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ORIGINAL ARTICLE

The challenge of administering anti-tuberculosis treatment in infants and pre-school children. pTBred Magistral Project☆,☆☆

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Tuberculosis;
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Abstract
Introduction: There are no paediatric formulations of anti-tuberculous drugs in Spain, with the only exception being rifampicin. Some paediatricians often prescribe composite formulations (CF), while others prefer to give crushed tablets. Nevertheless, there is no consensus in this regard, or any pharmacokinetic studies validating these procedures. In this situation, the Spanish Network for the Study of Paediatric Tuberculosis (pTBred) has launched the Magistral Project, which aims at its first phase to analyse the desirability of developing child-friendly pharmaceutical formulations and other aspects regarding the anti-tuberculous drug prescription in children.
Material and methods: A cross-sectional, multicentre, nationwide study was conducted, based on an online questionnaire sent to members of pTBred between February and March 2015.
Results: Fifty-four responses from 67 consulted institutions were received. Most of the respondents reported prescribing crushed tablets. A significant number of those surveyed, although being fewer, prescribe CF, for which availability varies widely among institutions. Eighty-three percent replied that it would be essential to have fixed dose combinations of anti-tuberculous drugs, specifically adapted to paediatric doses and administered by CF or tablets. Among the

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surveyed institutions, differences were found in the management of latent tuberculosis infection, in the use of directly observed therapy, and in the monitoring of adverse events.
Conclusions: Our survey reveals great diversity in anti-tuberculous drug prescription in children, due to the lack of suitable infant formulations, which could have an impact on treatment adherence and outcomes. pTBred intends to develop a pioneering and useful consensus document on the management of anti-tuberculous medication in children.

PALABRAS CLAVE
Tuberculosis;
Niños;
Fármacos antituberculosos;
Encuestas comunitarias;
Formulación magistral

El reto de la administración de antituberculosos en lactantes y preescolares. Proyecto Magistral de pTBred

Resumen
Introducción: En España no existen presentaciones pediátricas de fármacos antituberculosos, salvo para rifampicina. Algunos pediatras prescriben fórmulas magistrales (FM), mientras que otros administran comprimidos triturados. No existe consenso al respecto, ni estudios de farmacocinética que avalen estos procedimientos. Ante esta situación, la Red Española de Estudio de la Tuberculosis Pediátrica (pTBred) desarrolla el Proyecto Magistral, con el objetivo de analizar, en su primera fase, la conveniencia de desarrollar formas farmacéuticas específicas para niños, así como estudiar otros aspectos relacionados con la administración de antituberculosos en niños.
Material y métodos: Estudio transversal, multicéntrico y de ámbito nacional, mediante encuesta *on-line* enviada por correo electrónico a los instituciones pertenecientes a pTBred entre febrero y marzo del 2015.
Resultados: Se recibieron 54 respuestas de 67 instituciones consultadas. La mayoría de los centros trituran los comprimidos. Un porcentaje elevado, aunque menor, administra FM, cuya disponibilidad es variable entre las instituciones. El 83% responde que sería ideal disponer de combinaciones fijas de antituberculosos, adaptadas a las dosis pediátricas y administradas mediante FM o en un comprimido. Entre las instituciones encuestadas existen diferencias en el tratamiento de la infección tuberculosa latente, el uso de la terapia directamente observada y la monitorización de efectos adversos.
Conclusiones: Nuestra encuesta revela gran heterogeneidad en la prescripción de antituberculosos en niños debido a la falta de formulaciones específicas para esta edad, que podría tener implicaciones en la adherencia al tratamiento y evolución. pTBred propone elaborar un pionero y útil documento de consenso sobre la administración de medicación antituberculosa en niños.

Introduction and objectives

Between 2003 and 2010, the Working Group on Tuberculosis and Infection by Other Mycobacteria of the Sociedad Española de Infectología Pediátrica (Spanish Society of Paediatric Infectology [SEIP]) published the consensus documents[1–6] on the diagnosis and management of tuberculosis in children, collaborating with the Sociedad Española de Neumología Pediátrica (Spanish Society of Paediatric Pulmonology [SENP])[6] in the most recent one. These documents highlighted the lack of paediatric formulations prepared as solutions or suspensions for most antituberculosis agents, especially for those currently used as first-line treatment, which is one of the barriers to adherence.[5,6] As of today, the challenge most frequently faced by paediatric specialists in respiratory or infectious diseases in their everyday practice still remains: *how to administer antituberculosis agents to children that have yet to develop the ability to swallow solid dosage forms*.

In Spain, the only first-line antituberculosis agent that is commercially available as a liquid dosage form is rifampicin[7] (Table 1). Under these circumstances, some paediatricians prescribe compounded preparations (CPs), while others prescribe tablets to be crushed and subsequently diluted in various fluids for their administration. There is no consensus on these practices, nor any pharmacokinetic studies to support them. There is also wide variability in the use of CPs, with variations in stability between different dosage forms and the excipients used in their formulation and in the conditions surrounding their preparation. The published literature on the stability of CPs is also scarce.[8,9] There is also few data on the use of fixed dose combinations (FDCs) of antituberculosis drugs (Table 2), and furthermore their use is not approved in children aged less than 8 years.[10] In