 60th. This result was shown that a significant decrease in pain/colic figure [2].

The Urolithiasis Symptoms Score (USS) Chart Score in Haematuria over the time in table [2]. The score was in mild Haematuria at baseline, 2 (2%), at 30th day 2 (2%) and at 60th day 0 (0%). Which was not shown significantly decrease trend over the time (p=NS). Most of the patients had no Haematuria at baseline, at 30th day and 60th. There were not any changes over the time (p=NS) figure [3].

The Urolithiasis Symptoms Score (USS) Chart Score over the time in table [2]. The score was in no Dysuria at baseline, 85 (83.3%), at 30th day 96 (94.1%) and at 60th day 100 (99%). This showed significant increase in trend (p=<0.001). The mild Dysuria at baseline was 15 (14.7%), at 30th day was 5 (4.9%) and at 60th day 1 (1%) in. This was showing a significant decrease trend (p=<0.001). Whereas, moderate Dysuria at baseline, 2 (2%), at 30th day and 1 (1%) at 60th 0 (0%). This result was shown that significantly decrease (p=<0.001) figure [4].

Table [5] Urolithiasis Symptoms Score (USS) Chart Score Number of stones. The score was in >2 Number of stones at baseline, 15 (14.7%), at

30th day 13 (12.7%) and at 60th day 0 (0%). This was showing significant decreases trend (p=<0.001). The zero stones at baseline was 0 (0%), at 30th day was 2 (2%) and at 60th day 57 (56.4%). These were shows significant increase trend. The one stone was 53 (52%) at baseline, at 30th day and 52 (51%) and at 60th 41 (40.6%). This result was shown that significantly decrease trend (p=<0.001). Whereas, two stone at baseline, 34 (33.3%), at 30th day 35 (34.3%) and 3 (3%) at 60th day. This result was shown that significantly decrease trend (p=<0.001) figure [5].

In remaining all categorizes at day 60th as compare to baseline was shown that a decrease in the trend. Hence the results have shown a more significant decrease as comparable to baseline. This shows that the treatment effect was a more significant figure [1].

The Urolithiasis Symptoms Score (USS) Chart Score in Position of stones in kidney [7] The position of the kidney in the calyces of Kidney at baseline, 45 (44.1%), at 30th day 43 (42.2%) and 22 (47.8%). This was shown decrease trend over the time (p=<0.001). Pelvic Ureteric Stone/ Pelvis of Kidney was at baseline, 6 (5.9%), 5 (4.9%) at day 30th and 0 (0%) at 60th day, which was decreasing trend (p=<0.001). The pelvic Ureteric stone was 22 (21.6%) at baseline, 22 (21.6%) at 30th day and 6 (13%) at 60th day. This was decreasing in significant (p=<0.001). Pelvis of Kidney at baseline was 24 (23.5%), at 30th day 25 (24.5%) and at 60th day 16 (34.8%) was shows the significant decrease trend in proportion (p=<0.001). Which had shown changes over the time. Those patients were Pelvis of Kidney/ Calyces of kidney at baseline was 5 (4.9%) also at 30th day and 0 (0%) at 60th day. The result was shown that significant trend over the time figure [7]. All efficacy analysis was shown in the table [2].

The results show that all the patients have no change in the Position of the stone in the Bladder and Position of the stone in the ureter. Which has shown that there were no significant decrease or increase in the proportions.

Safety

All subjects received at least one dose of the study drug was included in the safety analysis. All subjects in the study were monitored for any adverse events and serious adverse events. Adverse events were recorded during and at the end of study treatment, and the investigator was assess the various parameters like severity, seriousness, expectedness, relationship to study medication (causality) outcomes. A summary of adverse events, adverse events that were occurring or not worsened during treatment table [2]. Most of the patients were reported pain, however, a smaller number of the patients expressed with worsening pain. At follow-up the patients with pain were shown more significant decrease trend during the treatment. Moreover, patients with Haematuria were shown decrease during the treatment. A patient with mild and moderate Dysuria was decreased during the treatment. Most of the patients who were reported with the position of stones in kidney the calyces of Kidney has shown change over the time. Whereas, pelvic ureteric stone and pelvis of the kidney which was not worsened during treatment. The Pelvis of Kidney/ Calyces of the kidney were not worsened during the treatment.

