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The Review on Study of Common Cold Disease

Ravindra Chatur Patil[1] * Assistant Prof. Rutuja S. Abhonkar[2*]

Swami Vivekananda Sanstha's Institute of Pharmacy,

Mungase Malegaon

Abstract:

Respiratory viral infections, also known as the common cold, are the most common infections in humans. Despite their benign nature, they are a major cause of morbidity and mortality on a worldwide basis. Several viruses have been associated with such illness, of which rhinovirus is the most common. Symptom production is a combination of viral cytopathic effects and the activation of inflammatory pathways. Therefore, antiviral treatment alone may not be able to prevent these events. The optimal use of such agents also requires earlier initiation; therefore, it is important to develop accurate and rapid diagnostic techniques for respiratory viruses. Before any reliable and effective treatment is available, symptomatic therapies may remain the only possible choice for management.

Keywords: Symptoms, Respiratory, Infections, Virus.

Introduction:

The common cold is the most commonly encountered infectious syndrome of human beings. Most observers consider colds to include symptoms of rhinitis with variable degrees of pharyngitis, but the major associated symptoms include nasal stuffiness and discharge, sneezing, sore throat, cough and hoarse voice. Patients frequently report chills, but a significantly high temperature is unusual. Colds are usually self-limiting to previously healthy individuals, but there are also recognised complications such as secondary bacterial infections, exacerbations of asthma, chronic obstructive airway disease and cystic fibrosis. Despite the benign nature of the illness in the majority of cases, it is still a significant economic burden on society.[1] It leads to an increase in consultations with clinicians, increased absence from school and work and subsequently causes loss of earnings.Transmission of parainfluenza virus (PIV) is by direct person-to-person contact or by large particle aerosol spread [2].The high rate of infection in childhood, coupled with the frequency of reinfection, suggests that they spread from person to person. There is evidence to suggest that the infectious dose of PIV is small, as two-thirds of volunteers developed flu-like symptoms following low-titre PIV intranasal challenge. RSV is spread by infected respiratory secretions. The major route of transmission appears to be by large particle aerosol or direct contact with self-inoculation. Spread requires either close contact with the infected individual or contamination of the hands followed by introduction into conjunctiva. Influenza tends to spread by small-particle aerosols. The relative efficacy of the various transmission routes under natural conditions for each virus is unknown.[3]

Since the discovery of rhinovirus in 1956, more than 100 serotypes have been identified, the relative prevalence of which seems to vary between different geographical areas and also over the course of time. These viruses are the most common cause of upper respiratory tract infections in all age groups. The reservoir for rhinovirus is school children, who transmit rhinovirus infections among their peers and infect other family members at home. Parainfluenza virus is the most common cause of croup (acute laryngotracheobronchitis) in young children and accounts for 5% of all causes of the common cold. [4]The human parainfluenza viruses are categorised into types 1 – 4, on the basis of antigenic differences. They are transmitted from person to person by direct contact with infectious respiratory secretions or by large-particle aerosols. The incubation period is about 3– 6 days. Bone marrow transplant recipients, children with bronchopulmonary dysplasia, prematurity, congenital heart disease or asthma are prone to

develop lower respiratory infection and require additional oxygen supplementation. One-third of children with lower respiratory infections due to parainfluenza are thought to develop secondary bacterial infections.[5]

Influenza virus infection accounts for 5 –15% of common colds. The small-particle aerosol spread has been implicated in several outbreaks, and it can retain its infectivity for prolonged periods after aerosolisation in conditions under low humidity. There are two features that distinguish influenza from other respiratory viruses. First, influenza viruses are able to produce new strains for which most of the population lacks immunity, leading to worldwide outbreaks. The unique feature of antigenic variation is referred to as antigenic shift or drift. Second, a recent outbreak in humans of the lethal H5N1 influenza subtype suggested that direct transmission between humans and infected birds without an intermediate host is possible. This avian influenza subtype caused high mortality, killing 70– 100% of chickens and also 6 humans. There was also a high proportion of amino acid changes in all gene products within the H5N1 influenza virus except the surface genes; this provides further support for antigenic drift.[6,7]

