PAIN SCORE COMPARISON IN PATIENTS RECEIVING LIGNOCAINE GEL 2% VERSUS PLAIN LUBRICATING GEL DURING FLEXIBLE CYSTOSCOPY,A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL,A CROSSOVER STUDY.

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CONTENTS

IV-ABSTRACT IN MALAY

Tujuan kajian: Buat masa ini, tiada bukti yang mengatakan gel lignocaine 2% adalah lebih baik daripada gel pelincir biasa dalam mengurangkan kesakitan semasa prosedur fleksibel cystoscopy (flex CE). Harga bagi lignocaine gel 2% adalah jauh lebih mahal daripada gel pelincir biasa.Oleh sebab itu kajian ini bertujuan untuk membandingkan skor kesakitan (*pain score*) di antara pesakit yang menerima lignocaine gel 2% dan gel pelincir biasa di samping perbandingan kos di antara dua gel tersebut.

Material dan kaedah:Kajian ini adalah kajian prospektif and rawak di mana para pesakit dibahagikan kepada dua kumpulan,sama ada yang menerima lignocaine gel 2% (kumpulan A) atau gel pelincir (kumpulan B) semasa prosedur fleksibel cystoscopy (Flex CE). Sejumlah 90 pesakit meyertai kajian ini dan pesakit-pesakit tersebut dibahagikan sama rata kepada dua kumpulan(45 setiap kumpulan) mengikut kaedah rawak berkomputer. Kajian ini merupakan kajian *single blind* di mana hanya pesakit tidak tahu mengenai jenis gel yang diterima manakala pakar/pegawai perubatan dan staf-staf perubatan yang terlibat tahu mengenai jenis gel yang diberikan. Sejumlah 10ml gel dimasukkan ke dalam urethra (salur kencing) pesakit mengikut kumpulan masing-masing, fleksibel cystoscopy(Flex CE) akan dimasukkan dengan ke salur tersebut sehingga ke pundi kencing.Skor tahap kesakitan (Visual Acuity score) kemudian direkodkan. Jikalau pesakit memerlukan tambahan gel untuk mengurangkan sakit,gel lignocaine 2% diberikan tidak kira sama ada pesakit itu di dalam kumpulan gel lignocaine atau gel pelincir (*cross-over study* atau kajian silang). Jumlah gel yang ditambah tersebut turut direkod dan dianalisis. Selain itu,kos untuk kedua-dua kumpulan tersebut turut dibandingkan dan dikaji.

Keputusan: Skor purata untuk gel lignocaine 2% adalah 4.53, manakala skor purata untuk gel pelincir adalah 4.33.Nilai *p* 0.388 menunjukkan tiada perbezaan ketara dari segi statistic di antara dua kumpulan gel tersebut. Ciri-ciri pesakit di dalam kedua dua kumpulan adalah homogenik. Dua puluh satu orang pesakit di dalam kumpulan A (gel lignocaine) memerlukan gel tambahan,manakala 26 orang pesakit yang pada asalnya menerima gel pelincir(kumpulan B) memerlukan tambahan gel lignocaine. Kos purata bagi gel lignocaine adalah RM 12.30 manakala gel pelincir adalah RM9.44. Walaupun kos tambahan lignocaine gel diambil kira untuk pesakit di dalam kumpulan B (gel pelincir), terdapat perbezaan ketara dari segi kos di antara gel lignocaine dan gel pelincir,di mana nilai *p* adalah 0.008.

Kesimpulan: Keberkesanan gel lignocaine untuk mengurangkan sakit semasa fleksibel cystoscopy (Flex CE) adalah tidak ketara berbanding gel pelincir biasa. Penggunaan gel lignocaine juga melibatkan kos yang lebih tinggi berbanding gel pelincir biasa.

