

Perineal pruritus after intravenous administration of hydrocortisone sodium phosphate

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Objectives: To determine the frequency of genital pruritus after intravenous administration of hydrocortisone and the associated risk factors.

Methods: Observational, prospective study of patients who received intravenous hydrocortisone sodium phosphate in the emergency department of La Paz Hospital between December 2007 and May 2008. The variables studied included age, sex, dose, form of administration, onset of pruritus, the severity of itching, and concomitant medication.

Results: We included 54 patients, of whom 39 were males (72.5%). The mean age was 56.9 years. The dose administered was 200 mg in 30 patients (55.6%) and 100 mg in the remainder. In total, 26 patients developed anogenital pruritus (48.1%). Itching lasted between 5 and 45 seconds and resolved spontaneously. Significant differences were observed with respect to age (the mean age of the patients with pruritus was lower) and the infusion method used (the higher the concentration used and the faster the drug was administered, the greater the probability of pruritus).

Conclusions: Transient pruritus following administration of intravenous hydrocortisone sodium phosphate is a common side effect that affects younger people and is associated with bolus administration. Dilution of the drug in 50 mL of saline solution, whenever possible, can prevent the appearance of this side effect. [Emergencias 2009;21:114-116]

Key words: Hydrocortisone sodium phosphate. Perineal pruritus. Intravenous administration.

Introducción

Within the pharmacological group of corticosteroids, there are basically three that are intravenously administered in emergency situations: hydrocortisone, 5-methyl prednisolone¹ and dexamethasone. Very few direct adverse effects have been associated with their intravenous administration, except for some allergic reactions². Occasionally, the appearance of genital, perineal or anorectal pruritus has been reported, associated with the use of hydrocortisone and dexamethasone. A review of the literature in Medline only revealed one reference to the association between hydrocortisone and anorectal pruritus³. In contrast, recent publications include ten articles⁴ referring to perineal pruritus associated with the administration of dexamethasone sodium phosphate⁵. The objective of this study was to determine the frequency of perineal pruritus after intravenous administration of hydrocortisone so-

dium phosphate, as well as to identify possible risk factors for the appearance of this adverse effect.

Method

We performed a prospective observational study of 54 non-consecutive patients treated at the Emergency Department of La Paz Hospital (Madrid) during a period of six months (December 2007-May 2008). The inclusion criterion was having received intravenous hydrocortisone sodium phosphate (Actocortina[®] laboratories Altana Pharma SA-Nycomed, Spain) as part of the treatment. The corticoid was administered by nursing staff who decided on the volume and dilution of the drug, but not the route which is habitually specified by the prescribing physician. The dilutions used were: 2 ml, 5 ml, 10 ml and 50 ml. For the first three, the drug was administered in bolus

form (2-5 seconds) and for the last, perfusion during 15-60 seconds was used.

Data collection included: age, sex, weight, reason for treatment with hydrocortisone, dose, form and perfusion time, appearance of pruritis or not, patient self-report on level of symptom intensity (categorized as slight, moderate or severe) and symptom duration, appearance of erythema, and co-administration of any other drug.

For statistical analysis of the data, quantitative variables are expressed as means \pm standard deviation (SD) and qualitative variables as percentages. The Student t test was used for the analysis of quantitative variables and Chi2 test was used for qualitative variables. Values of $p < 0.05$ were considered statistically significant. Statistical analysis was carried out using Windows SPSS, version 15.0.

Results

Of the 54 patients, 39 (72.2%) were men and 15 (27.8%) women. Mean age was 56.9 ± 23.5 years, range 14-95 years, and mean weight was 69.3 ± 13.5 Kg.

All received hydrocortisone for severe dyspnoea associated with bronchial spasm. Mean dose was 2.4 ± 0.9 mg/Kg; 24 (44.4%) received 100 mg and 30 (55.6%) received 200 mg. Form of intravenous administration was bolus diluted in saline solution, 2ml in 12 cases (22.2%); 5 ml in 8 cases (14.8%); and 10 ml in 22 cases (40.7%). Perfusion with 50 ml of saline solution was used in 12 cases (22.2%).

Anogenital pruritis was recorded in 26 patients (48.1%) (Table 1). Intensity of itching was reported as slight in 1, moderate in 8 and severe in 17 patients. Duration of pruritis varied from 5 to 45 seconds and resolved spontaneously. No skin alterations (erythema, etc.) or other symptoms were recorded. Some patients received other drugs simultaneously, mainly inhaled beta-2-adrenergic agonists (salbutamol) and anticholinergic agents (ipratropium). The patients with pruritis were significantly younger (44.7 vs 67.3 years) than those without ($p < 0.001$). In addition, the probability of pruritis increased with increased concentration of the drug and faster administration times (Table 1). No differences were found with respect to patient gender, drug dose per Kg body weight, or concomitant medication.

