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The effect of dilution and prolonged injection time on dexamethasone-induced perineal pruritus

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Dexamethasone has been widely used before general anesthesia induction. However, previous studies have found that a pre-induction bolus dose of dexamethasone sometimes causes perineal pruritus. We hypothesized that an appropriate prolongation of the injection time might suppress dexamethasone-induced perineal pruritus. Four hundred patients requiring general anaesthesia were randomly allocated into four groups: group I receiving 2 ml dexamethasone (5 mg/ml); group II receiving 4 ml dexamethasone (2.5 mg/ml); group III receiving 10 ml dexamethasone (1 mg/ml); and group IV receiving 20 ml dexamethasone (0.5 mg/ml). Dexamethasone was diluted with 0.9% sodium chloride. The injection time of dexamethasone was 5 s in groups I, II and III; while the injection time of dexamethasone was 30 s in group IV. Occurrence of perineal pruritus was significantly reduced in Group IV (0% vs 38%, 32% and 12% in Groups I, II and III, respectively, $p < 0.05$). The incidence was higher in females than in males ($p < 0.05$). The duration of perineal pruritus was longer in females than in males in groups I, II and III ($p < 0.05$). We conclude that the dilution of dexamethasone to 0.5 mg/ml with 0.9% sodium chloride combined with prolonged injection time to 30 s eliminates dexamethasone-induced perineal pruritus.

1. Introduction

Dexamethasone is widely used before general anesthesia induction to prevent postoperative nausea and vomiting (PONV) (Fujii et al. 2000). The same treatment (DEX 10 mg, IV) 5 min prior to fentanyl injection was also used to reduce fentanyl-induced cough (Lin et al. 2007). However, previous studies have found that a pre-induction bolus dose of dexamethasone sometimes causes perineal pruritus (Andrews et al. 1986; Crandell 2004; Klygis 1992; Neff et al. 2002; Perron et al. 2003; Thomas 1986). The incidence of perineal pruritus varies between 25% to 100%, depending on the dose of dexamethasone (Andrews et al. 1986; Crandell 2004; Kuczkowski 2004; Neff et al. 2002; Perron et al. 2003; Sanchez Ortega et al. 2005; Taleb 1988). Dexamethasone-induced perineal pruritus is common but has not been viewed as a serious drug problem. However, perineal pruritus is not always brief and benign. It may require immediate intervention, and may be associated with undesirable increase of unpleasant experience in the operation room. Prevention of dexamethasone-induced perineal pruritus in such situations is of great importance.

Previous studies have shown that dexamethasone-induced perineal pruritus can be alleviated by pretreatment with fentanyl (1 μg/kg) (Rewari et al. 2010). However, the incidence of fentanyl-induced cough was not observed in this study. The clinical acceptance of fentanyl-induced cough is somewhat limited. We hypothesized that an appropriate prolongation of the injection time might suppress dexamethasone-induced perineal pruritus. In clinical practice, however, prolonged injection of undiluted dexamethasone (5 mg/ml) is not easy to do. The present study was designed to find a simple and convenient method that could effectively attenuate dexamethasone-induced perineal pruritus.

2. Investigations, results and discussion

All patients completed the present study. There was no statistically significant difference between the four groups with regard to age, weight, sex, and ASA class (Table 1).

The incidence of dexamethasone-induced perineal pruritus was 38% in group I, 32% in group II, 12% in group III, and none in group IV. 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 and less severity of perineal pruritus than group II ($P < 0.05$). Group IV had a lower incidence and less severity of perineal pruritus than group III ($P < 0.05$) (Table 2).

The incidence of perineal pruritus was higher among females than among males in groups I and II ($p < 0.05$). The duration of perineal pruritus was longer in females than in males in groups I, II and III ($p < 0.05$) (Table 3).

Our study showed that dilution of dexamethasone to 0.5 mg/ml with 0.9% sodium chloride combined with prolonged injection time of 30 s completely eliminated dexamethasone-induced perineal pruritus.