V-ABSTRACT IN ENGLISH

Objective: There is no clear evidence that intraurethral 2% lignocaine gel is superior to plain lubricating gel in reducing pain during flexible cystoscopy (Flex CE).Since 2% lignocaine gel is far more expensive than plain lubricating gel, our study aimed to compare pain score in patients receiving 2% lignocaine gel and plain lubricating gel during flexible cystoscopy (Flex CE).At the same time, the cost difference was also compared in order to asses the benefit of both groups.

Materials and Methods: This is a randomize , prospective, single blind, cross over study. A total of 90 patients were involved in this study. The patients were then randomized by our computer generated randomization sequence to receive either 2% lignocaine gel (Group A) or plain lubricating gel (Group B). Initial 10ml of either 2% lignocaine gel or plain lubricating gel was instilled depending on the group assigned. Flexible cystoscopy was then inserted until the bladder mucosa is seen. Pain score was then recorded by Visual Analogue Score (VAS) with zero, 0 being no pain until 10 which is maximum pain. Additional 2% lignocaine gel was given to patients who requested to have additional gel if the pain was intolerable, regardless of the group assigned (cross-over study).The additional amount of 2% lignocaine gel and the subsequent final VAS score was also recorded. Besides, the cost difference between the two groups was also analyzed.

Results: Mean pain score for group A (2% lignocaine gel) was 4.53, while mean pain score for group B (plain lubricating gel) was 4.33.With a p value of 0.388,there was no statistically significant difference in pain score between the two groups. Patients' characteristics in the two groups were homogenous. Twenty one patients from 2% lignocaine gel group required additional 2% lignocaine gel while 26 patients from plain lubricating gel group required

additional 2% lignocaine gel. The mean cost for 2% lignocaine gel was RM12.30 compared with the mean cost for plain lubricating gel RM 9.44.Despite taking together the cost of additional lignocaine gel in plain lubricating gel group, there were still statistically significant cost difference with a p value of 0.008.

Conclusion: The efficacy of 2% lignocaine gel is not superior compared to plain lubricating gel in reducing pain during flexible cystoscopy. The cost of 2% lignocaine gel was proven to be higher than the cost of plain lubricating gel with little difference in mean pain score.

1-INTRODUCTION

1.1 INTRODUCTION

Flexible cystoscopy (flex CE) is a fundamental procedure in urology. The procedure is usually done in a daycare or office setting. The common indications of flexible cystoscopy are hematuria, insertion or removal of ureteric stents, surveillance for malignancy and lower urinary tract symptoms.

Before the mid 1990s the rigid cystoscopy was the only option. The invention of flexible cystoscopy significantly reduced pain and morbidity associated with rigid cystoscopy because it is flexible, adjustable to follow the curve of urethra and entry into the urethra and bladder is under direct vision, therefore minimising the pain. Together with the advent of modern, smaller caliber flexible cystoscopes the need for local anesthetic/lubricating agents has been questioned. However due to its invasive nature, topical anaesthesia is still required in order to minimize pain associated with the procedure. Two percent Lignocaine gel and lubricating gel has been extensively used prior to carrying out any intraurethral procedure that may be associated with discomfort such as catheterization, flexible cystoscopy or urethral dilatation in awake patients. Introduction of flexible cystoscopy in the urethra will cause some degree of discomfort especially in male patients due to longer urethra.

The ideal lubricant; traditionally,2% Lignocaine gel and lubricating gel has been extensively used prior to carrying out any intraurethral procedure that may be associated with discomfort ,such as catheterisation, flexible cystoscopy or urethral dilatation in awake patients. The clinical significance and the economic consequence with wide use of intraurethral lubricants in daily practice entail the justification of evaluating their efficacy. Intraurethral gel

