

Intravenous lidocaine suppresses dexamethasone-induced perineal pruritus during anesthesia induction: A randomized controlled, double blind study

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Abstract: Previous studies have found that intravenous dexamethasone may produce perineal pruritus in some patients when administered as premedicant in the preoperative period. This randomized controlled, double-blind study evaluated the efficacy of pretreatment of lidocaine on the incidence and severity of dexamethasone-induced perineal pruritus. 400 patients were enrolled in this study and allocated randomly into four groups (n=100, in each). Then, patients received intravenously anesthesia induction as the following sequence of medications: injecting 0.9% sodium chloride (placebo) 10 mL in group I, lidocaine 0.5mg/kg in group II, lidocaine 1mg/kg in group III, and lidocaine 1.5mg/kg in group IV, 1 minute later, injecting 10mg dexamethasone in all groups. The severity of perineal pruritus was graded based on the VAS as none (VAS 0), mild (VAS 1-3), moderate (4-6), or severe (VAS 7 to 10), and recorded the occurrence, the severity and the duration of perineal pruritus. Occurrence of perineal pruritus was significantly reduced in group III and group IV (8%, 9% vs 40% and 33% in Groups I and II, respectively, $p<0.05$). The incidence of perineal pruritus of females was higher than males in groups I and II ($P<0.05$). The duration of perineal pruritus was shorter in group IV compared to groups I, II and III ($p<0.05$). We conclude that pretreatment 1mg/kg or 1.5mg/kg lidocaine may effectively reduce the incidence of perineal pruritus.

Keywords: Anesthesia, dexamethasone, lidocaine, pruritus.

INTRODUCTION

Dexamethasone is a synthetic glucocorticosteroid with minimal mineralo corticoid activity, widely used before general anesthesia induction to prevent postoperative nausea and vomiting (PONV) (Henzi *et al.*, 2000). In our early study, we noted that Intravenous dexamethasone may produce perineal pain and perineal pruritus in some patients when administered as premedicant in the preoperative period (Gu *et al.*, 2012). Dexamethasone-induced perineal pruritus is common but has not caused enough attention as a serious drug problem. However, perineal pruritus is not good, and last for a long time. It will happen with drug use, requiring appropriate intervention, and may be associated with increase of unpleasant experience in the operation room.

Previous studies have shown that dexamethasone-induced perineal pruritus can be alleviated by pretreatment with fentanyl (1µg/kg) (Rewari *et al.*, 2010). In the clinic, we often use lidocaine for suppression of fentanyl-induced cough and reducing pain on injection of propofol (Pandey *et al.*, 2005; So *et al.*, 2013). We hypothesized that pretreatment of lidocaine might suppress dexamethasone-induced perineal pruritus. So, we designed a randomized controlled study to observe the effects of intravenous lidocaine on dexamethasone-induced perineal pruritus during anesthesia induction. The present study was

designed to find a simple and convenient method that could effectively attenuate dexamethasone-induced perineal pruritus.

SUBJECTS, MATERIALS AND METHODS

Participants

The Ethics Committee of The First People's Hospital of Wujiang approved the protocol of the present study, and informed written consent was obtained from all patients. A total of 400 patients of either sex, aged 25 to 60 years, American Society of Anesthesiologists (ASA) class I or II, scheduled for elective ENT and abdominal surgery with general anesthesia were enrolled in the present study. Patients who were on regular medications with analgesic or analgesic use within 24 hours of anesthesia, drug or alcohol abuse, contraindications to steroid use [diabetes mellitus /impaired glucose tolerance, peptic ulcer disease, endocrine disorder, morbid obesity (BMI>30)], impaired kidney or liver function were excluded from the study.

Trial design

According to the inclusion and exclusion criteria, Dr Wang decided whether a patient should be included in the present study. All patients were divided into 4 groups of 100 patients randomly by using a computer-generated table of random numbers. Dr Wang was responsible for the preparation of the drugs. The allocation sequences were put in some sealed envelopes, and all the patients and the implementers were blinded in the present study.

