Int. Adv. Otol. 2010; 6:(3) 408-409

SHORT REPORT

Ramsay Hunt and Antivirals: The Role of Evidence Based Medicine

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Chance of full recovery of facial nerve function following paralysis due to a herpes zoster infection is small. Therefore, treatment is imperative. A recently published systematic review published by the Cochrane Collaboration has caused us pause for thought. First of all, because the in our opinion incorrect conclusion that antiviral medication may not be helpful, might cause severe morbidity. Secondly, it concerns the current practice of only awarding any value to randomised trials. Although methodology, of course, is of importance, we are of the opinion that more attention should be paid to the medical content in all of its facets. Otherwise, we will have to face the fact that the methodological Puritanism - which usually results in rather nihilistic behaviour due to the fact that very little high-level evidence can be found for many diseases - will take precedence at the cost of proper patient care.

Submitted : 16 March 2010 *Accepted : 20 August 2010*

Introduction

Spontaneous and complete recovery following facial paralysis due to a herpes zoster infection, the Ramsay Hunt Syndrome (RHS), is the exception rather than the rule. Without treatment, the chance of full recovery is only 20 percent. Treatment promoting the full recovery is imperative considering the large (emotional) impact of facial paralysis. Based on the pathophysiology – swelling due to the inflammatory reaction against the virus, causing the nerve to be compressed in the narrow facial canal – a treatment regimen of prednisone and antiviral medication is the preferred therapy.

Apparently, there had been some doubt as to the efficacy of antiviral medication against this disease. This was sufficient ground to merit the execution of a systematic review of the randomized controlled trials (RCT's), in order to evaluate whether antiviral drugs support the recovery of the facial nerve function[1].

RHS is not a frequently occurring disease however. Taking into consideration that trial populations often consist of the relatively healthiest groups of patients, those with a single diagnosis and no concurrent disease, it follows that a large group of patients is excluded from participation in trial[2]. This, in advance, clearly decreases the chances that well executed RCT's exist. Nevertheless, the object of the literature search was limited to RCT's alone. This review was included in the Cochrane Library.

Main article

Only one RCT, concerning facial nerve palsy in general -discussing only a mere 15 patients with RHS, was found[3]. Based on the current understanding of the disease mechanism the conclusion of this RCT did not come as surprise to us. Within the group treated with antiviral medication 63% of the patients recovered to a House Brackmann (HB) I or II. In the group without antiviral medication, it was 43%. This is fully consistent with the a priori probability. Unfortunately, the limited size of this group rendered a non-significant result.

In light of the non-significant difference that they had found, the authors of the review concluded: "we found no evidence that antiviral agents offer any beneficial effect, despite their wide spread use in this condition. However, these drugs are associated with a number of adverse effects, and this must be taken into consideration when undertaking the requisite risk-benefit analysis before instigating treatment."

And, even though the above is not far from the truth, their phrasing is rather negative.

Moreover, according to the authors of the Cochrane Library, adverse effects of antiviral medication are transient and only exist of nausea and occasionally vomiting and headache, which occur in 10-20% of cases[1]. So, the likely benefits will probably exceed any potential harm.

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The addition of the following sentence does little to alter that sense of negativity: 'as usual the absence of positive evidence of benefit (or in this case the negative result of one small, statistically underpowered study) does not necessarily indicate that antiviral drugs are ineffective'. A non-significant positive effect is now termed a negative effect.

And this, even while the authors of the RCT in question, in their abstract state: there was a significant reduction of sequelae in patients treated with acyclovir.

To the ever-increasing group of students and physicians who consider the Cochrane Collaboration (CC) to be an authoritative institution representing the main source in evidence based medicine (EBM), it would now appear as if the administration of antiviral medication is not necessary when confronted with this disease.

Decision makers however, need to appraise all the available evidence irrespective of whether it has been derived from RCT or observational studies. It follows that the strengths and weaknesses of each need to be understood if reasonable and reliable conclusions are to be drawn[4]. In accordance with EBM principles one must therefore also assess the evidence of a lower level. It would have been sensible to plan for this in advance, as it seems more likely that with regard to infrequently occurring diseases, one will particularly find studies providing evidence of a 'lower' level. This indeed appears to be the case. The studies by Kinishi and Murakami clearly show a positive result, most definitely in comparison to the rather poor rate of spontaneous healing[5,6].

And even if one were inclined to criticize these studies with respect to methodology, due to an obvious lack of understanding of the daily reality, which limits the maximum achievable within a clinical study, we still have the additional expert opinions by Hato, Gilchrist, and Holland[7-9]. In short, there appears to be sufficient evidence supporting the favourable outcome of antiviral medication. (Of course, the questions with regard to the exact dosage and of which medications are of importance, however, these will be left in abeyance for the moment.) The answer, in our opinion, following the clinical question should have been that due to the limited number of patients within this group, a non-significant positive result has been found. However, studies with a lower level of evidence offer support for the established positive outcome; leading to the conclusion that antiviral medication probably does bring about an improvement.

The adverse effects of medication should not be underestimated, however, the gravity of the clinical picture in a facial paralysis merits an all-out effort, designating antiviral therapy to be the way forward.

If we were to adopt the advice given by the CC, and would actually embark on a new study reviewing the efficacy of antiviral medication in combination with prednisone, compared to prednisone alone, this would lead to the unjust undertreatment of an entire control group.

Conclusions

We conclude that practitioners of EBM need to expand their focus to levels of evidence other than level one alone, especially in rare cases. Furthermore, in a review of medical literature, a substantive and medically relevant assessment of, first, the subject and second the literature found, should play a more prominent role, prior to the focus on methodology. The most important conclusion is that antiviral medication in RHS has a positive effect on the recovery of the function of the facial nerve.

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