Discussion

In Spain, two hydrocortisone formulations for intravenous administration are commercially available:

Table 1. Patient characteristics and treatment according to the presence or absence of pruritis

	Pruritus (26 patients)	No Pruritus (28 patients)	p value p
Gender			
Male	17 (65.4%)	22 (78.6%)	
Female	9 (34.6%)	6 (21.4%)	0.2
Mean age (yrs)	44.7	67.3	< 0.001
Dose:			0.3
100 mg	10 (38.5%)	14 (50%)	
200 mg	16 (61.5%)	14 (50%)	
Dose mg/Kg	2.5	2.2	0.2
Form of administration			
Bolus diluted in 2 ml	10 (38.5%)	2 (7.1%)	
Bolus diluted in 5 ml	4 (15.4%)	4 (14.3%)	
Bolus diluted in 10 ml	12 (46.1%)	10 (35.7%)	
Perfusion diluted in 50 ml	0	12 (42.9%)	0.001

one is sodium phosphate (Actocortina® laboratories Altana Pharma SA-Nycomed, Spain) and the other is sodium succinate (Solu-cortef® laboratories Pfizer, Spain); the former is predominantly used. In a search of the literature, we found only one study, published in 1976, which reported that 16 of 18 (88%) of patients receiving the sodium phosphate formulation presented anogenital pruritis, versus none who received the sodium succinate. Since that publication, we found no further studies on this topic. The reason may be related to the passing and inconsequential nature of the adverse effect and its being mentioned only to nursing staff and not to the prescribing physician. The situation with respect to the administration of intravenous sodium phosphate dexamethasone is very different. This drug began to be used in the 1980s and isolated cases of genital pruritis were reported^{6,7} in patients with head injuries⁸ or pre-chemotherapy⁹. As from 2000, it has begun to be widely used by anaesthetists to prevent and treat post-operative nausea and vomiting^{11,12}. In this circumstance, it is the anaesthetists themselves who intravenously administer the drug and therefore witness at first hand the possible adverse effects¹³. Although the number of cases in these series is low, not more than 20 patients, these adverse effects clearly seem to be a frequent occurrence and are related with the speed of perfusion. Perron et al¹⁴ performed a small prospective study in which 20 patients received intravenous sodium phosphate dexamethasone. They found associations between the appearance of pruritis and female sex as well as rapid perfusion, and concluded with the recommendation that the steroid should be diluted in 50 ml of saline solution and perfused during 5-10 minutes. Their findings coincide with ours, except that in our study the frequency of pruritis in

the women, although higher, was not significantly different from that found in the men (Table 1).

Regarding the other corticoid widely used for intravenous administration, 5-methylprednisolone, there are also some case reports¹⁵ of pruritus in the genital area associated with sodium phosphate, but not with the formulation habitually used in Spain, which is methylprednisolone sodium succinate (Urbason® laboratories Sanofi-Aventis SA).

In the case of hydrocortisone, perfusion speed rate is usually decided on by the attending nurse, unless the physician decides on rapid bolus administration in certain patients whose severity of condition is considered to warrant bolus administration.

The etiopathogenic mechanism underlying the appearance of this pruritus is unknown, and has been related with ether phosphate corticoid more than with the phosphate ion itself, since the effect has only been reported for these three drugs (hydrocortisone, dexamethasone y methyl prednisolone and not for other phosphate drugs. The brief duration of the adverse effect is explained by rapid hydrolysis of the corticoid-phosphate complex.

Given the above considerations, the recommendations are to use 50 ml dilutions of the drug, whenever the clinical situation of the patient allows it, to avoid the risk of pruritus as an adverse effect. In cases where this is not feasible, the patient should be warned in advance of this possible effect and reassured as to its innocuous nature.

Addendum

This work was partially presented at the II National Congress of Health Science students held at Complutense University of Madrid, 17-18 April 2008.

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Prurito perineal tras la administración intravenosa de hidrocortisona fosfato sódico

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Objetivos: Establecer la frecuencia con la que aparece prurito genital tras administrar hidrocortisona iv y los factores que determinan su aparición.

Método: Estudio observacional, prospectivo de pacientes que recibieron hidrocortisona fosfato sódico i.v en el servicio de urgencias del Hospital La Paz entre diciembre de 2007 y mayo de 2008. Se rellenó un protocolo donde se incluyeron las variables: edad, sexo, dosis, forma de administración, aparición de prurito e intensidad del mismo y fármacos concomitantes.

Resultados: Se incluyeron 54 pacientes de los cuales 39 eran varones (72,2%). La edad media fue de 56,9 años. Las dosis administradas fueron 200 mg en 30 pacientes (55,6%) y 100 mg en el resto. Presentaron prurito en el área anogenital 26 enfermos (48,1%), que osciló entre 5 y 45 segundos y que cedió espontáneamente. Se encontraron diferencias significativas en relación con la edad (los pacientes con prurito tenían menor edad media) y con la forma de perfusión; de tal forma que cuanto más concentrado y más rápido (en bolo) se administre, mayor es la probabilidad de presentar prurito.

Conclusiones: La aparición de prurito tras la administración de hidrocortisona fosfato sódico intravenosa es un hecho frecuente y pasajero que aparece especialmente en personas jóvenes y cuando se administra en bolo. La administración de este fármaco diluido en 50 ml de suero, cuando sea posible, puede evitar la aparición de este efecto secundario. [*Emergencias* 2009;21:114-116]

Palabras clave: Hidrocortisona fosfato sódico. Prurito perineal. Intravenoso.