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ALKALINISED LIDOCAINE VERSUS LIDOCAINE GEL AS LOCAL ANAESTHESIA PRIOR TO INTRA-VESICAL BOTULINUM TOXIN (BONTA) INJECTIONS: A PROSPECTIVE, SINGLE CENTRE, RANDOMISED, DOUBLE-BLIND, PARALLEL GROUP TRIAL OF EFFICACY AND MORBIDITY

Hypothesis / aims of study
Alkalinised intra-vesical lidocaine should have enhanced mucosal absorption (1) that potentially makes it possible to perform more cystoscopic procedures comfortably under local anaesthetic. Intra-vesical botulinum toxin (BoNTA) injection under local anaesthetic using flexible cystoscopy is one of the relatively safe trans-cystoscopic procedures, but patients often find it painful or uncomfortable due to the sub-optimal level of local anaesthesia.
There are no randomised studies in the current literature that address the question of whether alkalinisation of a local anaesthetic solution increases its efficacy in achieving intra-vesical anaesthesia during cystoscopic procedures. Therefore in this study we aim to assess the efficacy and morbidity of alkalinised lidocaine solution compared to lidocaine gel for intra-vesical anaesthesia during BoNTA injections in a statistically powered, prospective, parallel group, double-blind randomised controlled trial.

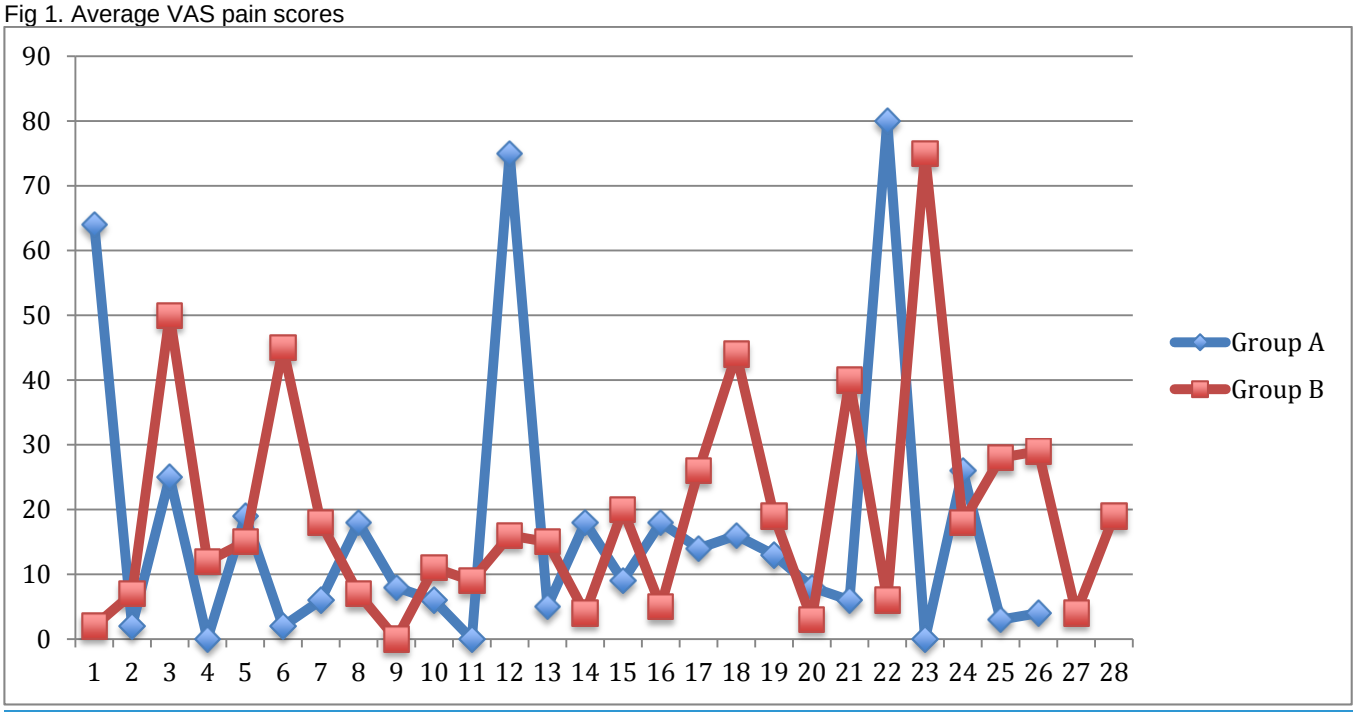
Study design, materials and methods
This was a single-centre, randomised, double-blind, parallel group superiority study in a 1:1 allocation. The main exclusion criteria were neurological disease that could affect bladder function or sensation, patients with long-term suprapubic or long-term catheters and patients with known allergy or sensitivity to any component of the study medication.
All patients were injected using the same type of needle of the same gauge under flexible cystoscopic guidance. The dose of BoNTA (prescribed on an individual patient basis) was diluted in 10ml saline and injected in 0.5ml aliquots to 20 sites in the bladder wall avoiding the dome and trigone.
Power calculation revealed the sample size necessary to detect at least a 20 mm difference (SD=23mm) in the mean of the VAS (pain) between the groups with a power of 0.80 and an alpha of 0.05 was 27 in each group. Randomisation was achieved using computer-generated block randomisation in a 1:1 allocation ratio and allocation concealment was done using opaque, sealed envelopes. Both participants and investigators performing the injection procedure were blinded to the allocation, as were the outcome assessors.
Participants were randomised to receive either **alkalinized lidocaine (AL)** solution (10ml 8.4% sodium bicarbonate + 20mls 2% lidocaine solution + 22ml sterile Aquagel®) or **lidocaine gel (LG)** (22 ml standard 2% lidocaine gel Instillagel® + 30ml 0.9% normal saline solution). The solutions were instilled by nursing staff on the ward who were blind to allocation, from pre-filled and unmarked syringes at least 20 minutes prior to injection. Both solutions had a similar appearance once instilled in the bladder therefore maintaining investigator blinding.
Primary outcome was average pain (assessed by 100mm visual analogue score) felt during intra-vesical BoNTA injections performed at least 20 minutes after instillation. Secondary outcome was the rate of adverse events. Sub-analysis based on previous experience of intra-vesical injections was also planned.