Out of 123 cases, there was an expulsion of calculi in 75 and in 44 cases, calculi remained but the symptom score reduced, and the stone size >9 at baseline was 11case which reduced to 4 cases, indicating improvement in the case. The symptom score at baseline and after treatment was analyzed and found statistically significant (P<0.001).

The incidence rate of adverse events was low and no patients reported serious adverse events, hence, demonstrating the favorable tolerability profile of Kidflame.

DISCUSSION:

Kidflame is a homeopathic product which is being marketed already for the treatment of inflammatory conditions and discomfort associated with conditions of the kidney and the bladder. Though the physicians are using it on patients with success and content, there is no study conducted which has tapped these effects. This is needed as this will help in bringing forward the positive effects of this medicine to worldwide physicians so that more patients of kidney stones can be benefitted. The perspective observational study of Indian population, no more study was done on this drug. The previous literature shows that no more evidence available for this drug. The study was conducted on Indian population with 123 sample size. In this study the symptoms pertaining to urolithiasis were assessed at baseline, at 30th day and 60th. Numerous studies have evaluated the efficacy of the Kidflame tablet in Urolithiasis and overall compliance to the drug treatment. Cantharis vesicatoria a study conducted in India by Siddiqui et al. Aimed to ascertain the role of homeopathic medicines in Urolithiasis. A prospective, multicentre observational study was conducted by Central Council for Research in Homoeopathy (CCRH) from October 2005 to January 2010 to find the usefulness of homeopathic medicines in cases of Urolithiasis. The symptoms pertaining to urolithiasis were assessed before and after treatment. Pain, Dysuria and Haematuria were graded from 0-3 as per severity of complaints. Calculi were graded as per Number, Size and Position of calculi. Out of 123 cases, there was an expulsion of calculi in 75 and in 44 cases, calculi remained but the symptom score reduced, and the stone size >9 at baseline was 11case which reduced to 4 cases, indicating improvement in the case. The symptom score at baseline and after treatment was analyzed and found statistically significant (P<0.001).

The symptom score at baseline, at 30th day and 60th was found statistically significant (P<0.05). Patients had more follow-up as compare to this study. The adverse event was founded to decrease during treatment.

Trill et al conducted a randomized controlled trial to evaluate Uva-ursi extract and ibuprofen as alternative treatments of adult female urinary tract infection. In their study protocol, which was published, they had mentioned that one trial has demonstrated that delayed antibiotic treatment offered without symptom relief results in a modest reduction in antibiotic use. There is some evidence that ibuprofen provides symptom relief and reduces antibiotic use. *Uva-ursi*, an herbal product, has a traditional use for urinary infection symptom relief. They set out to test: in adult women with suspected UTI who accept the delayed prescription strategy: Do NSAIDs or uva-ursi (an herbal product) provide relief from urinary symptoms and reduce antibiotic use. Currently the trial is in the works and the outcomes from this trial have the potential to modify the current approach to the management of acute urinary symptoms with less dependence on the use of antibiotics.

