Poster: **816**

Are urological patients at increased risks of developing haemostatic complications following shock wave lithotripsy (SWL) for solitary unilateral kidney stones?

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Background

Shock wave lithotripsy (SWL) is a non-invasive procedure, which is the most common way of treating kidney stones that cannot be passed on their own, in the urine. It involves using X-rays or ultrasound to pin-point where a kidney stone is, and sends shock waves of energy to the stone to break it into smaller pieces, so it can subsequently be passed in urine.

The number of SWL in Welsh hospitals (UK) for solitary unilateral kidney stones are increasing annually, with a 63% rise in upper urinary tract stones being reported in the UK over a 10-year period [1,2]. This trend is expected to continue and thus the risk of complications will potentially increase.

Serious complications of SWL include haematuria, acute kidney injury (AKI) and sepsis. However, currently there are no simple blood tests available, which can predict complications following SWL.

Aims

The main aim of this clinical pilot-study was to test the hypothesis that SWL results in changes to haemostatic function, increasing endothelial and haemostatic involvement postoperatively.

Methods

- **Subject Volunteers**

Ethical approval for this study was sought from the local Research Ethics Committee (Reference: 12/WA0117). Ten patients scheduled for elective SWL for solitary unilateral kidney stones, were recruited after informed consent (n=10). The patients (6 males and 4 females) were aged between 31 and 70 years old (mean age = 50).

- **Shock Wave Lithotripsy (SWL)**

Prior to SWL, a cannula was inserted into the ante-cubital fossa. A venous blood sample was then collected pre-operatively, which stood as a baseline measurement for that particular patient. After SWL, blood samples were collected at 30 minutes, 120 minutes and 240 minutes post-operatively.

- **Measurement of Haemostatic Biomarkers (D-dimer, vWF, PT and sE-Selectin)**

D-dimer was measured by a two-step enzyme immunoassay sandwich method, with a final fluorescent detection as described by others [3]. Measurement of this parameter was performed using a Mini-Vidas automated immunoassay system that uses ELFA (Enzyme-Linked Fluorescent Assay) technology. The Mini-Vidas system and immunoassay kits were supplied from Biomerieux, UK.

Plasma vWF concentration was measured as described previously by a sandwich-type ELISA technique using rabbit anti-human vWF and rabbit anti-human vWF peroxidase conjugate (Dako, UK) [4].

PT was measured using citrated collected blood samples employing a Randox Monza semi-automated system as described by manufacturer's instructions (Randox RX Monza Method Sheet: PTH 2752).

Measurement of sE-Selectin was performed using commercially available kits supplied by R&D Systems Europe, and involved using ELISA assay as described by the manufacturer (R&D Systems, Catalogue # SSLE00).

- **Statistical Analysis**

All results were presented as mean ± standard errors (SE) or median ± Iqr. Where data normally distributed, repeated measures one-way analysis of variance (ANOVA) between samples test was employed adopting a 5% level of significance. Post hoc testing was conducted using the Tukey test for pairwise comparisons between means. Data that did not comply with normality were analysed using the Friedman test. Where the Friedman test resulted in statistical significance, subsequent tests were performed using the Wilcoxon test. Statistical significance was accepted when $p \leq 0.05$.

Results

- **D-dimer**

The results are expressed as ng/ml and represent the changes in D-dimer concentration following SWL, for the treatment of kidney stones (Figure 1). This parameter was measured specifically to investigate the breakdown of fibrin degradation products (FFP). Following SWL, a significant increase in D-dimer was observed, p=0.05, as determined by the Friedman test. Specifically, D-dimer increased from baseline (283.5 ± 184.1), at 30 minutes post-operatively (1032.6 ± 1778.6) and peaking at 120 minutes (4943.0 ± 1021.6) postoperatively. D-dimer decreased toward basal levels at 240 minutes (600.7 ± 470.9) postoperatively, although remained at a higher level (2 fold) to those of basal values. Upon further analysis the Wilcoxon test showed significant differences between baseline (pre-operatively) vs 120 minutes post-operatively (p=0.022).

- **vWF**

The results are expressed as IU/dL and represent the changes in vWF following SWL, for the treatment of kidney stones (Figure 2). This parameter was measured to investigate endothelial activation, specifically to assess the release of vWF from endothelial storage organelles. Following SWL, a significant increase in vWF was observed, p=<0.01, as determined by ANOVA. vWF increased from baseline (140.02 ± 33.82), at 30 minutes post-operatively (151.72 ± 37.42), 120 minutes (153.60 ± 30.87) postoperatively, and peaking at 240 minutes (182.00 ± 41.5) postoperatively. Upon further analysis, pairwise comparisons showed significant differences between baseline (pre-operatively) vs 120 and 240 minutes post-operatively (p=<0.05).

