PROPANOLOL COURTE OU LONGUE ACTION DANS LA MIGRAINE ?

QUESTION : Ces deux formes du même médicament ont-elles la même efficacité?

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P : patients atteints de migraine

I : propranolol longue action (die)

C : propranolol courte action (BID)

O : contrôle de la migraine en prophylaxie

CONTEXTE : Pendant une de mes cliniques, j’ai vu une patiente qui prend du propanolol BID régulièrement en plus d’un triptan au besoin pour contrôler ses migraines. Le propanolol en longue action et donc DIE existe et je me demandais si ce n’était pas plus efficace (ou à tout le moins aussi efficace) que la forme BID pour une prophylaxie à long terme de la migraine.


RÉSULTATS : Aucune étude ni revue qui compare l’indéral LA à l’inderal BID n’a été trouvée. Il n’y avait rien dans Clinical Evidence ni dans TRIP Database d’intéressant. Par contre, il y a une revue systématique dans Cochrane sur l’indéral dans la prophylaxie de la migraine qui conclue que l’indéral est plus efficace que le placebo pour le traitement de la migraine en prophylaxie. De plus, plusieurs études sont présentes dans Cochrane et dans Pub Med. Elles comparent l’indéral LA avec le placebo ou comparent 2 doses différentes d’indéral LA. J’en cite quelques-unes (2 comparent l’indéral LA au placebo et 2 comparant différentes dose d’indéral LA)


Background : Propranolol is one of the most commonly prescribed drugs for migraine prophylaxis.

Objectives : We aimed to determine whether there is evidence that propranolol is more effective than placebo and as effective as other drugs for the interval (prophylactic) treatment of patients with migraine.
Search strategy: Potentially eligible studies were identified by searching MEDLINE/PubMed (1966 to May 2003) and the Cochrane Central Register of Controlled Trials (Issue 2, 2003), and by screening bibliographies of reviews and identified articles.

Selection criteria: We included randomised and quasi-randomised clinical trials of at least 4 weeks duration comparing clinical effects of propranolol with placebo or another drug in adult migraine sufferers.

Data collection and analysis: Two reviewers extracted information on patients, methods, interventions, outcomes measured, and results using a pre-tested form. Study quality was assessed using two checklists (Jadad scale and Delphi list). Due to the heterogeneity of outcome measures and insufficient reporting of the data, only selective quantitative meta-analyses were performed. As far as possible, effect size estimates were calculated for single trials. In addition, results were summarised descriptively and by a vote count among the reviewers.

Main results: A total of 58 trials with 5072 participants met the inclusion criteria. The 58 selected trials included 26 comparisons with placebo and 47 comparisons with other drugs. The methodological quality of the majority of trials was unsatisfactory. The principal shortcomings were high dropout rates and insufficient reporting and handling of this problem in the analysis. Overall, the 26 placebo-controlled trials showed clear short-term effects of propranolol over placebo. Due to the lack of studies with long-term follow up, it is unclear whether these effects are stable after stopping propranolol. The 47 comparisons with calcium antagonists, other beta-blockers, and a variety of other drugs did not yield any clear-cut differences. Sample size was, however, insufficient in most trials to establish equivalence.

Authors' conclusions: Although many trials have relevant methodological shortcomings, there is clear evidence that propranolol is more effective than placebo in the short-term interval treatment of migraine. Evidence on long-term effects is lacking. Propranolol seems to be as effective and safe as a variety of other drugs used for migraine prophylaxis.

Commentaires sur BANDOLIER: Overall there is a significant increase in the number of responders (usually at least 50% reduction in the number of migraine attacks, but occasionally at least 50% reduction in headache index or global assessment) with propranolol (53% compared with 31% with placebo). The relative benefit is 1.7 (95% confidence interval 1.2 to 2.4), and NNT 4.7 (2.9 to 12). However, as Figure 1 shows, the largest trial from 1996 with over 60% of the total number of patients showed no significant benefit. All the statistical significance comes from small trials from the 1970s with quality scores of 2/5 points, where some residual bias was possible even though the trials were described as randomised and double blind. There were comparisons with other drugs, but these were mostly small and without any clear indications of difference.

Étude comprise dans la revue de Cochrane

The efficacy and safety of long-acting propranolol (LA.P), 160 mg once-daily, in the prophylactic treatment of migraine have been tested against placebo in a multicentric, double-blind, randomized study. The two groups are compared in a parallel manner over a treatment period of 12 weeks, following a 4-week placebo run-in period. Fifty-five of the 74 patients who entered the trial were included at the end of the run-in period. Forty-one patients completed the study. None of the 14 patients who withdrew from the study did so because of side effects. The statistical analysis was done according to the "intention to treat" principle. LA.P was significantly more effective than placebo in reducing the frequency of migraine attacks (p = 0.01 by variance analysis). LA.P reduced the average number of monthly crises by 48% on day 84. There was a slight but significant reduction of the systolic blood pressure and heart rate in the erect position, but there was no significant difference between LA.P and placebo regarding either the number of complaints or the number of side effects elicited out of a 17-item questionnaire. None of the observed side effects led to a withdrawal from treatment.


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4) Al Quassab HK, Findley LJ. **Comparison of propranolol LA 80 mg and propranolol LA 160 mg in migraine prophylaxis: a placebo controlled study.** Cephalalgia. 1993 Apr;13(2):128-31.

Étude comprise dans la revue de Cochrane

Thirty patients with severe classical and common migraine participated in a double-blind placebo-controlled cross-over study of migraine prophylaxis with propranolol LA (long-acting) 80 mg once daily, or propranolol LA 160 mg once daily or placebo. Each treatment was given for two months. There were no significant differences between the three treatment periods in headache frequency, headache severity, nausea frequency or severity. There was a non-significant trend for reduced duration of headache with the two doses of propranolol. The possible reasons for this negative effect are discussed. The safety of propranolol and its lack of serious side effects were demonstrated.


Étude exclue de la revue de Cochrane

A randomized double-blind, cross-over study using treatment periods of 12 weeks with a 2-week washout, comparing two long-acting formulations of propranolol ('Inderal' LA 160 mg daily and Half-'Inderal' LA 80 mg daily) was performed after a placebo run-in of 4 weeks on 51 patients. The study indicated that both long-acting formulations were significantly better than placebo in reducing the frequency of migraine attacks (p less than 0.01). After 12 weeks there was a significantly lower (p = 0.03) frequency of migraine attacks in patients on the higher dose formulation than in those on the lower dose formulation. There was no significant difference in the frequency of side effects produced by the two formulations.

**CONCLUSION :**

Dans la plupart des études sus-mentionnées, l’indéral LA est meilleur que le placebo et l’indéral LA haute dose est plus efficace que l’indéral LA basse dose pour le traitement prophylactique de la migraine. Donc même si je n’ai pu répondre à ma question exactement comme elle était posée, j’offrirai dorénavant l’indéral LA lorsque je voudrai tenter du propanolol en prophylaxie pour mes patients migraineux.

Dans le CPS, il est dit qu’autant l’indéral LA que l’indéral BID peuvent être utilisés comme traitement de la migraine et que les effets secondaires sont les mêmes (assez peu fréquents).