

Nail polish for Random Pavarotti Disease: a systematic review

Michael P. Grayer

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Abstract

Objectives To determine the effectiveness of the topical application of nail polish as a cure for Random Pavarotti Disease (RPD).

Design Systematic review of randomized controlled trials.

Data sources PubMed (Medline) database.

Study selection Randomized controlled trials comparing topical application of nail polish with appropriate control group in human or plasticene canine patients with RPD. Quality assessed using 5-point Jadad scale; study excluded if Jadad score was less than 3.

Main outcome measure Mean change in frequency of Random Pavarotic episodes from baseline.

Results No relevant studies were found.

Conclusions The lack of evidence either supporting or refuting the effectiveness of nail polish as a cure for RPD suggests that rigorous randomized controlled trials are warranted. Failing that, other approaches, such as longitudinal studies, cross-sectional observational studies, or wild goose chases, may still contribute usefully to building further evidence.

1 Background

Random Pavarotti Disease (RPD) is a psychological disorder characterised by symptoms such as Tourette's-like spontaneous blurting out of random operatic passages [1]. There is anecdotal concern of RPD presenting in humans, though as yet, no cases have been officially documented. However, a case of RPD presenting in a plasticene dog was documented in a video case study [2]. Despite this case study being conducted over ten years previously, there is still very little known about this rare condition. Direct consequences of RPD include an increased risk of laryngitis, as well as increased social harms to the well-being of other people in the immediate neighbourhood, which may lead to increased stress levels and, in extreme cases, acts of physical harm directed at the person with the disease.

Nail polish (or nail varnish) is a lacquer applied to finger- and toe-nails for both aesthetic decoration and protection of the nail. Although modern nail polishes are made from nitrocellulose dissolved in an acetate solvent, coloured lacquer made from natural ingredients such as Arabica gum, egg whites, gelatin and beeswax has been used in Chinese civilisation since at least as long ago as the Chou dynasty of 600BC [3]. This historical point is salient in today's medical context: Traditional Chinese Medicine has a long history and is experiencing something of a resurgence in popularity in modern times. In terms of other medical uses or applications of nail polish, little is known, though nail polish is known to have little or no effect on pulse oximetry readings in mechanically ventilated patients [4].

Although there is no biomedical basis for suggesting that the topical application of nail polish may have any effect on the symptoms of Random Pavarotti Disease (the cure suggested in the case study presented above was the cerebral insertion of a miniaturized submarine—an invasive and potentially dangerous intervention), there may be a plausible explanation offered by other schools of medical thought. For example, reiki practitioners believe that therapeutic effects can be enacted from a universal life energy, presenting as a biofield around the body [5, 6]. A similar concept (“Qi”) exists in the Chinese Medicine literature, though according to this practice, Qi flows through “meridians”: channels of life energy flowing throughout the body. At least one website offering information on Chinese Medicine lists the Hand Jue Yin Pericardium, running from the end of the right hand (where nail polish is frequently applied) through the right armpit and into the right lung as related to symptoms such as “Delirious speech, restlessness, full in the chest and the lateral rib region, loss or impairment of the power to use or comprehend words usually resulting from brain damage (aphasia), palpitations, heartburn, constant laughter” [7]. These symptoms are not unlike those presented in Random Pavarotti Disease.

A rigorous critical appraisal of the evidence for an intervention with little or no plausible scientific theoretical basis is not without precedent. Examples of such systematic reviews include the following: on moxibustion [8, 9, 10] and cupping [11, 12]—modalities based on the flow of Qi through meridians—despite there being no scientific basis for the existence of either Qi or meridians within the human body; on reiki [5, 13] despite there being no scientific basis for the existence of biofields; on homeopathy [14, 15, 16] despite the fact that homeopathic remedies are diluted to such an extent that no molecules of the original substance remain; on laetrile [17, 18] in spite of there being concerns regarding the theoretical mechanism by which the substance's anti-cancer properties are purported to work¹.

The aim of this systematic review is to provide a critical appraisal of the current state of evidence supporting or refuting the effectiveness of the topical

¹From Milazzo et al. [18, p.592]: “Since rhodanese can convert cyanide into the relatively harmless compound thiocyanate [19], when Laetrile is broken down by the betaglucuronidase, producing cyanide, this would affect cancer cells more than healthy ones. However, there is no experimental evidence to show that malignant and healthy cells differ in rhodanese enzymes [20] nor that betaglucosidase is contained in tumor tissues [21].”

Table 1: Search strategy employed for reviewing the literature

Stage	Search terms
1	random OR aleatoric OR unpredictable OR spontaneous
2	Pavarotti OR opera OR operatic OR singing
3	disease OR disorder OR syndrome
4	#1 AND #2 AND #3
5	“nail polish” OR “nail varnish” OR “nail lacquer” OR nitrocellulose
6	#4 AND #5

application of nail polish as a cure for Random Pavarotti Disease.

2 Methods

2.1 Literature search strategy

A comprehensive search was carried out on the medical literature using the PubMed database. The database was searched from inception through to August 2010 (the point in time at which the review was conducted). The concepts embodied in the search strategy were as follows: nail polish, and Random Pavarotti Disease. The full list of search terms employed in the search strategy is detailed in Table 1.