A new pneumovirus, human metapneumovirus (HMPV), has recently been isolated in the Netherlands. It is closely related taxonomically to RSV. This virus possibly accounts for about 10% of unexplained respiratory infections in children during the winter season. Seroprevalence studies show that the virus has been circulating in humans for at least 50 years, that 25% of children by age 1 year have antibodies to the virus and that by age 5 years virtually all are seropositive. Analysis of the amplified sequences showed two clusters of HMPV. The clinical manifestation of HMPV can vary from mild upper respiratory symptoms to severe infections requiring hospital admissions. This clinical picture is an indistinguishable form that of other respiratory viruses. Coinfection of HMPV with other respiratory viruses is uncommon, and its role in human respiratory infections is still poorly understood. This new pathogen will certainly warrant long-term surveillance.[8]

Prevention:

The existence of diverse viral serotypes in causing the common cold has made vaccine preparation very difficult. Frequent mutations of viral proteins of RNA viruses (for example, genetic drift and shift of influenza) have further hampered the prevention of the illness. Influenza vaccines are the only commercially available vaccines. They are virtually all split products or purified subunit vaccines being used around the world. The strains (either A or B) that are used in immunisation are selected yearly, based on the recommendation by the World Health Organisation in conjunction with national public health institutions. Recent vaccines contain antigens of two influenzas A subtypes, strains of the currently circulating H3N2 and H1N1 subtypes and one influenza B virus. The waning of vaccine-induced immunity over time requires annual re-immunisation, even if the vaccine antigens are unchanged. The current recommendation for influenza vaccination in the UK is to offer it to those over the age of 65, those with chronic heart, respiratory or renal disease and those who are diabetic or immunosuppressed. The national policy also states that those living in long-stay residential and nursing homes should be prioritised for vaccination. Despite the wide availability of the vaccine against influenza A, it still causes 13,000 –20,000 excess deaths per year in the UK. Rhinovirus has more than 100 serotypes; it is unlikely that a unifying vaccine will be developed. However, the use of antivirals as chemoprophylaxis may have practical value. Topical application of interferon in the nose has been shown to be effective in reducing the incidence of colds in people who are exposed to others with a fresh cold. This strategy reduced the overall risk of cold by 40% and almost eliminated proven rhinovirus colds in contacts. The development of an RSV vaccine has been hampered by the experience with formalin-inactivated whole RSV vaccine in the 1960s, as it caused 80% of RSV vaccinees to become hospitalised compared with 5% of controls, as well as two fatalities.[9,10]

Current major research has focused on prophylaxis using a humanised mouse monoclonal antibody, Palizivumab, which has been shown to reduce the rate of RSV-associated hospitalisation in premature infants. However, its use on a wider population will require further research. There is currently no licensed Parainfluenza vaccine to date. The formalin-inactivated vaccine generated in the 1960s was not able to prevent PIV infection and was soon abandoned. At present, recombinant bovine PIV3 and human PIV3 attenuated vaccines are being evaluated in animal models as vectors for the delivery of other viral antigens such as RSV-G and RSV-F proteins. This bivalent vaccine combination provides a high level of resistance to challenge with PIV3 and RSV in animal models. The conventional methods of vaccination are via the intramuscular and subcutaneous routes. Mucosal immunisation has recently been explored and represents an attractive manner of delivering vaccines. It is fast, simple and noninvasive, and it can be carried out by unskilled individuals. The use of mucosal vaccination seems logical in that most respiratory viral

infections initially start at the mucosal sites. Therefore, inducing local immunity can help arrest the infection at an early phase before systemic complications arise. Thus far, there has been inconclusive evidence to support the use of vitamin C and extracts of the plant Echinacea in common cold prevention.[11,12]