- **PT**

The results are expressed as seconds and represent the changes in PT following SWL, for the treatment of kidney stones (Figure 3). This parameter was measured specifically to investigate the extrinsic coagulation pathway. Following SWL, a trend of increasing PT was observed, although these changes were not significant (p=>0.05, as determined by ANOVA). PT increased from baseline (12.0 ± 1.3), at 30 minutes post-operatively (13.1 ± 2.0) and peaking at 120 minutes (13.5 ± 2.5) postoperatively. PT decreased toward basal levels at 240 minutes (13.1 ± 1.5) postoperatively, although remained at a higher level to those of basal values.

- **sE-Selectin**

The results are expressed as ng/ml and represent the changes in sE-Selectin concentration following SWL, for the treatment of kidney stones (Figure 4). This parameter was measured to investigate endothelial activation, specifically to assess the shedding of this adhesion molecule from the endothelium. Following SWL, an initial trend of increasing sE-Selectin was observed from baseline (pre-operative) (68.49 ng/ml +3.02) and at 30 minutes post-operatively (72.94 ng/ml +2.36). sE-Selectin levels subsequently decreased towards basal levels at 120 and 240 minutes post-operatively (67.88 ng/ml +2.44; 62.26 ng/ml +2.04 respectively), (p>0.05 as determined by the Friedman test).

Discussion

Conventionally in the UK, patients are monitored in the post-operative period by a full blood count and urea and electrolyte; tests which cannot monitor or predict patient outcome. Findings from this clinical pilot-study demonstrate significant changes to parameters such as D-dimer and vWF following SWL. Clearly, the full effects of SWL on blood parameters, is not fully understood and warrants further investigation. Due to the lack of studies in this area, we are aiming to build on this pilot- study to investigate a larger cohort as well as novel parameters such as procalcitonin (PCT) and neutrophil gelatinase-associated lipocalin (NGAL), which may ultimately help monitor or predict post-operative outcome. Improvements in the monitoring of patients following SWL promises to provide financial benefits for the NHS and health benefits for the patients.

Conclusion

The significant increase in D-dimer and vWF concentrations following SWL suggests that these markers may provide a clinically relevant assessment of the extent of haemostatic involvement due to surgery. The analysis of such markers may have the potential to improve the detection of complications, such as haematuria and AKI that can occur following SWL

The results of this pilot-study provide a sound basis to continue research into this area, where D-dimer and vWF may be employed, as part of routine testing, in the monitoring of patients following SWL.

Acknowledgements

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Figures

Figure 1: Effect of SWL, for the treatment of kidney stones, on D-dimer concentration. The points represent median ± Iqr, p=0.05 as determined by the Friedman test. *p =0.022 baseline (pre-operative) vs 120 minutes post-operatively as determined by the Wilcoxon test.

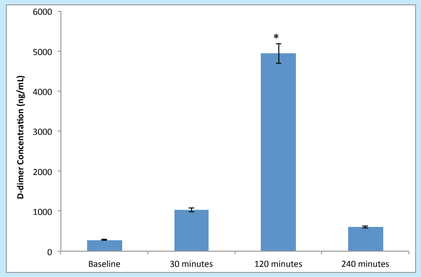


Figure 2: Effect of ESWL, for the treatment of kidney stones, on vWF concentration. The points represent mean ± SE, p=<0.01 as determined by ANOVA. *p = <0.05 baseline (pre-operative) vs 120 and 240 minutes post-operatively.

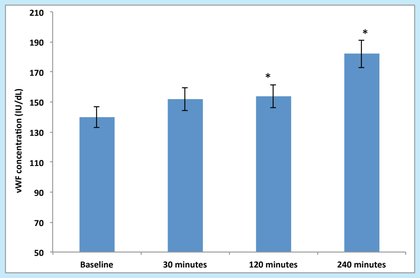


Figure 3: Effect of ESWL, for the treatment of kidney stones, on Prothrombin Time (PT). The points represent mean ± SE, p=0.426 as determined by ANOVA.

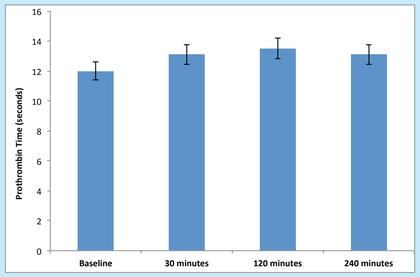
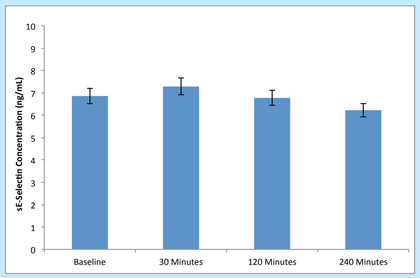


Figure 4: Effect of ESWL, for the treatment of kidney stones, on sE-Selectin. The points represent median ± Iqr, p=>0.05 as determined by the Friedman test.



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