2.2 Selection criteria

In this study, I sought to include randomized controlled trials (RCTs) comparing a group of patients who had received nail polish treatment for RPD with either a control group receiving comparable placebo or no treatment. Trials were excluded if nail polish treatment was administered as part of a complex intervention (for example in conjunction with cerebral submarine insertion). Trials assessing healthy subjects or subjects presenting with similar conditions were also excluded. Due to restraints imposed by the author’s knowledge of languages, trials were excluded if they were not published in English, German or French.

2.3 Extraction of data and assessment of methodological quality

I initially read the titles and abstracts of all relevant articles identified in the literature, excluding articles that clearly did not meet the inclusion criteria on this basis immediately. I then read the remaining articles in full. Data were

validated and extracted according to pre-determined criteria. Methodological quality of the articles was determined by the 5-point Jadad scale [22]. Studies with a Jadad score of 3 or greater were included in the study.

2.4 Meta-analysis

The statistical approach adopted was to assess the difference between intervention and control arms using the mean change in the frequency of Random Pavarottic episodes from baseline. Mean difference (MD) and 95% confidence intervals (CIs) were extracted from each study where given. For studies with insufficient information, the primary authors were contacted to obtain the relevant data wherever possible. A Student's *t*-test was used for statistical analysis of trials where data were available. All statistical analyses were conducted using Stata 10.1 for Unix.

3 Results

Unfortunately, no studies were found according to the given search strategy.

Widening the search to include all articles featuring "random", "Pavarotti" and "disease" or synonyms thereof (search #4 in Table 1 above) yielded eight articles [23, 24, 25, 26, 27, 28, 29, 30]. However, of these, none were RCTs. The closest study to an RCT of these eight was a large-scale longitudinal study [28], but this study was not concerned with RPD.

Widening the search criteria to simply "polish AND opera" yielded three published studies [31, 32, 33], but unfortunately as all three were written in the Polish language, none of them met the inclusion criteria for the review.

Hence, with no relevant studies available in the literature, no data could be extracted, therefore no evidence of the effectiveness of nail polish in curing RPD is currently available.

4 Discussion

The results point to a distinct lack of good quality evidence either in support of or against the use of nail polish in the treatment of RPD. While there is no evidence refuting the effectiveness of nail polish in treating RPD, the evidence in favour is equally unconvincing.

A limitation of the study was that, due to time and language constraints, only one database of published literature was consulted. Future systematic reviews should therefore aim not only to search this database, but to aim for a more comprehensive review of published articles, abstracts, foreign language literature, complementary and alternative medicine literature, catalogues of unpublished dissertations and theses, and conference proceedings. However, despite this limitation, the present review highlights the surprising lack of research conducted on Random Pavarotti Disease and the effectiveness of nail

polish as an intervention against it, despite the first case being documented over a decade ago.

One positive outcome arising from this review is with regard to safety. No adverse side effects of the topical application of nail polish in the treatment of RPD have been reported in the literature.

5 Conclusion

There is currently no convincing evidence supporting the use of nail polish in the treatment of Random Pavarotti Disease in humans or plasticene dogs, though good quality randomized controlled trials are lacking. More research on the etiology of RPD and the effectiveness of nail polish as a cure for the condition is required. Future studies should include high quality randomized controlled trials with particular focus on appropriate control-group interventions, effective double-blinding procedures, and should be conducted on a large enough sample size to be sufficiently powered to detect differences in mean change in Pavarottic episodes between the intervention and control. Furthermore, the researchers carrying out these trials will most likely need extensive prior training in skills required for the pursuit of wild geese.

6 Corollary to the conclusion

In case any reader is in any doubt, the above systematic review describes the evidence of an entirely implausible and arbitrarily chosen treatment for an entirely fictional debilitating condition. The reader may therefore be surprised at my conclusions: that more research—particularly large, complicated and expensive double-blind randomized controlled trials—is called for. However, there still remains a salient point to this exercise that should be stated.

The conclusions drawn from this present study bear striking similarities to those reached by other systematic reviews on interventions for which there is little or no *a priori* reason to suggest effectiveness. In many of these cases, however, randomized controlled trials were identified, with the vast majority being discarded for being of poor methodological quality where “positive” results were all but guaranteed due to inherent biases [34]. In many cases, even the trials which were included barely met the standards required by the pre-determined inclusion criteria.

Conclusions from the systematic reviews cited in the introduction above invariably call for more rigorous research to be conducted (see Appendix A for quotations). This would be largely justifiable if presented solely with the trial data, free from the context provided by the scientific plausibility of the theory underlying the intervention, the history of its development, and so on. However, with that context reinstated, and also recognising that there are not limitless resources that can be allocated to medical research, calling for more resources to be channelled in the direction of more rigorous research appears

less and less appropriate. Moreover, given the large number of studies with poor methodology identified by these systematic reviews (relative to the number trials identified with methodologies that met the inclusion criteria), it could be concluded that proponents of these and other medical interventions and treatments with no basis in scientific thought have already had plenty of opportunity to conduct trials where bias is minimised, but simply haven't done so.