In our study 1 tablet three times a day was a treatment regimen. Kidflame study shows more efficacy and less symptom score as compare to uva-ursi study. The Ufa-use was conducted on the only adult women with suspected UTI who accept the delayed prescription strategy, while the Kidflame study was conducted on male and female patients. It was a show better results during the treatment. The change over the time in vital measure was not found statistically significant (p=NS). The result is shown that the kidflame was not more affected on the vital measure. The Urolithiasis Symptoms Score (USS) Chart Score in no Pain/Colic patients 60 days was approximately double. Hence, that was shows treatment effect more significant. Moreover, the patients had mild pain/colic at baseline was more a compare to 60th day. Similarly the moderate and severe pain/colic was significantly decreased. The all results were showing that the treatment affects more significant reduction in pain/colic. The score in patients with no Haematuria was more, while the results was not shown more relevant. Because the data was skewed. There were those patients had mild haematuria show a little decrease trend. The score of the no Dysuria at 60th day as compared to baseline significantly increase. Patients Dysuria was more significant decrease. Treatment effect was show more effectively. Similarly, those patients with mild, moderate and severe Dysuria were showing more significant reduction after treatment. The number of the patients with zero number of the stones was an increasing trend. The size of the stone was shown significantly over the time. The decreasing trend shows over the time. The primary endpoint was achieved. Treatment effect was shows more signs. Moreover, those patients have one, two and more than two stone those patients were shows decreasing trend over the time. Since, the treatment is more effective. No patient was found with adverse and serious adverse event. The tolerability of the treatment was favorable.

CONCLUSION:

Kidflame at dose at least three times daily had more efficacious. A not higher incidence was found due to adverse events. The serious adverse event was not found. This is needed as this will help in bringing forward the positive effects of this medicine to worldwide physicians so that more patients of kidney stones can be benefitted. The incidence rate of adverse events was low and no patients reported serious adverse events, hence demonstrating the favorable tolerability profile of Kidflame. Based on analysis by each of the indigestion parameters, Pain/Colic, Haematuria, Dysuria, Number of stones, Size Of stones (mm) reduced at day 60 compared to baseline with significant p-value based. The treatment was safe as no significant treatment effect was seen on patient's vitals like SBP, DBP, Heart Rate, Respiratory Rate, Temperature and Weight after 60 days when compared to baseline. Overall, the 60th day Kidflame treatment regime was proven effective in reducing Pain/Colic, Haematuria, Dysuria, Number of stones, Size of stones (mm) Pain symptoms and safe. Data from this study demonstrated the favorable safety profile of Kidflame.

Supplementary results:

Table 1: Comparison vital measure at baseline, at 30th day and at 60th day.

Characteristics	Baseline (n=120)	At 30 Day	At 60 Day	p- value baseline vs 30 day	p- value baseline vs 60 day
Systolic BP (mmHg), Median (IQR)	120 (111- 125)	120(110-120)	120(110-120)	0.132	0.757
Diastolic BP(mmHg), Median (IQR)	80 (70- 80)	80 (70- 80)	70 (70- 80)	0.784	0.707
Heart Rate (bpm), Median (IQR)	80 (74- 84)	80 (74- 84)	74 (80- 82)	0.307	0.900
Respiratory rate(beats/mins) Median(IQR)	14 (14- 16)	14 (12- 16)	14 (12- 16)	0.668	0.633
Body temperature (degree Celsius), Median (IQR)	36.2 (34.83-37)	36.2(35.05-37)	36.6(34.4-37)	0.914	0.372
Body weight (kg), Median (IQR)	68(56.75-72.76)	68(56.75-72.57)	68(56.75-72.57)	0.317	0.317

Note: Description Categorical Variables were expressed in Frequency (Percentage) and Continuous variables are presented with Mean ± Standard Deviation.

Table 2: Efficacy, safety and tolerability assessment of the Kidflame drug.