facilitates insertion of flexible cystoscopy by lubrication and reduce friction, protecting the mucosa, optimal visibility due to its colourless character and provide anaesthetic effect. Randomized controlled trials of 2% ligocaine gel versus plain lubricating gel in men undergoing flexible cystoscopy has produced mixed results. Two percent lignocaine gel emerged as the anesthetic agent of choice based on its theoretical ability to act simultaneously as local anesthetic and lubricant. Two percent lignocaine gel contain 2g of lignocaine hydrochloride in 100g of gel and preservative agents. Lignocaine has been available as a local anaesthesia for over 50 years. It is a lipid soluble amide base that is capable of entering the hydrophobic components of neuronal cell membranes and preventing the transmembrane flow of sodium ions necessary for the initiation and propagation of nerve signal action potentials. Plain lubricating gel contains water and preservative agents only. Numerous studies have examined the volume of gel, instillation time, the waiting time and temperature of the gel as variables and yet no standard regime has been established. There are conflicting data regarding the efficacy of lignocaine gel in reducing pain versus plain lubricating gel in flexible cystoscopy.

In our local setting, both 2% lignocaine gel and plain lubricating gel has been used during flex CE since there is no standard guideline regarding the type of gel used. In the era of cost effective medicine, the cost factor should be taken into consideration as to whether the use of 2% lignocaine gel will result in significantly less pain compared to plain lubricating gel. Pain scores is compared between the patients receiving 2% lignocaine gel and plain lubricating gel. This study also compares the cost difference between the two groups since 2% lignocaine gel costs RM8.08 per 10ml while plain lubricating gel costs RM 4.50 per 10ml.Additional objective is to analyze whether patients require additional instillation of gel in addition to our proposed initial volume of 10ml.

1.2-LITERATURE REVIEW

Introduction of flexible cystoscopy in the urethra will cause some degree of discomfort especially in male patients. Tazhigadeh demonstrated that the most painful part during flexible cystoscopy is when the cystoscope passes through the external urinary sphincter (Tazhigadeh et al. 2006). The study by Tazhigadeh demonstrated how the pain is experienced moment by moment from administration of gel until the completion of cystoscopy which shows the most painful part to be at external sphincter. Theoretically the subepithelial plexus in the urethra is believed to subserve a sensory function and presumably represents the site at which topically applied lignocaine is active. When an instrument (catheter/cystoscopy) is passed into the urethra the sensation from distal urethra(navicular fossa, pendulous urethra) is tactile but not painful. However as the instrument transverse the level of pelvic floor, painful sensation is perceived, which implies that bilateral pudendal nerves supply the striated sphincter muscle, therefore confirming observation by Tazhigadeh. Randomized controlled trial of 2% lignocaine gel versus plain lubricating gel in men undergoing flexible cystoscopy has produced mixed results. Conflicting reports have been published regarding lignocaine gel efficacy prior to flexible cystoscopy.

Instillation time: Choong et al demonstrated that using lignocaine gel 2% would result in less pain provided that 20ml of 2% lignocaine gel was left in urethra for 15minutes (Choong et al. 1998). However Burke et al reported that cystoscopy performed 30 to 60 seconds after lignocaine gel instillation was similarly tolerated **(**Burke et al. 2002). Losco in a study has shown that delaying cystoscope insertion for few minutes in order to enhance efficacy of lignocaine gel in pain reduction to be futile **(**Losco et al. 2011). Likewise Herr in a study of 100 patients shows no difference in pain score between immediate and delayed

insertion of flexible cystoscopy **(**Herr et al. 2001) However the study by Herr involved all patients undergoing repeated surveillance flexible cystoscopy for bladder tumor, which might introduce bias in pain evaluation. Birch showed in a prospective, randomized, double blind trial that instillation of 11ml of 2% lignocaine gel for 10-15 min offered no statistical significant advantage over plain lubricating gel in reducing pain during flexible cystoscopy in awake patients regardless of age(younger or older than 55) (Birch et al.). Meanwhile Aaronson in a meta-analysis of 4 studies concluded that intraurethral instillation of lidocaine gel reduces the moderate to severe pain in flexible cystoscopy (Aaronson et al. 2006). However the 4 studies in the meta-analysis by Aaronson et al. has limitations which are 1) different quantities of lignocaine gel used and 2)different waiting time(dwell time) before the insertion of flexible cystoscopy.