Daily supplementation with large doses of vitamin C does not seem to prevent common colds; however, there seems to be a modest (8– 9%) reduction in the number of symptom days in individuals with established cold symptoms, with larger doses having a greater effect. For Echinacea, currently available data from studies conducted in the adult population show positive findings both in the treatment and prevention of upper respiratory infection. However, variations in the design of the clinical trial and in Echinacea preparations have to be taken into account. Zinc has been shown to possess antiviral properties in vitro, and different preparations of zinc have been proposed for the treatment of the common cold. Zinc lozenges appeared to have positive effects on adults, but negative effects on children in terms of duration and severity of common cold symptoms. Zinc nasal spray appears to reduce the total symptom score but has no effect on the duration of the common cold. Recent research shows that zinc nasal gel can reduce the median time to cold resolution compared to placebo (4.3 days vs. 6.0 days; $p = 0.02$) and decrease the median time to resolution of nasal congestion, nasal drainage, hoarseness and sore throat.[13]

Diagnosis:

The diagnosis of common cold is usually based on the patient's clinical presentation and the clinician's assessment of the disease. Sometimes, the diagnosis can be less straightforward for three reasons. First, clinical features of a common cold may overlap with those of pharyngitis and bronchitis, which are related syndromes of shared viral origins. To complicate matters, pharyngitis and sinusitis can also be caused by bacterial infections. Second, allergic diseases of the upper airway often have clinical features resembling those of common colds. Third, infants and young children are not able to express their symptoms, and clinicians have the challenge to distinguish between benign viral infections and severe invasive bacterial infections. Some respiratory viruses have typical clinical presentations that may be helpful in assessing the aetiology of illness when considered in conjunction with epidemiological factors such as age and clinical presentation of the patient and seasonality. Sometimes, it is virtually impossible to ascertain a specific virus inducing the common cold in the individual patient on clinical grounds alone. Determination of the aetiology of virus infections becomes increasingly essential with the introduction of new antivirals. The optional use of these new therapeutic options is problematic because all these drugs are virus-specific. Some therapies are initiated on the basis of a presumptive diagnosis; a specific diagnosis may be important to confirm the initial impression and to determine the length of time for treatment. Conversely, viral detection is important to avoid unnecessary antibiotic prescriptions. The principal laboratory methods of respiratory virus diagnosis rely on their detection in respiratory secretions.[14,15]

Antigen testing The major advantage of antigen detection in respiratory secretions by immunofluorescence assay (IFA) or enzyme-linkedimmunoabsorbent assay (ELISA) is that they can be performed rapidly and can provide results within 24 h of receiving the specimen in the laboratory. IFA can be divided into direct and indirect methods. Direct immunofluorescence utilises a fluorochrome-labelled antibody that is specific to viral proteins or antigens. It involves fixing the specimens containing viral materials onto a slide so that virus-specific monoclonal antibodies labelled with the fluorochrome can bind to the antigen. Following the addition of a substrate, a colour change with the fluorochrome can be induced, which in turn can be detected by a fluorescence microscope.[16]

Indirect immune fluorescence uses an unlabelled monoclonal antibody that binds to the viral antigen. It is then washed away, and any bound monoclonal antibody is detected with a labelled anti-mouse antibody. The use of multiple antibodies can, in theory, improve the sensitivity of the detection because multiple conjugate molecules can attach to virus-specific antibodies. ELISA is very similar to IFA; however, instead of using a fluorescent label, an enzyme label is used. This assay utilises a double antibody sandwich. A 'capture' antibody specific for the viral antigen being sought is bound to a reaction surface. When the specimen or viral antigen is added, it binds to the capture antibody. The bound antigen is detected by a second antiviral antibody, the 'detector' antibody. This detector antibody carries an enzyme label and, once bound, this enzyme produces a colour change. This colour change can be detected by photometry. The disadvantages of ELISA are that it is usually less sensitive and the reagents are only available for a limited number of viruses. In addition, adults tend to have lower viral titres in nasopharyngeal aspirates, making the sensitivity of this test understandably lower.[17]

Treatment:

There are, so far, no effective therapeutic options available to treat the common cold since so many viruses are involved in its aetiology. Recent studies have focused on three areas for the treatment of the common cold: symptomatic management, pharmacological treatment and antiviral agents. The most disturbing symptoms of the common cold are nasal discharge and stuffiness. Alpha agonists, either alone or in combination with a nonsteroidal anti-inflammatory drug, are effective in reducing nasal blockage and rhinorrhoea. Nasal decongestants improve cold symptoms in adults and improve nasal patency in children; however, their side effects, such as rebound obstruction and nasal epithelial drying, have impeded their use. First-generation antihistamines have shown favourable effects on nasal symptoms in adult studies, probably because of their anticholinergic effects. Topical application of ipratropium (an anticholinergic drug) at a moderate dose, which is minimally absorbed across biologic membranes, reduces rhinorrhoea and sneezing in colds. The routine use of cough medications in healthy children and adults should Amantadine have been the conventional antiviral against of influenza. However, it is strain-specific as it is only effective against influenza A and has common side effects, such as insomnia, poor concentration and irritability; it is now being replaced by newer agents such as zanamivir and oseltamivir.[18]

They are licensed for the treatment of influenza A and B. Early initiation of these therapies, i.e., within 48 hours of the onset of symptoms, can reduce the duration of common cold symptoms by 1 – 2 days. Zanamivir has poor oral bioavailability, and intranasal application has been shown to be effective in treating experimental influenza infection with a reduction in symptoms caused, virus shedding and the development of otitis media. Ribavarin, a synthetic guanosine nucleoside that has a broad spectrum of antiviral activity, has been approved for the treatment of RSV-related respiratory infections in children since 1986. It is the only approved therapy for lower respiratory tract disease caused by RSV [98]. Potential benefits of ribavirin therapy include the inhibition of RSV-specific IgE production in nasal secretions, which has been associated with the development of hypoxaemia and wheezing [99], and improved pulmonary function. Controlled studies also show that the use of ribavirin is effective in reducing the clinical severity score, duration of mechanical ventilation, supplemental oxygen use and days of hospitalisation. Although rhinovirus is the major cause of colds, its vast amount of serotypes has made the development of antivirals against it problematic. Some 90% of rhinovirus serotypes gain entry into epithelial cells using ICAM-1 cellular receptors. Blockade of these receptors in experimental studies showed reduced infection severity, but further study is required before this treatment option becomes widely available.[19,20,21]

Management of the common cold and flu:

Pharmacotherapy is directed at alleviating associated symptoms. Antibiotics are often prescribed erroneously and in the absence of a secondary bacterial infection. Antibiotics should only be administered when a bacterial infection has been identified as a pathogen, and should not be used as a preventative measure. The following measures can be used to either prevent or treat the symptoms of the common cold and flu. (Each of these recommendations will be discussed separately):

• A flu vaccine is recommended by the Centrefor Disease Control and Prevention as a preventative measure against the acquisition of the influenza virus

• Combinations of active ingredients, e.g. decongestants, cough suppressants and paracetamol, are available for use as over-the counter (OTC) products

• Drinking plenty of fluids: Water has been shown to be the best fluid with which to lubricate the mucous membranes • Vitamins and minerals, e.g. vitamin C and zinc sulphate

• Antiviral drugs, e.g. neuraminidase inhibitors (zanamivir and oseltamivir)

• Antiviral drugs, e.g. N-methyl D-aspartate receptor antagonists (amantadine and rimantadine)

• Other [orally inhaled anticholinergics, inhaled corticosteroids, herbal solutions and nonsteroidal anti-inflammatory drugs (NSAIDs)]. [22]

Vitamins and minerals:

Evidence supporting the use of high dosages of vitamin C to reduce the severity of the disease is lacking and inconclusive.The prophylactic use of vitamin C has only been shown to produce a marked reduction in the risk of developing a cold or flu in defined populations, e.g. athletes, with a reduction of approximately 6% in the disease duration. High dosages of vitamin C also provide the following challenges:

• Intestinal and urinary problems, with a higher tendency to develop headaches

• Vitamin C enhances the absorption of iron, and patients with certain blood disorders, such as haemochromatosis, thalassaemia or sideroblastic anaemia, should avoid high dosages

• High dosages of vitamin C may also interfere with anticoagulant medication, and blood tests used in diabetes and stool tests.