Results
Of 60 randomised patients 54 received the allocated intervention and were analysed. Mean pain score in the AL group was 17.11mm (95% CI 8.65-25.57mm) and in the LG group was 19.53mm (95% CI 13.03-26.03mm) with no significant difference between the groups (p=0.656). Cost of interventional medication in the AL group was almost double that of the LG group. No adverse events were attributable to local anaesthetic instillation in either group, and all were Clavien-Dindo Grade 1.
Sub-analysis based on number of previous injections showed the average VAS score for treatment naïve patients in group A was 21mm and in group B was 19mm (p=0.404). The average VAS score for non-naïve patients in group A was 12mm and in group B 20mm (p=0.062). No inter or intra-group comparison reached statistical significance, but the numbers were too small in these comparisons to conclude that no difference actually exists.

Table 1. Baseline characteristics

Characteristic	**AL group**	**LG group**
Age (Mean +/- SD)	55.30±9.40	64.07±10.15
Sex		
Female	26	26
Male	0	2
Previous Botox injections		
One	6	12
Two or more	3	2

Fig 1. Average VAS pain scores



Interpretation of results

This is the first randomised study comparing the use of alkalinised lidocaine solution versus lidocaine gel as a local anaesthetic for intra-vesical procedures. The study has a strong methodological foundation but the use of an average VAS pain score to represent the nature of pain felt throughout the procedure could be argued as an oversimplification. However the study has helped to define our local protocol for intra-vesical injections and the higher cost of alkalinised lidocaine precludes its use over lidocaine gel at our centre. It also raises the question whether lidocaine gel could be used to mitigate pain in patients with painful bladder syndrome.

Concluding message

Based on this statistically powered, randomised study there is not enough evidence to conclude that alkalinised lidocaine solution is superior to lidocaine gel for anaesthesia during intravesical BoNTA injections, and the higher cost precludes its use over lidocaine gel at our centre. We have used the results of this study to adapt our local protocol for BoNTA injections and continue to use lidocaine gel as the local anaesthetic of choice.

References

1. Henry R, Patterson L, Avery N et al. Absorption of alkalized intravesical lidocaine in normal and inflamed bladders: a simple method for improving bladder anesthesia. J Urol 2001; 165: 1900–3

Disclosures

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CTA number: 35930/0001/001-0001 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Regional Ethics Committee for Wales (REC Wales)
Medicines and Healthcare Regulatory Authority (MHRA) **Helsinki:** Yes **Informed Consent:** Yes