Volume: The volume of lignocaine gel used was 10-20ml and dwell time was 5-25min**.** Meanwhile in our study we chose the volume of 10ml with options of additional lignocaine gel if pain is more than minimal or as requested by the patient. It is not practical for us to have dwell time of up to 25 minutes before flexible cystoscopy insertion due to the workload and limited resource that we have. In a study by McFarlane there was no statistical difference in pain sensation in a randomized controlled study regardless of the volume instilled (Mc Farlane et al. 2001). The study by McFarlane included only patients undergoing their first cystoscopic examination, which helps to eliminate any bias caused by patients' recollection of past experience. Meanwhile in another study by Holmes which compared 10ml and 20ml of gel and found that men treated with 20ml of lignocaine gel had less pain than those receiving 10ml (Holmes et al. 2001). The results of the study by Holmes seems to relate to a study by Dawkins and colleagues (Dawkins et al. 1995) who noted that a mean urethral

volume of 16ml (range 12-20ml) in awake male patients, as assessed by the volume of gel required to pass through the bladder neck while observing with ultrasonography. This observation by Dawkins suggest theoretically that 10ml is an inadequate volume to completely lubricate the urethra prior to cystoscopy, while 20ml should fill entire urethra in all patients. Studies by Holmes and Dawkins suggest that 20ml of lignocaine gel(versus 20ml of plain lubricating gel) would result in greater pain reduction that is attributable to adequate filling of the entire urethra, therefore allowing sufficient anaesthesia of urethra. However the studies was done in Caucasian males with a bigger body habitus and may not represent the population of our study .In our study we chose 10ml of initial gel instillation because it seem sensible to lubricate (anaesthetize) the entire urethra because of shorter urethra in our population and the additional instillation of lignocaine gel will be given to patients as requested.The amount of additional 2% lignocaine gel initially is 10ml,however if patient still complain of pain and the pain score is not reduced,another series of 5ml gel will be given until the pain score has reduced.

Rate of instillation: Khan et al in a prospective, randomized study involving 100 patients who were randomized to receive 11ml of 2% lignocaine gel over either 2seconds or 10 seconds has demonstrated that slow administration of gel over 10 seconds is associated with significantly reduced discomfort compared to rapid administration over 2seconds (Khan et al. 2002). This can be explained by rapid shearing force to the urethral wall when the lignocaine gel was rapidly given over 2 seconds. It is for this reason that we chose to instill lignocaine gel/plain lubricating gel for 10 seconds in all of our patients in the study.

Indwelling time: Rodriguez-Rubio in a study of 185 patients who were randomly assigned to receive 2% lignocaine gel or plain lubricating gel demonstrated no significant

difference in pain if the flexible cystoscopy was inserted less than 5 minutes from the gel instillation (Rodriguez-Rubio et al. 2004). However the study by Rodriguez-Rubio differs from our study in two aspects which are 1)patients with previous experience with flexible cystoscopy was also included in their study 2)all the procedures were done by experienced urologist. Previous exposure to poorly tolerated flexible cystoscopy might influence patient's perception in a negative way. Patients with previous experience may become accustomed to the procedure to some degree and may tolerate minor discomfort. For these reasons we chose to include only patients undergoing flexible cystoscopy for their first time in our study. All of our procedures were done by medical officers as it is unrealistic to have experienced urologist doing the procedure due to clinical load at our center.

Patel in a meta analysis of 7 randomized controlled trial(excluding crossover trials, which is our study) with 417 patients receiving 2% lignocaine gel versus 400 patients receiving plain lubricating gel showed no statistical effect of pain using lignocaine gel (Patel et al. 2008).This meta-analysis refutes the general belief among clinicians that 2% lignocaine gel is superior in reducing pain during flexible cystoscopy.