Zinc may inhibit viral growth, and could possibly reduce the duration of cold symptoms. However, not enough high-quality trials support the routine and high-dosage use of zinc in preventing a cold or flu. Some reports have been lodged with the US Food and Drug Administration (FDA) that nasal preparations containing zinc may cause loss of smell.Zinc may also reduce the absorption of certain antibiotics. Food containing calcium and phosphorus can impair the absorption of zinc.[23,24]

Hydration for the common cold and flu:

Contradictory literature exists for the recommendation of hydration for the common cold and flu. Some studies have suggested that providing extra fluid to a patient with an acute respiratory condition may cause hyponatraemia and fluid overload, because of the release of the antidiuretic hormone. This hormone is released in adults and children with lower respiratory tract infections. The combination of increased production of the antidiuretic hormone and extra fluid may lead to hyponatraemia and fluid overload. It has not been as clearly illustrated in upper respiratory tract infections, and extra fluid (water still remains the first choice) may help to lubricate the membranes in these patients.[25]

Other strategies used to treat the common cold and flu:

Anticholinergic agents, such as inhaled ipratropium bromide, may be used to treat a cough caused by the common cold. Nasal preparations have shown some efficacy in reducing rhinorrhoea and sneezing. Inhaled corticosteroids can be used to reduce the swelling and inflammation of the nasal mucosa, but have not been shown to provide any benefit in patients diagnosed with a “common cold”.[26] There has been conflicting evidence on the use of nasal irrigations with hypertonic saline or a nasal wash. Some studies have shown that nasal preparations that contain benzalkonium chloride as a preservative may worsen symptoms and infections. Traditional nasal washes that do not contain baking soda may be used (plentiful fluid and minimal salt) to remove mucus from the nose.Medication used to alleviate the pain and fever associated with the common cold and flu include aspirin, ibuprofen, naproxen or paracetamol. Aspirin should only be used in adults, and not in children, as there is a risk of the latter acquiring Reye’s syndrome; especially in children with a viral infection.[27,28]

Conclusion:

The recent discovery of human metapneumovirus and the development of molecular techniques in viral detection represent an exciting time in the study of the common cold. Further research into host inflammatory response and the use of combination therapies may provide a long-term treatment option for this debilitating disease. In the meantime, we as clinicians will have to concentrate on patient education regarding vaccination and avoid unnecessary antibiotic prescriptions.

Antibiotics should not be used to treat a common cold or the flu. There is also not enough evidence to support the use of OTC drugs in the prevention thereof. Receiving an influenza vaccine may reduce the likelihood of acquiring seasonal influenza. Treatment is aimed at alleviating symptoms. However, many OTC medicines are not supported

by evidence in the scientific literature. Herbal remedies may be effective, and include P. sidoides extract, A. paniculata and elderberry. The use of codeine and antihistamines as monotherapy is not effective in the management of coughs or other cold symptoms. Medications, such as paracetamol and other NSAIDs, may be used to manage pain and fever in adults. Antivirals, especially neuraminidase inhibitors, can be utilised to treat and prevent influenza A and B but should be used within two days of the correct diagnosis having been made. Large-scale resistance to amantadine by influenza has limited its usefulness.

References:

1. NHS National Prescribing Centre. Common cold. NHS [homepage on the Internet]. 2006. c2014. Available from: http://www.npc.nhs.uk/merec/infect/commonintro/resources/ merec_bulletin_vol17_no3_common_cold.pdf

2. Rutter P. Community pharmacy. 2nd ed. London: Elsevier; 2009

3. Simon H, Zieve D. Colds and flu: an in-depth report on the diagnosis, treatment and prevention of colds and flu. University of Maryland Medical Centre [homepage on the Internet]. 2013. c2014. Available from: http://health/medical/reports/articles/colds-and-the-flu

4. Hermsen ED, Rupp ME. Influenza. Pharmacotherapy: a pathophysiologic approach. In: DiPiro JT, editor. New York: McGraw Hill, 2008; p.1791-1799.

5. Ebell MH, Alfonso A. A systematic review of clinical decision rules for the diagnosis of influenza. Ann Fam Med. 2011:9(1):69-77.

