Author's response to reviews

Title: Extended varenicline treatment in a severe cardiopathic smoker: a case report

Authors:

Elena Munarini (elenamunarini@hotmail.com)
Chiara M Marabelli (chiaramaria.marabelli@istitutotumori.mi.it)
Paolo Pozzi (paolo.pozzi@istitutotumori.mi.it)
Roberto Boffi (roberto.boffi@istitutotumori.mi.it)

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Title: Extended varenicline treatment in a severe cardiopathic smoker: a case report

Authors:

Munarini Elena (elena.munarini@istitutotumori.mi.it)
Marabelli Chiara (chiaramaria.marabelli@istitutotumori.mi.it)
Pozzi Paolo (paolo.pozzi@istitutotumori.mi.it)
Boffi Roberto (roberto.boffi@istitutotumori.mi.it)

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Author's response to reviews: see over
The Biomed Central Editorial Team

Object: MS: MS: 1928887980141764 - Extended varenicline treatment in a severe cardiopathic smoker: a case report. Dr Elena Munarini et al.

Thank you for consideration of our manuscript for publication in your journal.

We have reviewed the above manuscript according to your reviewer’s comments. Moreover we made language correction: they are all the highlighted sentences that aren’t reported below.

Reviewer 1 (Dr Paredi)

Major Points

I have the following minor suggestions to improve this already well written report:

1) A more thorough description of the medication in question is required. More specifically, its mechanism of action, advised dosage, side effects etc need to be included in the text.

   • We added the information required. The following statements now appear in the background section:

Varenicline is a nicotinic receptor partial agonist and it stimulates nicotine receptors more weakly than nicotine itself does. As a partial agonist it both reduces cravings for and decreases the pleasurable effects of cigarettes and other tobacco products. Through these mechanisms it can assist smokers who want to quit. The summary of product characteristics (SPC) states that smokers should set a date to stop smoking and treatment with varenicline should start 1 to 2 weeks before this date. The usual starting dose of varenicline is 0.5 mg once daily for the first 3 days, then 0.5 mg twice daily for the next 4 days, then continue on 0.5 mg twice daily or increase to 1 mg twice daily thereafter. The maximum dose of varenicline is 1 mg twice daily. Varenicline should be taken with a full glass of water, after eating. About side effects, nausea occurs commonly in people taking varenicline. Other less common side effects include headache, difficulty sleeping, and abnormal dreams. Rare side effects reported by people taking varenicline compared to placebo include change in taste, vomiting, abdominal pain, flatulence, and constipation. Serious side effects related to varenicline are uncommon and very serious side effects are rare and they include burning feeling in feet/toes, unusual pain in the legs when walking, chest/jaw/left arm pain, weakness on one side of the body, severe headache, vision changes, confusion, slurred speech, seizure.

2) It may be of benefit to include a brief chronological history of the FDA concerns and public warning for Varenicline. Within this history it is crucial to describe more clearly:

a) what is meant by “cardiovascular events” as this was the main outcome of the meta-analysis

   • Now they are specified in background section, fifth paragraph

b) Please clarify that that meta-analysis was ordered by the FDA and was sponsored by the producer of the drug, Pfeizer. Include number of patients enrolled, number of centers, etc.
So, FDA required the manufacturer of the drug, Pfizer, to conduct a meta-analysis to further evaluate the cardiovascular safety of the drug: it incorporated data from 7,002 patients (4,190 varenicline and 2,812 placebo) that were enrolled in 15 Pfizer-sponsored, randomized, double-blind, placebo-controlled clinical trials of ≥12 weeks treatment duration; findings of cardiovascular risk are similar to the findings in the smoking cessation clinical trial of patients with stable cardiovascular disease that was described in FDA’s June 2011 announcement.

c) It is crucial to highlight that occurrence of cardiovascular events was higher in the varenicline treated group but this was NOT statistically significant

3) A better description of the cardiological history of the patient described in this case report is required. More specifically. How many vessels disease? Where were the stents placed? What type of stents? Was there a history of arrhythmia?

March 2003 he had an ischemic heart disease in the diagonal branch of the anterior interventricular artery and it was treated with plain old balloon angioplasty (POBA) and one drug-eluting stent (DES) application; in July 2011 he suffered from an intrastent restenosis and he underwent a second angioplasty (POBA). He hadn’t a history of arrhythmia. What were the current medications at the time of the smoking cessation intervention? Blood pressure? Heart rate? Was the patient suffering from COPD as well? Weight, height?

4) Of course, as this is a case report, it is vital to tone down the strength of general conclusions as these cannot be drawn based on a single case. More specifically, please acknowledge that even though varenicline was safe and successful in this specific case, it is still vital to “weigh the risks of Chantix against the benefits of its use” as indicated by the FDA.
weighing the risks of these therapies against the benefits of their use. About Varenicline FDA declare “Health care professionals are advised to weigh the risks of varenicline against the benefits of its use. It is important to note that smoking is a major risk factor for cardiovascular disease, and varenicline is effective in helping patients to quit smoking and abstain from it for as long as one year. The health benefits of quitting smoking are immediate and substantial” [20].

Minor Points

1) Replace “serious” with “severe” in the title
   • Change made as indicated by the reviewer.

2) Abstract: a) replace “even more” with “particularly” in heart patients
   • Change made as indicated by the reviewer.

Replace “The extended varenicline therapy was clinically monitored and it allowed the patient to consolidate the abstinence” with “The extended varenicline therapy was clinically monitored and allowed the patient to consolidate the abstinence”
   • Change made as indicated by the reviewer.

Reviewer 2 (Dr Linhartova)

Comments to authors:
A single case report is not a suitable way of proving safety of the drug
   • No statement was made on the basis of the result of this specific case, but each sentence was supported by references. As we said for the last point of Reviewer 1, we add also the FDA recommendations about the use of varenicline.