Chen et al. in a prospective, randomized double blind controlled trial involving 91 patients (45 lignocaine gel/46 plain lubricating gel) demonstrated no statistically significant difference in pain score between the two. The mean and median pain score between the two groups were similar (Chen et al 2005). The difference between the study by Chen and our study is that the amount of gel instilled was 20ml and the dwell time was 15minutes. Meanwhile after review with our local ethical committee, our study is a crossover study whereby if patients request for additional gel regardless of their pain score or initial type of gel given, they would receive additional 2% lignocaine gel. This crossover is to prevent any

ethical argument that may arise if we continue to instill plain lubricating gel despite patient requesting for additional gel to reduce the pain.

Conclusion: In our local setting we have been doing flexible cystoscopy for many years with smearing of lubricant jelly around cystoscope and into external urethral meatus. Both 2% lignocaine gel and plain lubricating gel have been used and there is no proper guideline regarding the type of gel used in flexible cystoscopy. Considering the above mentioned studies, there is no consensus regarding the choice of gel in flexible cystoscopy.

1.3 -RATIONALE OF STUDY

Previous data regarding the efficacy of lignocaine gel versus plain lubricating gel in reducing pain during flexible cystoscopy have produced mixed results. No consensus is available regarding the use of gel during flexible cystoscopy. In the era of cost effective medicine, the cost factor should be taken into consideration as to whether the use of 2% lignocaine gel will result in significantly less pain compared to plain lubricating gel since lignocaine gel costs RM 8.08 per 10ml while plain lubricating gel costs RM4.50 per 10ml.This is a prospective randomized controlled, single blind cross over trial analyzing the difference in pain score in between patients receiving 2% lignocaine gel and plain lubricating gel during flexible cystoscopy. Additional objective is to analyze whether patients require additional instillation of gel in addition to our proposed volume of 10ml.This study will also compare the cost between the two groups (together with the cost of additional instillation of gel).

2-STUDY PROTOCOL

2.1- DOCUMENT SUBMITED FOR ETHICAL APPROVAL

PAIN SCORE COMPARISON IN PATIENTS RECEIVING LIGNOCAINE GEL 2% VERSUS PLAIN LUBRICATING GEL DURING FLEXIBLE CYSTOSCOPY,A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL,A CROSSOVER STUDY.

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This study is a prospective randomized controlled trial in comparing pain scores between the two groups of patients receiving lignocaine gel 2% versus plain lubricating gel during flexible cystoscopy. This study involves urology patients who undergo elective flexible cystoscopy in Hospital Universiti Sains Malaysia. The potential patients involving in this study will be screened with our inclusions and exclusion criterias. The patients will give their written consent. Randomization of patients will be done by computer generated sequence to reduce selection bias. The initial pain score right after the introduction of flexible cystoscopy into the bladder will be recorded in both groups. In addition to pain score comparison, this study also will analyse the additional gel requirement during the flexible cystoscopy to further reduce the pain score. In patients receiving lignocaine gel 2%,the initial pain score right after introduction of flexible cystoscopy into the bladder will be recorded ,subsequently if additional lignocaine gel is required to further reduce the pain ,the amount of additional gel as requested by patients and the subsequent reduced pain score will also be recorded. In another group of patients who receive plain lubricating gel, the initial pain score will be recorded. If additional gel is required as requested by patients, we will subsequently instill lignocaine gel 2%. Additional 2% lignocaine gel is given regardless of the patient's group. The volume of additional lignocaine gel is 10ml initially, and the subsequent pain score is then recorded. If there is still no reduction in pain score, series of 5ml lignocaine gel is added until pain score reduction is achieved. The subsequent reduction in pain score is also recorded. The cost difference between the two groups is also analyzed.

Introduction

Literature review and scientific background

Flexible cystoscopy is a fundamental procedure. It is usually done on outpatient basis. Common indications of flexible cystoscopy include lower urinary tracts symptoms, hematuria, surveillance of urological malignancies and insertion/removal of stent. It has been shown that some patients experience certain degree and discomfort related to the procedure. There are conflicting data regarding the efficacy of lignocaine gel in reducing pain versus plain lubricating gel in flexible cystoscopy .