Dexamethasone-induced perineal pruritus is commonly observed during induction of anaesthesia (Crandell 2004;

Table 1: Demographic data and clinical characteristics

Group	I(n = 100)	II(n = 100)	III(n = 100)	IV(n = 100)
Age (year)	40 ± 8	41 ± 10	40 ± 11	39 ± 10
Sex (M/F)	43/57	41/59	43/57	42/58
Weight (kg)	59 ± 8	61 ± 10	61 ± 7	61 ± 9
ASA class (I/II)	97/3	96/4	98/2	97/3

* Values are mean ± SD; There was no significant difference with regard to demographics in the four groups

Perron et al. 2003). Our study has shown that undiluted dexamethasone, when administered through a peripheral venous line, provokes perineal pruritus in up to 38% of the patients. Since 2000, the use of dexamethasone has extended to prophylaxis and the treatment of post operative nausea and vomiting. Another method of abolishing this discomfort is to administer dexamethasone after induction of anaesthesia. It was found that the prophylactic IV administration of dexamethasone immediately before the induction, rather than at the end of anesthesia, was more effective in preventing PONV (Wang et al. 2000). So it is even more important to find a way to reduce dexamethasone-induced perineal pruritus. Previous studies have shown that the incidence of dexamethasone-induced perineal pruritus varies between 25% and 100% (Kuczkowski 2004; Sanchez Ortega et al. 2005; Taleb et al. 1988). These studies did not observe the effect of the injection time. Rewari et al. (2010) reported that 71% of patients had perineal pruritus after 8 mg dexamethasone intravenously through a peripheral venous line. These symptoms were alleviated by pretreatment with fentanyl (1 μg/kg).

In a study by Singh et al. (2011), 43% of patients were perineal pruritused after receiving 0.15 mg/kg dexamethasone via a peripheral intravenous line. This discrepancy can be explained by differences in injection dose and time. Therefore, in the present study, we chose a medium dose of dexamethasone (10 mg), which is commonly used in daily practice. Injection time had considerable impact on the incidence of perineal pruritus, which decreased significantly as the injection time was prolonged in a pilot study. We adopted an injection time of 5 s in Groups I, II and III because we found the injection of the volume of diluted dexamethasone solution could not be achieved within 2 s when dexamethasone was diluted to 1 mg/ml with 0.9% sodium chloride. In our pilot study with 20 patients, we concluded that the time required for the completion of the injection of diluted dexamethasone was 3–5 s. Interestingly, in our study, we found that the incidence and severity of perineal pruritus could even be effectively reduced by the dilution of dexamethasone to 1 mg/ml with 0.9% sodium chloride alone without prolonged injection time. This result is obviously different from that of previous studies. We obtained the gradually decreased incidence of perineal pruritus with increased dilution of 10 mg dexamethasone, which was injeccted at the same rate. This strategy significantly reduced the incidence of perineal pruritus from 38% to 12%.

The mechanism by which dilution of dexamethasone reduces the incidence of perineal pruritus is not known. Some studies speculate that perineal pruritus could be related to the phosphate ester of the corticosteroid since perineal irritation has been described with hydrocortisone-21-phosphate sodium and prednisolone phosphate (Neff et al. 2002; Perron et al. 2003; Taleb et al. 1988; Thomas 1986). Therefore, the low incidence of perineal pruritus in groups II, III and IV in our study may be attributed to actions on neurotransmitter mechanisms. The neurotransmitter may be phosphate itself or be stimulated by phosphate. We speculate that dilution and prolonged injection time on dexamethasone may result in a slower release of neurotransmitters. Neurotransmitters released by injections of small doses of diluted dexamethasone may not reach threshold levels, hence resulting in no dexamethasone-induced perineal pruritus.

The effect of gender on the incidence of perineal pruritus was already seen in previous studies (Rewari et al. 2010; Singh et al. 2011). In our daily clinical practice, we have observed that females had a higher incidence of dexamethasone-induced perineal pruritus. In our study, we found that the incidence was higher in females than in males in groups I and II. We speculate that the threshold levels of released neurotransmitters were lower in females than in males.