VAS		Baseline					Visit Day 30					Visit Day 60					p-value
Symptom	Type				95% CI					95% CI					95% CI		
		n	n'	%	LL	UL	n	n'	%	LL	UL	n	n'	%	LL	UL	
Pain/Colic	Mild	123.00	27.00	26.50	0.10	0.43	123.00	23.00	22.50	0.05	0.40	123.00	6.00	5.90	-0.13	0.25	<0.001
	Moderate	123.00	9.00	8.80	-0.10	0.27	123.00	2.00	2.00	-0.17	0.21	123.00	-	-	-	-	
	No Discomfort	123.00	55.00	53.90	0.41	0.67	123.00	74.00	72.50	0.62	0.83	123.00	95.00	94.10	0.89	0.99	
	Severe	123.00	11.00	10.80	-0.08	0.29	123.00	3.00	2.90	-0.16	0.22	123.00	-	-	-	-	
Haematuria	Mild	123.00	2.00	2.00	-0.17	0.21	123.00	2.00	2.00	-0.17	0.21	123.00	-	-	-	-	<0.198
	No Discomfort	123.00	100.00	98.00	0.95	1.01	123.00	100.00	98.00	0.95	1.01	123.00	101.00	100.00	1.00	1.00	
Dysuria	Mild	123.00	15.00	14.70	-0.03	0.33	123.00	5.00	4.90	-0.14	0.24	123.00	1.00	1.00	-0.19	0.21	<0.001
	Moderate	123.00	2.00	2.00	-0.17	0.21	123.00	1.00	1.00	-0.19	0.21	123.00	-	-	-	-	
	No Discomfort	123.00	85.00	83.30	0.75	0.91	123.00	96.00	94.10	0.89	0.99	123.00	100.00	99.00	0.97	1.01	
Number of stones	0	123.00	-	-	-	-	123.00	2.00	2.00	-0.17	0.21	123.00	57.00	56.40	0.44	0.69	<0.001
	1	123.00	53.00	52.00	0.39	0.65	123.00	52.00	52.00	0.37	0.65	123.00	41.00	40.60	0.26	0.56	
	2	123.00	34.00	33.30	0.17	0.49	123.00	35.00	34.30	0.19	0.50	123.00	3.00	3.00	-0.16	0.22	
	>2	123.00	15.00	14.70	-0.03	0.33	123.00	13.00	12.70	-0.05	0.31	123.00	0.00				
Size of Stones (mm)	0	123.00	-	-	-	-	123.00	2.00	2.00	-0.01	0.21	123.00	57.00	56.40	0.44	0.69	<0.001
	3mm	123.00	17.00	16.70	-0.01	0.34	123.00	16.00	15.70	-0.02	0.34	123.00	11.00	10.90	-0.08	0.29	
	3-6mm	123.00	43.00	42.20	0.27	0.57	123.00	38.00	37.30	0.22	0.53	123.00	15.00	14.90	-0.03	0.33	
	6-9mm	123.00	31.00	30.40	0.14	0.47	123.00	36.00	35.30	0.20	0.51	123.00	14.00	13.90	-0.04	0.32	
	>9mm	123.00	11.00	10.80	-0.08	0.29	123.00	-	-	-	-	123.00	4.00	4.00	-0.15	0.23	
Position of Stones in Kidney	No	123.00					123.00	2.00	2.00	-0.17	0.21	123.00					<0.001
	Calyces of Kidney	123.00	45.00	44.10	0.30	0.59	123.00	43.00	42.20	0.27	0.57	123.00	22.00	47.80	0.27	0.69	
	Pelvic Ureteric stone/ Pelvis of Kidney	123.00	6.00	5.90	-0.13	0.25	123.00	5.00	4.90	-0.14	0.24	123.00	2.00	4.30	-0.24	0.32	
	Pelvic Ureteric Stone	123.00	22.00	21.60	0.04	0.39	123.00	22.00	21.60	0.04	0.39	123.00	6.00	13.00	-0.14	0.40	
	Pelvis of Kidney	123.00	24.00	23.50	0.07	0.40	123.00	25.00	24.50	0.08	0.41	123.00	16.00	34.80	0.11	0.58	
	Pelvis of Kidney/ Calyces of Kidney	123.00	5.00	4.90	-0.14	0.24	123.00	5.00	4.90	-0.14	0.24	123.00	-	-	-	-	
Position of Stone in Ureter	No	123.00	102.00	100.00	-	-	123.00	103.00	-	-	-	123.00	101.00	-	-	-	NA
Position of Stone in Bladder	No	123.00	102.00	100.00	-	-	123.00	103.00	-	-	-	123.00	101.00				NA