Introduction of flexible cystoscopy in the urethra will cause some degree of discomfort especially in male patients. Tazhigadeh demonstrated that the most painful part during flexible cystoscopy is when the cystoscope passes through the external urinary sphincter[1].2% Lignocaine gel and lubricating gel has been extensively used prior to carrying out any intraurethral procedure that may be associated with discomfort ,such as catheterization, flexible cystoscopy or urethral dilatation in awake patients. Randomized controlled trial of 2% lignocaine gel versus plain lubricating gel in men undergoing flexible cystoscopy has produced mixed results. Patel in a meta analysis of 7 randomized controlled trial with 817 patients showed no statistical effect of pain using lignocaine gel[2].

Instillation time: Birch et al showed in a prospective, randomized, double blind trial that instillation of 10ml 2% lignocaine gel for 10-15 min offered no advantage over plain lubricating gel in reducing pain during flexible cystoscopy[3]. Meanwhile Aaronson in a meta-analysis concluded that intraurethral instillation of lidocaine gel reduces the moderate to severe pain in flexible cystoscopy[4]. Khan has demonstrated slow administration of gel over

10seconds is associated with significantly reduced discomfort compared to rapid administration over 2seconds[5].

Volume: Mc Farlane found no difference in pain sensation in a randomized controlled study regardless of the volume instilled[6].Rodriguez-Rubio demonstrated no significant difference in pain and discomfort between lignocaine gel and plain lubricating gel during cystoscopy[7]. Holmes found that men treated with 20ml of of lignocaine gel had less pain than those receiving 10ml[8].However Choong demonstrated that using lignocaine gel 2% would result in less pain provided that 20ml of 2% lignocaine gel was left in urethra for 15minutes[9].

Indwelling time: Herr in a study of 288 patients shows no difference in pain score between immediate and delayed insertion of flexible cystoscopy[10]. Losco in a study has shown that delaying cystoscope insertion for few minutes in order to enhance efficacy of lignocaine gel in pain reduction to be futile[11].It has been shown by studies that the most painful part during flexible cystoscopy is when the cystoscope passes through external urinary sphincter(membranous urethra)[12].

In our local setting we have been doing flexible cystoscopy for many years with smearing of lubricant jelly around cystoscope and into external urethral meatus. Flexible cystoscope is then immediately inserted following gel instillation. Both 2% lignocaine gel and plain lubricating gel have been used and there is no proper guideline regarding the type of gel used in flexible cystoscopy. Considering the above mentioned studies, there is no consensus regarding the choice of gel in flexible cystoscopy.

Rationale of studies

Previous data regarding the efficacy of lignocaine gel versus plain lubricating gel in reducing pain during flexible cystoscopy have produced mixed results. No consensus is available regarding the use of gel during flexible cystoscopy. In the era of cost effective medicine,the cost factor should be taken into consideration as to whether the use of 2% lignocaine gel will result in significantly less pain compared to plain lubricating gel. Lignocaine gel costs RM8.08 per tube while plain lubricating gel costs RM4.50 per tube. This study will analyze the difference in pain score in between patients receiving 10ml 2% lignocaine gel and patients receiving 10ml of plain lubricating gel during flexible cystoscopy. Additional objective is to analyze whether patients require additional instillation of gel in addition to our proposed volume of 10ml.This study will also compare the cost between the two groups (together with the cost of additional instillation of gel).

Hypotheses

Null hypotheses

- There is no difference in pain score between the two groups of patients receiving lignocaine gel and lubricating gel during flexible cystoscopy.

Objectives

General objective

- To determine visual analogue score (VAS) between patients receiving lignocaine gel 2% and patients receiving plain lubricating gel during flexible cystoscopy.

Specific objectives

- 1st specific objective: To determine mean/median pain score between the two groups.
- 2nd specific objective: To analyze the difference in pain score between the two groups.
- 3rd specific objective: To analyze if there is any additional instillation of gel required to reduce pain in each group.
- 4th specific objective: To analyze cost difference between the two groups (taking together the cost of additional instillation of gel)

Research Methodology

Trial Design

- Prospective, randomize controlled trial, single blind.