In conclusion, our study suggests that the dilution of dexamethasone may effectively reduce the incidence of perineal pruritus.

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

Group		I (n = 100)	II (n = 100)	III (n = 100)	IV (n = 100)
Incidence (%)		38 (38)	32 (32)	12 (12) [ab]	0 (0) [abc]
	None	62 (62)	68 (68)	88 (88)	100 (100)
Severity	Mild	23 (23)	19 (19)	6 (6)	0 (0)
	Moderate	10 (10)	10 (10)	6 (6)	0 (0)
	Severe	5 (5)	3 (3)	0 (0)	0 (0)

* Data are expressed as number (percentage)
[a] $P < 0.05$, groups II, III, and IV vs group I; [b] $P < 0.05$, groups III and IV vs group II; [c] $P < 0.05$, groups IV vs group III

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	38 (38)	100	32 (32)	100	12(12)	100	0 (0)
	Male	43	9(20.9)	41	7(17.1)	43	3(7.0)	42	0(0)
	Female	57	29(50.9) [a]	59	25(42.4) [a]	57	9(15.8)	58	0(0)
Duration of perineal pruritus (s)	Total	38	69 ± 36	32	58 ± 24	12	26 ± 9	0	0
	Male	9	28 ± 12	7	23 ± 11	3	13 ± 3	0	0
	Female	29	79 ± 29 [a]	25	71 ± 19 [a]	9	30 ± 6 [a]	0	0

* Values are expressed as number (percentage) or mean ± SD
[a] $P < 0.05$, Female vs Male.

The dilution of dexamethasone to 0.5 mg/ml with 0.9% sodium chloride combined with a prolonged injection time of 30 s eliminates dexamethasone-induced perineal pruritus. This is a simple and cost-effective method to prevent this adverse effect.

3. Experimental

3.1. Patients

Four hundred American Society of Anesthesiologists physical status class II or II patients of either sex, aged 22–70 yr and weighing 42–81 kg, scheduled for elective surgery under general anesthesia were enrolled in the present study. Exclusion criteria included: body weight exceeding 20% of ideal body weight (on the basis of body mass index recommended); impaired kidney or liver function; presence of a gastric tube; alcohol abuse; diabetes mellitus or impaired glucose tolerance; endocrine disorder.

3.2. Methods

Dr. Gu decided whether a patient should be included in the present study according to the inclusion and exclusion criteria, randomized the patients to four groups of 100 patients by using a computer generated table of random numbers, and was responsible for drug preparation. The allocation sequences were contained in a set of sealed envelopes, and the observer and all the patients involved in the present study were blinded.

This double-blind, randomized, and controlled study was conducted after approval from the Institute's Ethics Committee and after obtaining written informed consent from the patients. The tests were completed in the operating room. Phenobarbital sodium 0.1 g and atropine 0.5 mg were injected intra-muscularly 30 min before anesthesia. Venous access to the median cubital vein was established with an 18 gauge cannula. The vertical distance between the drip bottle and the venous access was 1 m in all patients. Electrocardiogram, noninvasive blood pressure, and pulse oximeter were applied throughout the tests. Patients were left undisturbed for more than 5 min. Then, participants were randomly assigned into four groups and all received 10 mg dexamethasone (Tianyao. Corp®, Tianjing, China): group I receiving 2 ml dexamethasone (5 mg/ml); group II receiving 4 ml dexamethasone (2.5 mg/ml); group III receiving 10 ml dexamethasone (1 mg/ml); and group IV receiving 20 ml dexamethasone (0.5 mg/ml). Dexamethasone was diluted with 0.9% sodium chloride. The injection time of dexamethasone was 5 s in groups I, II and III; while the injection time of dexamethasone was 30 s in group IV. Induction of anaesthesia was conducted 10 min after the end of injection of dexamethasone.

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, unaware of the type of medications 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).

3.3. Statistical analysis

Data are 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.

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