Confidence Interval (CI): Exact 95% CI for proportion, LCB: Lower confidence bound, UCB: Upper confidence bound

Figure 1: Box plot shows comparison change over the time

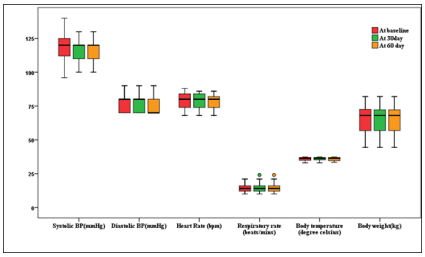


Figure 2: Percentage bar for Urolithiasis Symptoms Score (USS) Chart Score in pain/colic.

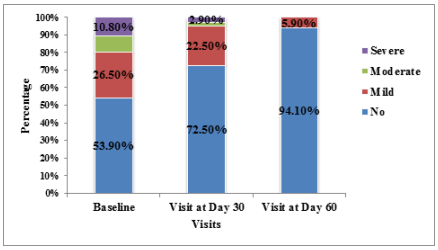


Figure 3: Percentage bar for Urolithiasis Symptoms Score (USS) Chart Score in Haematuria.

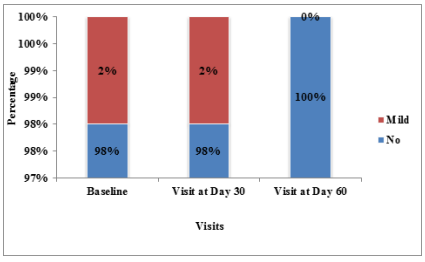


Figure 4: Percentage bar for Urolithiasis Symptoms Score (USS) Chart Score in Dysuria

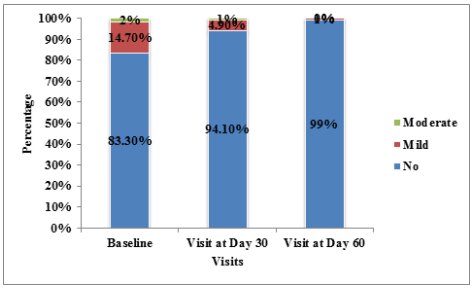
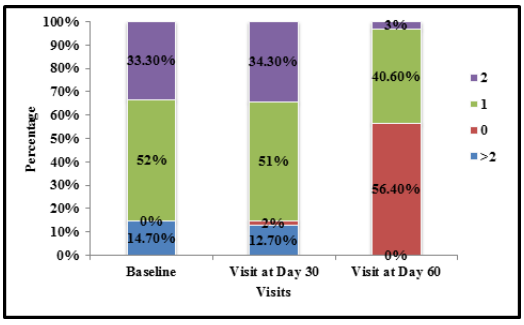
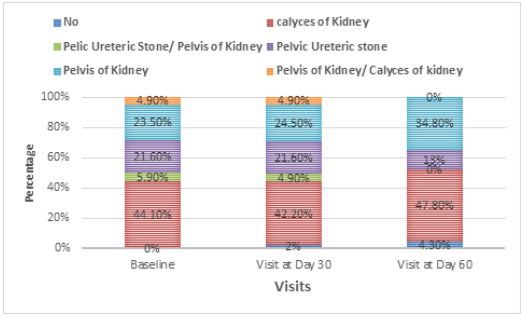


Figure 5: Percentage bar for Urolithiasis Symptoms Score (USS) Chart Score in Number of stones.



Graph: Percentage bar for Urolithiasis Symptoms Score (USS) Chart Score in Position of stones in kidney.



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