On the Diagnosis and Management of Viral Respiratory Infections

AKADEMISK AVHANDLING

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av
Robin Brittain-Long
Leg. Läkare

Fakultetsopponent
Professor Annika Linde
Smittskyddsinstitutet
Stockholm

Avhandlingen baseras på följande arbeten:


Abstract

Acute respiratory tract infections (ARTIs), are the most common infections in man, and represent a major global health burden. Viruses, most often causing a mild and self-limiting disease, yet with substantial morbidity and high costs for society, mainly cause upper respiratory tract infections. 70% of all infections in primary care in Sweden are due to ARTIs. Lower respiratory infections on the other hand constitute the third leading cause of death worldwide, mainly in children <5 years of age in resource poor settings. Distinguishing virus from bacteria can be difficult, and often lead to an over-prescription of antibiotics. Modern molecular based diagnostic methods have increased the possibility of an etiologic diagnosis of ARTIs significantly. This thesis aims to evaluate the use of a multiplex real time PCR assay targeting 13 respiratory viruses and two bacteria, from a clinical perspective.

In paper I, a retrospective study of 954 nasopharyngeal samples, the PCR assay, which is based on automated specimen extraction and multiplex amplification, is described. Detection rate was 48%. Streamlined testing and cost limitation (€ 33 per sample) along with high accuracy and prompt result delivery, is key to successful implementation of broad molecular testing.

Paper II evaluates in a prospective study of 209 adults with ARTI in primary care, and 100 asymptomatic controls, the impact duration of symptoms have on detection rate. Overall positive yield was 43% in patients and 2% in controls, with a significantly higher detection rate in patients with < 6 days duration of symptoms (51%) compared to ≥ 7 days (30%, p<0.01).

Having access to the PCR assay reduced antibiotic prescription rates by 50%, in a prospective study (paper III) of 426 adults with ARTI. Patients receiving a result within 48 hours were prescribed antibiotics in 6.8% (n=14) compared to 15.1% (n=33, p<0.01) in the delayed result group.

The diagnostic yield in paper IV, a retrospective study of 8753 patients of all ages during 36 consecutive months, was significantly higher during winter (54.7%) than in summer (31.1%, p<0.001), and in children (61.5%) compared with adults (30.5%, p<0.001). Rhinovirus was the most frequently found virus (32.5%), independent of season, and displayed a high genetic variability across seasons.

The findings of this thesis support the implementation of similar methods in routine clinical care.

Keywords: Respiratory virus, Respiratory tract infection, Real-time PCR, Multiplex PCR, Antibiotic use.

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