Effects of untreated Rhinitis on actual driving. A patient study

Dr. Eric Vuurman
Department of Neuropsychology and Psychopharmacology
Maastricht University, The Netherlands

Abstract

Background. Allergic Rhinitis (AR), also known as Hay Fever, affects up to 30% of the adult population. While symptomatic, patients usually continue to engage in daily life activities, including car driving. Previous studies have shown that AR can impair cognitive functions, especially during longer lasting tasks and it has been identified as the cause of at least one fatal car accident. Treatment of AR is often done with drugs that might also induce somnolence and impair driving performance. This impairment is however exclusively based on studies with healthy volunteers. Not much is known on the (combined) effects of AR and drug treatment on driving performance of patients.

Aims. Primary objective was to determine the effect of AR per se on actual driving performance and compare it to the effects of AR treated with two types of drugs.

Methods. Nineteen patients with documented AR history engaged in a 1-hour on the road driving test outside the pollen season. In a 4-leg repeated measures design patients underwent a nasal provocation test with a pollen mixture to provoke AR symptoms or a placebo sham provocation. In the three conditions with pollen provocation patients were pre-treated with either cetirizine 10 mg, fluticasone furoate 27.5ug or placebo to alleviate the provoked AR symptoms.

Results. The driving performance of patients when symptomatic and not treated with medication was significantly impaired compared to their non-symptomatic performance in the placebo condition. When engaging in a secondary memory task during the driving task their performance deteriorated further and impairment was comparable to that seen at a blood alcohol level of 0.05%.

Conclusions. Untreated allergic rhinitis can seriously impair driving performance and put AR patients at increased risk, especially when engaging in other activities requiring attention during driving. Patients with AR should be cautioned that their condition can cause impairment.

Background

Allergic rhinitis (AR) is a very common condition, affecting between 15 – 30% of the general population with prevalence reported to be increasing over the last decades (Wallace et al. 2008). Untreated AR is associated with diminished productivity, discomfort, reduced functional ability and also reduced health-related quality of life (HRQOL, for an overview see Melzer, 2001). More specifically, the latter not only relates to psychological wellbeing but also to diminished cognitive functions such as memory and concentration (Kremer et al, 2002). Allergic Rhinitis or AR treatment is further also implicated in road safety and at least one report claims a direct relationship between AR and a lethal car accident (Spector, 2010). However, experimental studies on the effect of AR on driving are missing and long overdue (Smolensky 2011).

Besides AR itself also the treatment for alleviating symptoms can impair cognitive and psychomotor performance. Most of the first generation and some second-generation antihistamines cause sedation as a side effect and subsequently impair performance.
Effects of untreated Rhinitis on actual driving. A patient study

(Vuurman et al 2004). This can be particularly relevant in safety related behavior, such as car driving or operating dangerous machinery. The impact of antihistamines on driving behavior has been shown in a series of studies employing a realistic on-the-road driving test (O’Hanlon 1995). This model, that is also used in the present study, differs from most laboratory tests aimed at measuring driving impairment in that it requires sustained performance and attention over a relatively long period of time (1 hour) and is more realistic. Furthermore, a recent meta-analysis showed that laboratory tests poorly predict impairment on actual driving (Verster and Roth, 2012).

**Aims**

The primary objective of this study was to evaluate the effects of untreated AR on driving and cognition as well as the effects of two types of AR treatment & placebo in counteracting AR’s effects on driving and cognition. The main hypothesis was that patients suffering from AR symptoms would show impaired driving performance. This detrimental effect would be (partially) counteracted by the use of AR drugs.

**Methods**

Nineteen Dutch speaking patients (nine female) completed the study. Main inclusion criteria were age between 22 and 45 years with a documented positive medical history of AR and documented AR treatment in the season preceding the study. Participants were required to be experienced drivers holding a license for at least two years and driving over 5000 km/year. Main exclusion criteria were the presence of any other form of (allergic) rhinitis, the presence or a history of psychiatric disorders or other contraindicated illness, e.g. asthma, diseases or trauma’s of the central nervous system or impaired visual or auditory functions. Written informed consent was given before inclusion and patients were paid for their participation. The study was approved by the Medical Ethical Committee of Maastricht University and was conducted in accordance with the World Medical Associations Declaration of Helsinki [Seoul revision, 2008].