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Table 1: Demographic data of patients

Group	I (n=100)	II (n=100)	III (n=100)	IV (n=100)
Age (year)	43±7	42±10	44±9	41±8
Sex (M/F)	46/54	44/56	44/56	45/55
Weight (kg)	62±10	63±9	65±7	64±8
ASA class (I/II)	98/2	95/5	94/6	96/4

Data are expressed as the mean ± standard deviation, or number of cases. There were no significant differences between groups with regard to the demographics

Table 2: Dexamethasone-induced perineal pruritus and its severity in the four groups

Group	I (n=100)	II (n=100)	III (n=100)	IV (n=100)
Incidence (%)	40 (40)	33 (33)	9 (9) *#	8 (8) * #
Severity	None	60(60)	67 (67)	91 (91)
	Mild	25 (25)	20 (20)	6 (6)
	Moderate	11(11)	9 (9)	2 (2)
	Severe	4 (4)	4 (4)	1 (0)

Data are expressed as number (percentage). * P<0.05, groups II, III, and IV versus group I; # P < 0.05, groups III and IV versus group II

Table 3: The effect of gender on dexamethasone-induced perineal pruritus

		n	Group I	n	Group II	n	Group III	n	Group IV
Incidence (%)	Total	100	40 (40)	100	33 (33)	100	9 (9)	100	8 (8)
	Male	46	8(17.4)	44	7(15.9)	44	2(4.5)	45	3(6.7)
	Female	54	32(59.3)*	56	26(46.4)*	56	7(12.5)	55	5(9.1)
Duration of perineal pruritus (second)	Total	40	65±15	33	53±16	9	29±6 #	8	16±6 #†
	Male	8	25±7	7	26±10	2	16±3	3	9±4
	Female	32	76±12*	26	61±14*	7	33±5*	5	21±5*

Data are expressed as number (percentage) or Mean ± SD. * P<0.05, Female versus Male. P<0.05, groups II, III, and IV versus group I; # P<0.05, groups III and IV versus group II † P<0.05, group IV vs. group III

The premedication was phenobarbital sodium 0.1 g and atropine 0.5 mg intramuscular injection 30 min before anesthesia. In the operating room, venous access to the median cubital vein was established with an 18-gauge cannula. All patients in the operation room were established with an 18-gauge cannula in median cubital vein. The vertical distance between the infusion bottle and the operation bed was 1 meter in all patients. Non-invasive blood pressure, heart rate, electrocardiogram, and pulse oximeter were applied throughout the surgery. All patients in the operation room keep sedation at least 5 minutes. Then, patients received intravenously anesthesia induction as the following sequence of medications: injecting 0.9% sodium chloride (placebo) 10 ml in group I, lidocaine 0.5mg/kg (20mg/ml, Dameng. Corp®, Guangdong, China) in group II, lidocaine 1mg/kg in group III, and lidocaine 1.5mg/kg in group IV (all lidocaine was diluted with 0.9% sodium chloride to a volume of 10 ml), 1 minute later, injection of 2ml dexamethasone sodium phosphate (5 mg/ml, Tianyao. Corp®, Tianjing, China) in all groups. All the bolus time of dexamethasone was controlled, less than 2 seconds, and was recorded in the present study. Induction of anaesthesia was conducted 3 min after the end of injection

of dexamethasone. All patients were successfully endotracheally intubated, and they underwent surgery favorably.

Measurements of the severity of perineal pruritus

The day before surgery, patients could cooperate and understand the Visual Analogue Score (VAS) scale. Patients were explained about the use of VAS for grading the severity of perineal pruritus on a scale of 0 to 10. We defined the range of perineal pruritus including vagina, vulva, anus, scrotum, and penis. An observer, not knowing what the type of drug was given to the patients, recorded the occurrence, the severity and the duration of perineal pruritus. The severity of perineal pruritus was graded based on the VAS as none (VAS 0), mild (VAS 1-3), moderate (4-6), or severe (VAS 7 to 10).

STATISTICAL ANALYSIS

Data were expressed as mean ± SD, number, proportion, or percentage. Statistical analysis was performed by Statistical Product for Social Sciences (SPSS) software 13.0(SPSS Corp®, USA). The number of perineal pruritus and the proportions of sex and ASA class were

compared using Chi-square test or Fisher exact test with Bonferroni correction. One-way analysis of variance was used to compare the age and weight among the four groups. $P < 0.05$ was considered statistically significant.

RESULTS

Demographic data

All patients completed our study. There was no statistically significant difference of age, sex, weight, and ASA class between the four groups (table 1).

Dexamethasone-induced perineal pruritus and its severity in the four groups

The incidence of dexamethasone-induced perineal pruritus was 40%, 33%, 9%, and 8% in groups I, II, III, and IV, respectively. Groups III and IV had a lower incidence and less severity of perineal pruritus than groups I and II ($P < 0.05$). Groups III and IV had a lower incidence less severity of perineal pruritus than group II ($P < 0.05$). There was no significant difference in the incidence and severity of perineal pruritus between groups III and IV ($P > 0.05$) (table 2).

