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## Rhabdomyolysis During Isotretinoin Therapy

### Rabdomiólisis durante el tratamiento con isotretinoína

To the Editor:

Isotretinoin therapy is used in nodular-cystic acne and acne vulgaris when they do not respond to other treatments. Muscle toxicity is a little-known complication and its true incidence and management remain to be determined.

A 16-year old male started therapy with 30 mg per day of isotretinoin (0.4 mg/kg/d) for papulopustular acne that was resistant to other treatments. In routine laboratory tests prior to the start of therapy with retinoids all parameters were normal. After 2 months the patient presented with severe cheilitis, so the dose was reduced to 20 mg per day (0.3 mg/kg/d). No adverse events were detected during follow-up with bimonthly physical examination and laboratory tests (complete blood count, basic biochemistry, and lipid profile), and the acne improved significantly. Because of the dose reduction the therapy was continued longer than usual. In a routine examination conducted after 11 months and close to the end of the therapy, the patient reported moderate fatigue. Blood tests revealed elevated creatine phosphokinase (CK) and myoglobin plasma levels, with values of 801 IU/l (normal range, 5-110 IU/L) and 504 ng/mL (normal range, 0-75 ng/mL), respectively. A

few days before the sample was collected the patient had done weight-lifting exercises, which was not a usual activity for him. We discontinued the isotretinoin therapy and recommended abundant fluid intake and avoidance of strenuous exercise. In the results of laboratory tests after 3 weeks all parameters had returned to normal.

Rhabdomyolysis is caused by necrosis of striated muscle cells and subsequent release of toxic intracellular material into the blood stream.<sup>1</sup> It has been defined as an elevation of CK greater than 5 times the upper limit of normal.<sup>2</sup> It can be caused by toxins (substance abuse, alcohol, and drugs), trauma, overexertion, and muscle metabolic defects.<sup>2</sup> Drugs are one of the most common causes of rhabdomyolysis, although in most patients various causes are found simultaneously. The drugs involved are usually the antipsychotics and statins.<sup>2</sup> The typical clinical presentation of weakness, muscle pain, and reddish urine occurs in less than half of patients<sup>1</sup> and high levels of CK can be found in the absence of symptoms.<sup>3</sup>

Isotretinoin is a vitamin A derivative that is widely used in dermatology and is usually well tolerated. Shortly after its introduction several cases of elevated CK in patients receiving this therapy were reported. In recent years there have been almost no publications on the subject, probably because of the tendency to reduce the frequency and thoroughness of monitoring.<sup>4</sup> In some of the cases described the patients had severe muscle pain and weakness of acute onset.<sup>5-7</sup> In others rhabdomyolysis was detected in asymptomatic patients through the finding of elevated CK in routine

laboratory tests.<sup>8</sup> The elevation of CK in patients undergoing isotretinoin therapy is usually mild and asymptomatic<sup>3</sup> and its incidence is variable (5.5% to 37.3%).<sup>3,4</sup> In addition, some patients with symptoms of pain and muscle weakness have CK within the normal range.<sup>3,7</sup>

CK levels are influenced by the level of physical activity. They are higher in athletes than in physically active nonathletes and higher in the latter than in sedentary people.<sup>9</sup> Some authors have suggested that normal ranges should take into account the level of physical activity of the individual. The upper limit of the normal range could be 350-532 IU/L in physically active male nonathletes.<sup>9</sup>

It is believed that isotretinoin and exercise can have a synergistic effect in causing muscle damage,<sup>3</sup> a hypothesis that could explain the differences in CK levels found in different studies. Landau et al<sup>4</sup> found elevated levels of CK in 37.3% of patients in a study performed on soldiers, whose physical activity is higher than that of the general population. On the other hand, Kaymac<sup>3</sup> found elevated levels of CK in only 5.5% of patients from the general population treated with isotretinoin.

There are disagreements concerning the management of isolated CK elevation. Although some authors recommend not starting isotretinoin therapy if the baseline CK is elevated and discontinuing therapy if CK rises during therapy,<sup>10</sup> most prefer to decrease the dose or temporarily discontinue therapy until the enzyme levels return to normal.<sup>3,4</sup> In patients performing strenuous exercise, avoidance of this activity may be sufficient.<sup>3,4</sup>

In conclusion, we present a case of rhabdomyolysis in a patient treated with isotretinoin. We believe that the dermatologist should be able to recognize this adverse effect and know how to manage it. It is recommended to avoid strenuous exercise during isotretinoin therapy and CK levels should be determined in the routine laboratory tests in athlete patients to detect asymptomatic cases. Although we discontinued the isotretinoin therapy, it may be sufficient to avoid exercise, decrease the dose, or interrupt therapy until CK has returned to normal levels.

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## Physiological Desquamation of the Newborn: Epidemiology and Predisposing Factors

### Descamación fisiológica en el recién nacido: epidemiología y factores predisponentes

*To the Editor:*

Physiological desquamation is the name given to surface scaling that appears in most newborn infants within a few days after birth. It begins on the ankles in the first 24 to 48 hours after birth and can remain localized, often confined to the hands and feet, or gradually spread. It is usually most intense and widespread between the sixth and tenth days.<sup>1,2</sup>

When involvement is generalized or more intense it must be distinguished from certain forms of ichthyosis or hypohidrotic ectodermal dysplasia, which are rare conditions

with a very different clinical course and management. Furthermore, newborns with physiological desquamation do not present findings consistent with ichthyosis, such as poor general condition, ectropion, family history, characteristic distribution, continuous flaking, or erythema of the underlying skin. It is important to recognize this transitory benign skin condition in order to avoid unnecessary tests and treatment and parental anxiety.<sup>3</sup>

Although physiological desquamation is a common disorder, few studies have analyzed the frequency and predisposing factors involved. Our aim was to determine the prevalence of physiological desquamation and the areas of the body affected in 1000 newborn infants in our health care district, and how neonatal and maternal parameters, time of examination, and mode of delivery influence its appearance.

We undertook a descriptive study of 1000 newborn infants seen in the perinatology outpatient clinic of the