Study population

Reference population

- All Urology patients in Hospital Universiti Sains Malaysia

Source population

- All patients undergoing flexible cystoscopy under Urology Department in Hospital Universiti Sains Malaysia.
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Inclusion criteria

- All adults male age 18 years and older scheduled for elective flexible cystoscopy.

Exclusion criteria

- Patients using sedatives.
- Patients with spinal cord disease.
- Patients with a known hypersensitivity to anaesthetic agents.
- Patients on regular analgesia.
- Inability to asses pain(altered mental status,language barrier,dementia).
- Other significant known illness associated with pain and discomfort.
- Mentally challenged patients.

Study settings

Study Location

- Operation theater,Hospital Universiti Sains Malaysia

Study Duration

- June 2016 to Feb 2017

Intervention.

During flexible cystoscopy, patients will be divided into either group A or group B by our computer generated sequence randomization. Patients in group A will receive 10ml of lignocaine gel intraurethrally which will be administered slowly over 10-20seconds.Patients in group B will receive 10ml of plain lubricating gel intraurethrally which will be also administered slowly over 10-20sec.Flexible cystoscopy will be inserted 30seconds after instillation of gel and patient will be asked regarding his pain according to visual acuity (VAS) score and the score is recorded. Subsequently during the cystoscopy if patient still complains of pain, additional lignocaine gel 2% is given regardless of the patient's group. The volume of additional lignocaine gel is 10ml initially,and the subsequent pain score is then recorded. If there is still no reduction in pain score, series of 5ml lignocaine gel is added until pain score reduction is achieved.

Outcome

The primary outcome is the initial pain score right after the flexible cystoscopy enter the bladder. The secondary outcomes are the additional volume of lignocaine gel required and the resulting pain score.

Sampling size

Sample size determination

The sample size was determined by Two Mean formula by using G*Power software according to study by Chen et al(2005)[3]

t tests - Means: Difference between two independent means (two groups)		
Analysis:	A priori: Compute required sample size	
Input:	Tail(s)	= Two
	Effect size d	= 0.6
	α err prob	= 0.05
	Power (1-β err prob)	= 0.8
	Allocation ratio N2/N1	= 1

Sample size, n = 90

Sample size + 10% drop out = 100

Therefore, the total sample size for this study will be 100 (50 samples for each group).

Randomization.

Sequence generation

The selection of patients for each group in the study will be carried out using Microsoft Excel,in which this method is a simple computer generated sequence to reduce selection bias.Each patient will have equal probability to be assigned to either group.

Type of randomization: blocked randomization

Blocked randomization assures that the number of patients allocated in Lignocaine gel and plain lubricating gel are the same size with allocation ratio of 1:1.Blocked randomization can ensure close balance of the numbers in each group at any time of the trial.

Allocation concealment mechanism

Once randomization completes, each number will be placed into an envelope that fulfills the characteristics: opaque, sealed and sequential. The number for each group will be revealed on the day of the trial.

Implementation.

Patients will be enrolled by medical officers/surgeons in Urology department. Patients' assignement to intervention will also be implemented by the clinicians in Urology department of Hospital Universiti Sains Malaysia.

Blinding

This study is a single blind study, only the patient is blinded to the type of gel used during his flexible cystoscopy. The clinicians and care providers are aware of the type of gel given. This is important since our study is a crossover study, whereby if the patient complains of pain after insertion of flexible cystoscopy, additional lignocaine gel will be given.

Statistical methods

- 1st specific objective: Determining mean/median pain score for the two groups is descriptive.
- 2nd specific objective: Independent t-test in analyzing the difference in pain score between the two groups.
- 3rd specific objective: Independent t-test in analyzing the additional lignocaine gel instillation required to relieve the pain.
- 4th specific objective :Independent t-test in comparing the costs between the two groups.