



SPANISH ASSOCIATION OF PAEDIATRICS

Tuberculosis treatment for children: An update^{☆,☆☆}



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Abstract Tuberculosis (TB) is the most important infectious disease all over the world, with a high morbidity and mortality. Paediatric tuberculosis has been a neglected epidemic, due to the difficulties in assessing its global impact, reduced incidence and lower infectivity compared to adults. In 2015, the WHO reported 1 million cases of paediatric TB and 169,000 deaths. In Europe, the emergence of MDR TB is a major concern, representing 16% of the new diagnosis in Eastern Europe. In 2014, it was estimated that about 219,000 children were infected by MDR-TB-strains in Europe, and 2120 developed the disease. Spain is the Western European country with more paediatric cases, with an incidence 4.3/100,000 inhabitants in 2014. Paediatric tuberculosis mortality in Spain is rare, but extra-pulmonary disease is associated with significant complications. The prevalence of paediatric drug resistant TB in Spain is over 4%, higher than the estimated incidence in adult population, representing mayor difficulties for therapeutic intervention. These data reveal that paediatric TB is still a Public Health priority in our country.

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^{☆☆} This project is endorsed by all the signing societies and institutions. In the case of RITIP and TEDDY, there is no endorsement as such, since the document was requested by these research networks. The SENP has also agreed to endorse the project.

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The difficulties in diagnosis and the lack of optimal paediatric drug formulations are the major challenges for controlling the childhood's tuberculosis epidemic. A group of national paediatric TB experts has reviewed the international guidelines and the most recent evidences, and has established new recommendations for the management of paediatric TB contacts, latent infection and active TB disease, especially focused in drug resistant cases. This document replaces the former national guidelines from the Spanish Society for Pediatric Infectious Diseases, although the prior recommendations on the diagnosis remain valid.

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PALABRAS CLAVE

Tratamiento tuberculosis;
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Resistencia

Actualización del tratamiento de la tuberculosis en niños

Resumen La tuberculosis (TB) es la enfermedad infecciosa más importante del mundo, asociando enorme morbimortalidad. La TB pediátrica ha sido una epidemia oculta por su escasa capacidad infectiva y menor incidencia comparada con adultos. El informe-OMS 2015 estimó un millón de niños enfermos de TB en el mundo y 169.000 fallecidos. En Europa, el problema acuciante es la tuberculosis multirresistente, con tasas del 16% en nuevos diagnósticos, especialmente en países del este. En 2014, 219.000 niños se infectaron por cepas-MDR en Europa, 2.120 desarrollaron enfermedad. España es el país de Europa con mayor número de casos pediátricos, con una incidencia en 2014: 4,3/100.000 habitantes. La mortalidad por TB pediátrica en nuestro país es excepcional, pero las formas extrapulmonares ocasionan importantes complicaciones. La TB resistente en niños en España presenta una prevalencia >4%, superando incluso la notificada en adultos. Estos datos reflejan que la TB en niños en nuestro medio continúa siendo un problema de salud pública prioritario.

Las dificultades diagnósticas del niño y la falta de formulaciones pediátricas óptimas son el mayor desafío para control de TB infantil. El Grupo de expertos de TB pediátrica realiza un análisis de las nuevas tendencias internacionales y guías terapéuticas de tuberculosis en niños, según nuevas evidencias disponibles; y considera una prioridad actualizar las guías pediátricas nacionales de exposición a TB, infección tuberculosa latente y enfermedad, y particularmente los casos de resistencia a fármacos. Este documento, por tanto, sustituye a todos los previos en cuanto a las pautas terapéuticas, aunque siguen estando vigentes las indicaciones diagnósticas. © 2017 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Current epidemiology of tuberculosis

Tuberculosis (TB) is the most important infectious disease worldwide and one of the 10 leading causes of death, although its incidence and associated mortality are experiencing a marked decline. In 2015, there were 104 million new cases, 480,000 of them of multidrug-resistant TB (MDR-TB), and 1.4 million deaths caused by this disease. Through its *End TB* strategy, the WHO intends to decrease the incidence of TB by 80% and its mortality by 90% by year 2030.

Paediatric TB has been a hidden global epidemic for decades due to the difficulty of estimating its true impact. In highly endemic countries, the main barriers are poverty and the limited accessibility of health care. International policies have neglected this population due to the lower incidence of TB in children compared to adults and the low infectivity of TB. Even the *Stop TB* strategy, based on the quantification and treatment of individuals with active disease, excluded children because they rarely have positive sputum-smear results. Since 2012, there has been an increasing awareness of the need to include children in these

programmes.² The latest reports of the WHO¹ provide more accurate data on the impact of childhood TB, with an actual incidence that exceeds published data by 25%, an estimated one million diseased children worldwide, and 169,000 dying from TB in 2015.

In Europe, the overall prevalence of childhood TB has been decreasing each year, but TB continues to be a public health priority, with more than 40,000 cases reported in the past decade and an overall prevalence of MDR-TB of 16% in newly diagnosed cases and 48% in previously treated cases. Eastern European countries are the most important contributors to these figures and pose a serious threat to the overall control of the disease.³ It is estimated that in 2014 there were 219,000 children infected with MDR strains in Europe, of who 2120 developed the disease.⁴

Spain is the country in Western Europe with the highest number of paediatric cases, although the incidence is progressively decreasing. In 2014, 303 cases were reported in children, corresponding to an incidence of 4.3 cases per 100,000 inhabitants.³ The epidemiology of TB, marked by HIV infection in the last two decades of the 20th century, has

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