An earlier special Christmas edition of the British Medical Journal contained a systematic review of randomised controlled trials investigating the efficacy of parachutes in preventing death and major trauma related to "gravitational challenge" [35]. Similarly, no studies meeting the search criteria were found. Several other parallels between Smith and Pell's study and this one can be drawn: both they and I argue that a systematic review of randomised controlled trials produce spurious calls for more research when contextual information is ignored. Whereas they highlight the case for including observational data for common sense situations (if you fall from a great height then your chances of survival are greatly improved if you have a parachute), I present the opposite case, where disease, intervention and the theory underpinning the link between the two are entirely made-up. The argument presented by this study is this: simply calling for more rigorous research after conducting a systematic review in which very little in the way of good-quality evidence was found, without taking into account how sandy are the foundations upon which the evidence is built, risks creating an artificially strong case for diverting the limited funds available for medical research towards wild goose chases.

7 Declaration of interests

I am a PhD student, researching life expectancy trends in London. I receive funding from the ESRC with respect to my PhD, though this study is unrelated. From time to time I write a blog (<http://www.nontoxic.org.uk>) discussing the abuse of statistics in the reporting of current affairs. I do not personally self-identify as a "skeptic" though share some of the character traits that that label would suggest. No funding from any external source was received in relation to this study.

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A Conclusions from selected systematic reviews of alternative treatments

“Well designed controlled clinical trials to assess whether Laetrile or amygdalin have any beneficial effects for cancer patients could also be considered.” [17, p.11]

“In conclusion, there is no reliable evidence for the effectiveness of laetrile, and considerable doubt about its safety exists. The risk–benefit balance of laetrile as a treatment for cancer is therefore negative. Well-designed, controlled clinical trials to test laetrile or amygdalin could be considered.” [18, p.593]

“There are currently only a few trials of moxibustion for the management of hypertension that have been published. Collectively, the existing evidence

does not suggest that moxibustion is an effective therapy for this indication. Future studies should be of high quality with particular emphasis on using adequate control interventions and differentiating between specific and non-specific effects." [8, p.5]

"The evidence is limited to suggest moxibustion is an effective supportive cancer care in nausea and vomiting. However, all studies have a high risk of bias so effectively there is not enough evidence to draw any conclusion. Further research is required to investigate whether there are specific benefits of moxibustion for supportive cancer care." [9, pp.6-7]

"Conclusion Current evidence from these three randomized controlled trials is insufficient to suggest that moxibustion is an effective treatment for constipation. More rigorous studies are warranted." [10, p.4]

"However the evidence base is currently weak. The main problem in RCTs of homeopathy for depression has been recruitment. In principle it is possible to overcome this problem by using a very large recruitment base. However, this would be inefficient and the low recruitment ratio such a design implies means that the recruited subjects would likely be atypical. Further research is required, and should include well-designed controlled studies with sufficient numbers of participants." [14, p.158]

"Further RCTs of homeopathic medicines for adverse symptoms and skin reactions related to radiotherapy are needed to confirm the results described in this review." [15, p.15]

"Homeopaths often treat insomnia. However, there is currently a lack of high-quality studies assessing the effectiveness of homeopathy in treating this condition. The limited evidence available does not demonstrate a statistically significant effect of homeopathic medicines for the treatment of insomnia. Existing RCTs were of poor quality and were likely to have been underpowered. Well-conducted studies of homeopathic medicines and treatment by a homeopath are required to fully examine the clinical and cost effectiveness of homeopathy for insomnia." [16, p.8]

"Future trials testing the effectiveness of reiki should adhere to rigorous trial designs which are adequately suited to the research question that is being asked. Such trials should preferably be randomised, control for placebo effects, assessor blinded, adequately allocation concealed, have optimal treatment time and sample sizes based on proper sample size calculations, use validated outcome measures and include a full description of the actual interventions that are being tested." [5, p.953]

"The serious methodological and reporting limitations of limited existing Reiki studies preclude a definitive conclusion on its effectiveness. High-quality randomized controlled trials are needed to address the effectiveness of Reiki over placebo." [13, abstract]

"In conclusion, the results of our systematic review provide some suggestive evidence for the effectiveness of cupping in the management of pain conditions. However, the total number of RCTs included in the analysis and the methodological quality were too low to draw firm conclusions. Future RCTs seem warranted but must overcome the methodological shortcomings of the

existing evidence." [11, p.6]

"Carrying out studies with comparable controls would be one way to establish or contribute to the current evidence of cupping. One should note, however, that design features such as placebo or blinding are difficult to incorporate in studies on cupping. Moreover, research funds for these studies are scarce... Future investigations of this topic should adopt rigorous trial methodology in order to minimize bias. They should also have sufficiently large sample sizes and employ validated outcome measures. The unsolved problem of an adequate sham procedure needs to be addressed, and we suggest that future RCTs should pilot a sham procedure in order to identify the optimal way of controlling for non-specific effects... Future RCTs seem warranted but must overcome the methodological shortcomings of the existing evidence." [12, p.73]