Effect of gender on dexamethasone-induced perineal pruritus

The females had higher incidence of perineal pruritus than males in groups I and II ($P < 0.05$). The females had longer duration of perineal pruritus than males in groups I, II, III and IV ($P < 0.05$). Groups III and IV had a lower duration of perineal pruritus than groups I and II ($P < 0.05$). Groups IV had a lower duration of perineal pruritus than group III ($P < 0.05$) (table 3).

DISCUSSION

Our study showed that intravenous lidocaine suppresses dexamethasone-induced perineal pruritus during anesthesia induction. Since year 2000, dexamethasone was widely used to prophylaxis or treatment of post operative nausea and vomiting (Pandey *et al.*, 2005; So *et al.*, 2013). Dexamethasone-induced perineal pruritus is commonly observed during induction of anaesthesia (Thomas *et al.*, 1986; Klygis *et al.*, 1992; Andrews *et al.*, 1986). Singh *et al.* performed a small prospective study in which 60 patients experienced pruritus in many patients after administration of intravenous dexamethasone sodium phosphate (Singh *et al.*, 2011). Perineal itching or excruciating pain in patients receiving dexamethasone is more common in female patients with incidence more than 55%. Their results are also similar to our study where the incidence of perineal pruritus was more in group I (female patient) and it was statistically significant. Another method of abolishing this discomfort is to administer dexamethasone after induction of anaesthesia. Wang *et al.* found that it was more effective in preventing PONV prophylactic using dexamethasone immediately

before anesthesia, rather than at the end of anesthesia (Wang *et al.*, 2000). So it is more important to find a way to reduce the dexamethasone-induced perineal pruritus.

Lidocaine was widely used to suppress fentanyl-induced cough and reduce pain on injection of propofol during induction of anaesthesia (Pandey *et al.*, 2005; So *et al.*, 2013). In our study, we find that 1mg/kg or 1.5mg/kg intravenous lidocaine could effectively suppress the incidence and severity dexamethasone-induced perineal pruritus during anesthesia induction. We observed that a pretreatment dose of 0.5mg/kg lidocaine was able to suppress the duration of perineal pruritus significantly and higher doses of lidocaine (1mg/kg or 2mg/kg) were more effective in suppressing the duration of perineal pruritus. So, we presume that lidocaine had dose dependent manner in suppressing the duration of dexamethasone-induced perineal pruritus. We still did not know the perineum pruritus mechanisms induced by dexamethasone. Some studies found that hydrocortisone-21-phosphate sodium and prednisolone phosphate may lead to perineal irritation.

So, they speculate that perineal pruritus could be related to the phosphate ester of the corticosteroid (Thomas *et al.*, 1986; Neff *et al.*, 2002; Taleb *et al.*, 1988). Dexamethasone sodium phosphate, instead of dexamethasone acetate salt, was used in our study. Whether dexamethasone acetate salt will lead perineal pruritus is unknown.

Previous studies have shown the difference incidence of dexamethasone-induced perineal pruritus from 25% to 100% (Gu *et al.*, 2012; Rewari *et al.*, 2010; Thomas *et al.*, 1986; Singh *et al.*, 2011). These difference results were due to different drug doses and the injection time. Therefore, in our study, we chose a moderate dose of dexamethasone (10mg), the clinical usually using of this dose in every operation. In addition, our previous study showed that the dexamethasone-induced perineal pruritus was associated with injection time, prolonged injection time could significantly reduce the incidence of perineal pruritus. So we controlled the bolus time of dexamethasone less than 2 seconds. Interestingly, in our study, we found that pretreatment with lidocaine, do not prolong the injection time, could effectively reduce the incidence and severity of dexamethasone-induced perineal pruritus. The results of this study were obviously different from the previous studies. We found that with the increase of the lidocaine dose, the duration of duration perineal pruritus was gradually shortened. This strategy significantly reduced the duration of perineal pruritus from 65 s to 16 s.

Topical local anesthetics such as lidocaine have been shown to have anti-pruritic properties (Villamil *et al.*, 2005; Joffe *et al.*, 1985; Fishman *et al.*, 1997). Therefore,

the low incidence of perineal pruritus in groups II, III, IV and low duration of perineal pruritus in present study may be associated with neurotransmitter mechanisms. The neurotransmitter may be phosphate itself or be stimulated by phosphate. We speculate that dexamethasone may participate in the pathogenesis of pruritus through activate the sodium channels in peripheral unmyelinated C-fiber polymodal afferents within superficial layers of skin and mucous membrane (Villamil *et al.*, 2005). Using lidocaine may result in slow release of neurotransmitters. Previous studies have shown the relationship between gender and perineum pruritus (Gu *et al.*, 2012; Singh *et al.*, 2011). In our daily clinical practice, we found that the incidence of perineal pruritus in females was significantly higher than that of males. In our study, we found that the incidence was higher in females as compared to males in groups I and II. We speculate that the threshold levels of released neurotransmitters were lower in females than in males.