6. Simasek M, Blandino DA. Treatment of the common cold. Am Fam Physician. 2007;75(4):515-520.

7. Rossiter D, editor. South African medicines formulary. 11th ed. Cape Town: Health and Medical Publishing Group; 2014.

8. Guppy MPB, Mickan SM, Del Mar CB. "Drink plenty of fluids": a systematic review of evidence for this recommendation in acute respiratory infections. BMJ. 2004328(7438):499- 500.

9. Fashner J, Ericson K, Werner S. Treatment of the common cold in children and adults. Am Fam Physician. 2012;86(2):153-159.

10.Johnston SL, Pattemore PK, Sanderson G, et al. Community study of role of viral infections in exacerbations of asthma in 9 – 11 year old children. BMJ 1995;310(6989):1225 – 9.

11. Seemungal T, Harper-Owen R, Bhowmik A, et al. Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001;164(9):1618 – 23.

12. Hiatt PW, Grace SC, Kozinetz CA, Raboudi SH, Treece DG, Taber LH, Piedra PA. Effects of viral lower respiratory tract infection on lung function in infants with cystic fibrosis. Pediatr 1999;103:619 – 26.

13. Wang EE, Prober CG, Manson B, Corey M, Levison H. Associations of respiratory viral infections with pulmonary deterioration in patients with cystic fibrosis. N Eng J Med 1984;311:1653 – 8.

14. Prober CG. The impact of respiratory viral infections in patients with cystic fibrosis. Clin Rev Allergy 1991;9:87 – 102.

15. Gwaltney Jr JM, Moskalski PB, Hendley JO. Hand-to-hand transmission of rhinovirus colds. Ann Intern Med 1978;88(4):463 – 7.

16. Meschievitz CK, Schultz SB, Dick EC. A model for obtaining predictable natural transmission of rhinoviruses in human volunteers. J Infect Dis 1984;150(2):195 – 201.

17. Smith CB, Purcell RH, Bellanti JA, Chanock RM. Protective effect of antibody to parainfluenza type 1 virus. N Engl J Med 1966; 275(21): 1145 – 52.

18. Nicholson K. Human influenza. In: Nicholson K.G.W.R., Hay AJ, editors. Textbook of influenza 275. Oxford: Blackwell; 1998. p. 219 – 64.

19. Pelon W, Mogabgab W, Philips I, et al. A cytopathic agent isolated from nasal recruits and mild respiratory illness. Proc Soc Exp Biol Med 1957;94:262 – 7.

20. Price W. The isolation of the new virus associated with respiratory clincal disease in humans. Proc Natl Acad Sci U S A 1956;42: 892 – 6.

21. Monto AS, Bryan ER, Ohmit S. Rhinovirus infections in Tecumseh, Michigan: frequency of illness and number of serotypes. J Infect Dis 1987;156(1):43 – 9.

22. Beem MO. Acute respiratory illness in nursery school children: a longitudinal study of the occurrence of illness and respiratory viruses. Am J Epidemiol 1969;90(1):30 – 44.

23. Hendley JO, Gwaltney Jr JM, Jordan Jr WS. Rhinovirus infections in an industrial population: IV. Infections within families of employees during two fall peaks of respiratory illness. Am J Epidemiol 1969;89(2):184 – 96.

24. Lewis VA, Champlin R, Englund J, et al. Respiratory disease due to parainfluenza virus in adult bone marrow transplant recipients. Clin Infect Dis 1996;23(5):1033 – 7.

25. Heidemann SM. Clinical characteristics of parainfluenza virus infection in hospitalized children. Pediatr Pulmonol 1992;13(2):86 – 9.

26. Korppi M, Leinonen M, Makela PH, Launiala K. Bacterial involvement in parainfluenza virus infection in children. Scand J Infect Dis 1990;22(3):307 – 12.

27. Makela MJ, Puhakka T, Ruuskanen O, et al. Viruses and bacteria in the etiology of the common cold. J Clin Microbiol 1998;36(2):539 – 42.

28. Larson HE, Reed SE, Tyrrell DA. Isolation of rhinoviruses and coronaviruses from 38 colds in adults. J Med Virol 1980;5(3): 221 – 9

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