**Study design**

In this study AR patients were studied outside of the pollen season when natural exposure to allergens was minimal. This offered the experimenter control over AR symptoms experimentally by administering a nasal provocation test with pollen (or placebo). The study was organized following a double blind randomized 4-leg crossover repeated measures design. In each condition patients were challenged with either an allergen solution (sprayed in the nose) or placebo in combination with one of two medicinal allergy treatments or placebo. Table 1 summarizes the conditions and treatments. Drug treatment and nasal pollen provocation was administered in a double dummy fashion. On the four days prior to each testing day patients were treated once daily with a nose spray containing 27.5 microgram fluticasone furoate or placebo. On each testing day a final dose of the same spray was administered together with a single dose (capsule) containing either 10 mg cetirizine or placebo. Only either the capsule or the nasal spray could contain an active compound on a given test day. Both the active nasal spray and placebo were packed in blinded and identical containers as were capsules containing cetirizine or placebo.
Effects of untreated Rhinitis on actual driving. A patient study

### Driving Test

The on the road driving test developed in our laboratory aims at overcoming common problems associated with driving simulators which seem a more safe and logical choice as an instrument to study driving. Contrary to almost all driving simulators this test is more sensitive, has been validated and does not provoke motion sickness, a side effect affecting almost half of the subjects tested in simulators (Classen et al 2011). The main outcome variable “weaving” as defined by the Standard Deviation of Lateral Position (SDLP) is a very reliable index (test-retest r=0.7-0.9) of individual driving performance and has proven to be sensitive to many sedating drugs. A clinically relevant increase in SDLP has been established in a series of studies investigating the effect of alcohol. The driving test consisted of two distinct parts. The first 45 minutes the participants’ task was just to drive the car under silent conditions. During the last 15 minutes a verbal Word Learning Test was administered through the speaker system of the car. The participant now also had to repeat and remember as many words presented to them during three successive presentations of a list of 15 words (1 per 2 seconds) forcing him/her to allocate attention to two tasks simultaneously.

### Results

#### Driving Test

Figure 1 shows the results of the driving test. The left panel shows mean SDLP scores for the entire 60-minute test (overall SDLP) and the right panel shows the SDLP while patients were driving and simultaneously performing a memory task. The overall SDLP was different between conditions ($F_{(3,16)}=7.44 ; p=0.002$) and significantly higher for the untreated provocation condition compared to placebo : PROV > PLAC ($F_{(1,18)}= 42.18 ; p<0.001$). The SDLP during the memory test section showed a similar pattern although the SDLP was larger in all 4 conditions. Comparing over conditions showed them to be significantly different ($F_{(3,16)}= 21.15 ; p< 0.001$). Pair wise comparisons showed that both the untreated provocation condition as well as the condition with cetirizine treatment yielded a higher SDLP compared to placebo: PROV > PLAC $F_{(1,18)}=52.15 ; p< 0.001$ and CETR > PLAC ($F_{(1,18)} = 4.61 ; p=0.046$). The SDLP in the condition with fluticasone furoate treatment did not show a difference from placebo.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Provocation type</th>
<th>Drug treatment type</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLAC</td>
<td>Placebo</td>
<td>Placebo</td>
</tr>
<tr>
<td>PROV</td>
<td>Grass / Tree pollen</td>
<td>Placebo</td>
</tr>
<tr>
<td>CETR</td>
<td>Grass / Tree pollen</td>
<td>Cetirizine</td>
</tr>
<tr>
<td>FLUT</td>
<td>Grass / Tree pollen</td>
<td>Fluticasone furoate</td>
</tr>
</tbody>
</table>
Discussion and conclusions

This study set out to study the effects of AR on the driving ability of patients. The method of nasal provocation to induce AR symptoms was reliable and caused different levels of AR symptoms in the experimental conditions. Without treatment AR symptoms were above clinically relevant levels for the duration of almost the entire test. Both systemic treatment with cetirizine as well as topical treatment with fluticasone furoate suppressed symptoms relative to the non-treated condition although not completely.

The impairing effects of AR per se on driving were large and significant. An increase in SDLP of 2.07 cm was seen in the untreated provocation condition which is comparable to the effect of driving with a BAC of 0.03 %\(^\text{26}\). Although this BAC level is under the legal limit in most countries it is nevertheless of some concern. In individual cases the effect could be larger which is particularly true if patients would also be taking a small dose of alcohol while symptomatic. The combined effects could then easily produce an SDLP increase of 2.5 cm, which is seen at the legal BAC limit of 0.05 % and putting the patient at risk. When an additional task is presented during the test the driving performance deteriorates further. While performing the memory test SDLP increases 2.35 cm relative to placebo in the untreated provocation condition. This (mean) effect is close to that of a BAC of 0.05 % and in individual cases it was higher.

We can conclude that patients suffering from untreated AR symptoms show impaired driving that, under conditions of extra cognitive load while driving, are almost comparable to the effects of a BAC of 0.05 percent. Furthermore, cognitive performance in this dual task
Effects of untreated Rhinitis on actual driving. A patient study

situation can be significantly impaired which may further interfere with other activities needed for safe travel. Treatment with either a systemic or topical treatment can partially correct this situation. Not treating AR symptoms will put patients at risk in situations where a maximal continuous attention and performance is required such as driving a car.

Declaration of funding sources

This study was investigator initiated and financially funded by an unrestricted grant of GlaxoSmithKline (GSK) company, the Netherlands. The author declares to have no conflict of interest regarding the funding by this company, directly or indirectly.

References


