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A RANDOMIZED SHAM CONTROLLED STUDY OF LIDOCAINE EMDA FOR BLADDER ANAESTHESIA

Hypothesis / aims of study

Effective bladder anaesthesia is an essential urological tool. It allows for invasive procedures to be performed in an office setting, for blinding of clinical trials using intravesical and endoscopic therapy, and for treatment of the endogenous bladder pain in disease such as interstitial cystitis (IC). Improved anaesthetic techniques could advance urological practice and improve patient care. Electromotive Drug Administration (EMDA) uses an electrical current to improve a drug's permeability into tissue. In this randomized, double blind, sham controlled study we ask: 1) Does intravesical lidocaine administered with EMDA provide more effective immediate anaesthesia to the bladder then lidocaine alone? 2) Does lidocaine with EMDA provide a longer lasting anaesthesia then lidocaine alone?

Study design, materials and methods

24 subjects ages 18 to 80 years with chronic bladder pain (see Table below) were recruited from clinic and randomized to intravesical lidocaine (150cc 2% lidocaine, 2 cc 1:1,000 epinephrine) with treatment EMDA (30 mAmps, 25 minutes) or the same solution with sham (minimal) EMDA (5 mAmps, 25 minutes). Three metrics used. 1) Immediate pain relief: Visual Analog Pain Scale (VAS) administered before and immediately after anaesthesia. 2) Immediate change in bladder capacity measured by gravity fill at 20cm pressure. 3) Duration of anaesthesia: Patient determined time to "return of baseline" bladder sensation and additional VAS scores. Inclusion criteria: Bladder pain of 6 months duration that is consistently present and reasonably stable (ICS definition of Painful Bladder Syndrome or IC). Blinding: patients and primary investigator blinded to treatment vs. sham allocation. EMDA was performed as previously reported [1] Participants returned their final VAS scores and times via mail. If there were unable to do this, their time of pain return was communicated over the phone. The maximum study end point was four weeks post treatment. If the subjects had not returned to their pre-EMDA pain level at the end of the study, a pain relief time of 4 weeks (672 hours) was recorded. Statistics were done with Microsoft Excel and web base statistical tool: http://www.physics.csbsju.edu/stats/t-test_bulk_form.html

Results

Total Subjects n = 24	Average Age	ICSI	ICPI
Sham n = 11, all female, 1 with ulcer	51	16 ± 3	14 ± 2
Treatment n = 13, one male with ulcers	49	15 ± 3	12 ± 3

Complete in-office data were obtained for 23 subjects (EMDA Sham n = 11, EMDA treatment n = 13). Participant number 10 (female, sham) withdrew from the study due to fear of being catheterized. Follow-up data was obtained for 19 subjects (EMDA Sham n = 8, EMDA treatment n = 11, See Table below). EMDA extended the duration of lidocaine anaesthesia by an average of 119 hours (4.9 days) Although a definite trend was observed, this did not reach statistical significance (Student's paired t=-1.32, DF=18, P= 0.20). Using an estimated effect size of 40 hours (sdev. = 48 hours) we calculated a need for 46 subjects to sufficiently power this experiment. (ά = .5, β = .20). However, the study was underpowered due to time and funding restrictions. The mean immediate change in bladder capacity was 74% greater for the treatment group vs. sham but statistical significance was not reached (Student's paired t= -1.26, DF = 21 P= .22). Immediate pain reduction was similar for both groups.

Allocation	**Participant Number**	**Percentage Reduction in Pain** (Post EMDA VAS/ Pre EMDA VAS * 100)	**Percentage change in bladder capacity** (Post EMDA volume/ pre EMDA volume * 100)	**Duration of Aesthetic effect (hours)**
Sham	1	9	124	29
	2	42	313	360
	7	32	300	53
	8	91	500	54
	9	54	-25	101
	11	100	136	no data
	12	46	25	no data
	17	82	124	8
	18	100	-3	24

	24	54	129	8
Mean ± SD		**61 ± 31**	**162 ± 155**	**80 ± 117**
Treatment	3	67	250	96
	4	44	340	30
	5	32	317	46
	6	76	200	168
	13	64	70	672*
	14	100	142	323
	15	35	140	103
	16	31	260	56
	19	79	188	72
	20	13	206	no data
	21	31	133	72
	22	71	300	72
	23	100	525	672*
Mean ± SD		**57 ± 28**	**236 ± 118**	**199 ± 234**
***** patients reported pain relief > 4 weeks				

Interpretation of results

Although statistical significance was not reached, a strong trend emerged whereby EMDA administered intravesical lidocaine was associated with both immediate increased bladder capacity and longer duration of anaesthetic effect in patients with IC/PBS.

Concluding message:

EMDA may increase the depth and duration of lidocaine anaesthesia in the bladder. These findings have important clinical implications. EMDA could increase the range of endoscopic office procedures available to patients. EMDA could be used to blind clinical trials of intravesical and bladder instillation therapies such as vanilloids and botulinum toxin. However, because certain individuals demonstrate prolonged improvement with EMDA alone, caution needs to be exercised when evaluating any additional therapeutic intervention, since the EMDA effect is a potent confounder. The prolonged remission of bladder pain seen here supports the utility of EMDA as a promising independent treatment modality for patients with IC/PBS. Future studies are indicated to explore the role of EMDA in the care of urological patients.

References

[1]Int Urogynecol J Pelvic Floor Dysfunct. 199;8:142–5

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CLINICAL TRIAL REGISTRATION: This clinical trial has not yet been registered in a public clinical trials registry.
HUMAN SUBJECTS: This study was approved by the Stanford University Institutional Review Board and followed the Declaration of Helsinki Informed consent was obtained from the patients.