Abstract

- Epstein–Barr virus (EBV) infection is the cause of infectious mononucleosis (IM). Many drugs have been investigated in the management of IM including antibiotics, steroids, aciclovir and H2 blockers. The aim of this paper is to review current knowledge in the evidence based management strategies of primary EBV infection, with special emphasis on the use of antibiotics and steroids.

- Current data seem to suggest that in uncomplicated cases none of these drugs has a substantial clinical benefit.

- Steroids appear to be an exception, but because of the marginal benefits and potential complications, routine administration is not recommended. Nevertheless, steroids do have a role in the treatment of EBV related complications such as upper airway obstruction.

Keywords

Infectious mononucleosis, antibiotics, steroids, management.

Introduction

During the last 40 years, a large amount of knowledge and evidence has been accumulated for the spectrum of human diseases associated with EBV infection as well as the molecular pathogenesis, diagnosis and treatment of primary EBV infection.

A search of the literature revealed a paucity of publications related to otolaryngology, despite a significant number originating from non ENT literature. The aim of this article is to review the current literature regarding management strategies from an ENT perspective.

Methodology

The literature review was conducted using a Medline search and the keywords mentioned above over a period of one month. In addition, the references in each captured publication were examined to identify earlier publications that had escaped the Medline search. It has been difficult to compare the results from different reports because so many variables affect the disease. The criteria used between different authors to measure outcomes varied between different reports and between different specialities.

We tried to find if there was any evidence to support the use of:

1) Antibiotics for symptom control
2) Steroids for general symptom control
3) Steroids for pain relief
4) Steroids for management of the airway
5) Finally, if there was any evidence to link the use of steroids with specific ENT complications.

EVIDENCE BASED MANAGEMENT:

Infectious mononucleosis is a benign and usually self-limiting illness and one should carefully balance the risk to benefit ratio of various therapeutic drug regimens. During the last 50 years many drugs have been tested though the strength of evidence varies greatly between studies. This can be attributed to the study design, sample size, patient selection and finally route and dosage of study drugs.

Our search yielded only three papers producing level one evidence.

ANTIBIOTIC TREATMENT

General considerations:

- In uncomplicated cases treatment is largely supportive.
- Tonsillitis can be severe and can impair the ability to drink & swallow. This coupled with anorexia and abdominal discomfort may lead to dehydration. Two studies have shown different group A Streptococci growing in throat cultures, with a prevalence ranging from 3%1 to 30%.2 Both studies conclude that there is no indication for theroutine use of antibiotics, although the use of antibiotics only in positive cultures to avoid post-streptococcal sequelae is acceptable.
- The drug of choice is either oral penicillin (phenoxymethylpenicillin) or erythromycin. Ampicillin & amoxicillin should be avoided as they can cause rash in IM patients. Penicillin hypersensitivity in the general population was found to range from 5% (Calnan 1964) to 30% (Guthe 1958) while ampicillin hypersensitivity ranges from 3% to 22% (Kennedy 1963) & appears to be dose related. In contrast sensitivity to antibiotics in patients with infectious mononucleosis was found to be 95% in patients receiving ampicillin and 43% in patients receiving penicillin.3

References


A. Tsikoudas
FRCS, DLO

M. Davage
Q. Gardiner
FRCS (ORL)

Dept of ORL
Ninewells Hospital
Dundee,
Scotland
UK

Correspondence:
Mr Alexandros
Tsikoudas
FRCS, DLO
Specialist Registrar in
ENT Surgery
Ninewells Hospital
Dept of ORL
Dundee, Scotland
DD1 9SY
UK

Review
Evidence based management of infectious mononucleosis with antibiotics & steroids. An ENT perspective

**Antibiotics for symptom control:**
A review of the literature found only two studies that evaluated the use of antibiotics in patients with glandular fever. The studies, one retrospective and one RCT (not blinded) differ in methodology, patient selection and severity of illness. Both conclude that antibiotics had no effect in the febrile phase nor the duration of hospitalisation. Both showed a very small number of complications.

**Antibiotics against anaerobes:**
A small number of studies evaluated the efficacy of metronidazole and tinidazole in patients with glandular fever. Findings suggest that therapy was beneficial for the resolution of fever and tonsillitis. It is interesting that the benefit of the anaerobic antibiotics did not seem to be related to the eradication of the throat anaerobes, but via an unexplained immuno-modulatory mechanism. Data is insufficient to recommend routine administration.

**STEROID TREATMENT:**
The use of steroids in infectious mononucleosis has been investigated in a number of clinical studies summarised in Table 1. Again, studies differ significantly from one another in methodology, severity of illness, patient selection, power, steroid dosage and clinical endpoints. All of these studies originate from non ORL literature. It can be concluded that steroids shorten the duration of illness, fever & pharyngitis in uncomplicated IM.

**Steroids for pain relief:**
Roy M. *et al* in a recent double blind RCT in a paediatric population has shown that a single dose of dexamethasone (0.5 mg/kg) achieved greater pain relief in comparison to the placebo group. He concluded that a single dose is not sufficient and more may be necessary.

**Steroids for airway management:**
Two studies suggest that steroids are beneficial in the improvement of the airway. They both lack definitions of a sufficient airway, methods of airway measurement or definitions for patient selection. Two more studies seem to suggest that steroids make no significant difference. Again, there are no clear definitions of methods of airway measurement. It is worth noting that Antila *et al* is comparing steroids with antibiotics and not with placebo. Chan *et al* makes the assumption that patients with symptoms severe enough to warrant steroid treatment may be more prone to recurrent tonsillitis and have a more prompt response after acute tonsillectomy. Nevertheless he concludes that steroids made no difference to the tonsillectomy rate. No statistical analysis was made in his study, as the number of patients was considered too small for a reliable result.

**Steroids & ORL complications**
A number of studies implicate steroids in the formation of peritonsillar abscess while Burstin et al presents a case of an infectious mononucleosis patient with bilateral quinsies. On the other hand, Hanna *et al* concludes that there is no strong evidence (RCT's) to suggest such a connection and that existing trials are not powered sufficiently. He goes further by giving an explanation of why steroids cannot be connected with peritonsillar abscess: The capsule of bacteria like *Bacteroides fragilis* contains polysaccharides which activate CD4 T lymphocytes leading to abscess formation. After steroid injection there is a downregulation of CD4 T cells. It is therefore unlikely that steroids are responsible for the abscess formation.

In 1992, the Infectious Diseases Society of America issued guidelines for the selective use of steroids in patients with infectious mononucleosis:
- Steroids should not be routinely used. Can be prescribed when risk of impending airway obstruction.
- Steroids can help in persistent or severe disease or exhaustion. Those patients can be identified by high fever, weight loss, arthritis or prolonged illness.
- Recommended dose: 80mg/day prednisone in divided doses for 2-3 days

<table>
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<th>Study and year</th>
<th>Design</th>
<th>Pts</th>
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<th>Physical signs</th>
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Table 1. Summary of studies of steroids.
Evidence based management of infectious mononucleosis with antibiotics & steroids. An ENT perspective

Key Learning Points

• Many drugs have been investigated in the management of IM.
• Available data suggest that in uncomplicated cases none has a substantial clinical benefit.
• Steroids are an exception, but owing to only marginal benefits & potential complications routine administration is not recommended. They do have a role in complications such as airway obstruction.

References