There are four major limitations in interpreting the results of the present study. First, the sample size was small, only three groups of patients using lidocaine, and so we may not find the optimal dose of lidocaine to reduce the incidence of perineal pruritus. Second, the preoperative medication with phenobarbital sodium 0.1 g and atropine 0.5 mg must be used, but premedication may interfere with the experimental results. Third, we only observed the influence of gender on dexamethasone-induced perineal pruritus and patients were not grouped according to the age or weight factors. Last, we only observed the effects of dexamethasone sodium phosphate-induced perineal pruritus but not observed dexamethasone acetate salt.

In conclusion, our study suggests that pretreatment 1mg/kg or 1.5mg/kg lidocaine may effectively reduce the incidence of perineal pruritus. High dosage of lidocaine do not reduce the incidence of perineal pruritus, but suppress the duration of dexamethasone-induced perineal pruritus in a dose dependent manner.

REFERENCES

- Andrews D and Grunau VJ (1986). An uncommon adverse effect following bolus administration of intravenous dexamethasone. *J. Can. Dent. Assoc.*, **52**(4): 309-311.
- Fishman SM, Caneris OA, Stojanovic MP and Borsook D (1997). Intravenous lidocaine for treatment-resistant pruritus. *Am. J. Med.*, **102**(6): 584-585.
- Gu CY, Wu YM, Zhou MT, Li F and Tang QF (2012). The effect of dilution and prolonged injection time on dexamethasone-induced perineal pruritus. *Pharmazie*, **67**(12): 1015-1017.
- Henzi I, Walder B and Tramèr MR (2000). Dexamethasone for the prevention of postoperative nausea and vomiting: A quantitative systematic review. *Anesth. Analg.*, **90**(1): 186-194.
- Joffe P, Andersen LW, Mølviig J, Kyst A and Johannessen A (1985). Intravenous lidocaine in the treatment of pruritus in hemodialysis patients. *Clin. Nephrol.*, **24**(4): 214.
- Klygis LM (1992). Dexamethasone-induced perineal irritation in head injury. *Am. J. Emerg. Med.*, **10**(3): 268.
- Neff SP, Stapelberg F and Warmington A (2002). Excruciating perineal pain after intravenous dexamethasone. *Anaesth. Intensive. Care*, **30**(3): 370-371.
- Pandey CK, Raza M, Ranjan R, Singhal V, Kumar M, Lakra A, Navkar DV, Agarwal A, Singh RB, Singh U and Singh PK (2005). Intravenous lidocaine 0.5 mg.kg⁻¹ effectively suppresses fentanyl-induced cough. *Can. J. Anaesth.*, **52**(2): 172-175.
- Rewari V, Garg R, Trikha A and Chandralekhia (2010). Fentanyl pretreatment for alleviation of perineal symptoms following preoperative administration of intravenous dexamethasone sodium phosphate-a prospective, randomized, double blind, placebo controlled study. *Middle East J. Anesthesiol.*, **20**(6): 803-808.
- Singh M, Sharma CS, Rautela RS and Taneja A (2011). Intravenous dexamethasone causes perineal pain and pruritus. *J. Anesthe001.. Clinic. Res.*, S1:001.doi:10.4172/2155-6148.S1-Pages 1-3.
- So SY, Kim YH, Ko YK, Park SI, Pak HJ and Jung WS (2013). Effect of lidocaine (40mg) mixed to prevent injection pain of propofol on the intubating conditions and onset time of rocuronium. *Korean J. Anesthesiol.*, **64**(1): 29-33.
- Taleb N, Geahchan N, Ghosn M, Brihi E and Sacre P (1988). Vulvar pruritus after high-dose dexamethasone. *Eur. J. Cancer Clin. Oncol.*, **24**(3): 495.
- Thomas VL (1986). More on dexamethasone-induced perineal irritation. *N. Engl. J. Med.*, **314**(25): 1643-1644.
- Villamil AG, Bandi JC, Galdame OA, Gerona S and Gadano AC (2005). Efficacy of lidocaine in the treatment of pruritus in patients with chronic cholestatic liver diseases. *Am. J. Med.*, **118**(10): 1160-1163.
- Wang JJ, Ho ST, Tzeng JI and Tang CS (2000). The effect of timing of dexamethasone administration on its efficacy as a prophylactic anti-emetic for postoperative nausea and vomiting. *Anesth. Analg.*, **91**(1): 136-139.