

Improving medicine selection in homeopathy

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May 2007

Abstract

Homeopathic medicines cannot be prescribed on diagnosis only. The fact that multiple criteria (personal traits, symptoms) lead to a number of preferred medicines resembles the diagnostic process. Homeopathic reasoning can be modelled using Bayes' theorem. The presence of certain symptoms increases chances that corresponding medicines will work. In the past this information has been collected in the homeopathic repertories based on expert opinion. This process is liable to chance variations. We assessed homeopathic symptoms the same way as diagnostic instruments, obtaining Likelihood Ratios. This assessment confirmed that a symptom indicates certain medicines more than others. It also confirmed our expectation that frequently used medicines are over-rated and infrequently used medicines are underestimated in the repertory.

Introduction

Homeopathy is developed around 1800 and its mechanism of action is still unknown. It is unlikely that the mechanism of action could be explained by chemical interaction. This corresponds with the experience of homeopathic doctors that these medicines have effects different from conventional medicine. It causes gradual improvement of more than just the presented complaint; the resemblance is more to a signal than to a chemical reaction. Especially in chronic disorders with co-morbidity the method seems useful as an addition to conventional medicine. The effect of a homeopathic medicine seems to be not confined to one complaint or one diagnosis.

The method has an empirical basis and most of its methodology stems from the 19th century. There are two essential aspects that influence assessment of the method.

1. It appears that a homeopathic medicine cannot be prescribed solely on the basis of a conventional diagnosis. The reproducibility of success prescribing a certain homeopathic medicine increases if the patient also has other features that are characteristic for that medicine. This resembles susceptibility for conventional medicines on genetic grounds. The characteristic features could be assessed as effect modifiers. The number of possible features indicating a homeopathic medicine is large, mostly several hundreds.

2. The homeopathic doctors have developed their own methodology to deal with this complexity in the nineteenth century. There are two major steps involved in selecting a homeopathic medicine. The first is making a differential diagnosis of medicines that could be considered. The next step is comparison of a complex pattern of the medicines out of the differential diagnosis with the complex pattern of the patient.

Homeopathic methodology

Homeopathic doctors have two main instruments, the materia medica and the repertory to the materia medica. The materia medica describes the patterns of the homeopathic medicine, the repertory indexes all possible features/symptoms leading to different medicines. There are ten thousands of rubrics in the repertory. These rubrics refer to mental and physical complaints and properties, some are common, some are rare. Common symptoms or properties refer to a large number of medicines, rare symptom or properties refer to a small number of medicines.

One of the rubrics, with the constituting medicines, is (RADAR synth 8.1.40, modern to 1987):

Diarrhoea after anticipation: Aethusa, Argentum nitricum (arg-n), Gelsemium (gels.), Phosphoricum acidum (ph-ac.).

This symptom is not especially rare, but the number of indexed medicines is still small. This is one of the problems arising from the developmental history of the method; some symptoms received much attention of professionals, others few. Some rubrics are over-complete, others incomplete.

In order to establish a differential diagnosis homeopathic doctors arrange a number of characteristic features of the patient in a spreadsheet. An example based on the original repertory containing six symptoms is presented in table 1. The numbers in the columns below the abbreviations of the medicines

indicate the strength of each indication, e.g. the number 3 for the fifth symptom in the first medicine row indicates that sensitivity to injustice is a strong indication for the medicine Causticum (caust.).

Symptom nr.	Symptom	number of entries
1	RECTUM - DIARRHOEA - anticipation, after	4
2	MIND - FEAR - death, of	145
3	TEETH - GRINDING - sleep, during	43
4	FACE - ERUPTIONS - herpes - Lips - About	44
5	MIND - INJUSTICE, cannot support	10
6	MIND - LOQUACITY	139

Symptom nr.	medicines							
	caust.	ph-ac.	sep.	gels.	calc.	ign.	verat	arg-n.
1:	-	2	-	3	-	-	-	2
2:	2	2	1	3	3	1	2	2
3:	1	-	1	-	1	2	2	-
4:	1	1	3	-	-	-	-	-
5:	3	-	1	-	1	1	1	-
6:	1	-	-	2	1	1	2	-

Table 1: Entries of six repertory rubrics arranged to discover medicines that could be considered in a patient that has these symptoms. Value 1 under the medicine means that the symptom is occasionally seen in patients responding well to this medicine. Values 2 and 3 indicate that the symptom is seen more frequently.

This system should be handled carefully, all symptom-rubrics mentioned in the repertory were originally constituted separately, as if the symptoms were mutually independent. This is probably not true for a number of medicines. Symptoms should also be chosen carefully, because they could be related. If, say, the patient has rheumatoid arthritis (RA) adding the symptom 'amelioration from motion' gives few extra information because most RA patients have this symptom. Homeopathic doctors use such tables only to concentrate on a limited number of possible medicines to be explored further. The next step consists of pattern recognition. Metaphorically we could compare this with a weather-forecast; a small number of variables like temperature, wind and precipitation can help to make decisions in a far more complex choice about activities for the next day. The three given variables however have different interrelations for each activity.

Bayes theorem

Knowledge about homeopathic medicines is, among others, based on practice experience. Characteristics of patients responding well to a certain homeopathic medicine can be used to predict successful application of that medicine. This is theoretically based on Bayes' theorem, which says:

posterior odds = LR * prior odds.

Where LR (Likelihood Ratio) = prevalence in target population / prevalence in rest-population.

If the symptom 'Diarrhoea after anticipation' occurs 10 times as frequently in the population responding well to the homeopathic medicine Argentinum nitricum as in the rest-population, LR=10. Such knowledge is implicitly, but with much chance variation, available via practice experience.

Bayes formula enables us to estimate growth of chances of success if a symptom is present. Suppose that chances of success from Argentinum nitricum regarding a certain patient are estimated to be 5%, then odds are 0.05. If subsequently the symptom 'diarrhoea from anticipation' appears to be present, the odds will rise to 0.5, chances becoming 33%.

Bias in the repertory

The interrelatedness of symptoms is handled by homeopathic doctors by referring to materia medica in order to make a more complex decision about the right medicine. But there is also serious bias in the repertory which was originally constituted in the beginning of the twentieth century. Entries in a symptom rubric are made on expert opinion and there is no sound protocol. If a symptom is seen repeatedly in patients responding well to a certain medicine, this medicine is entered in grade 2 or 3 in the repertory-rubric suggesting the symptom is more important in relation to this medicine. Symptoms with greater prevalence and medicines which are more frequently used have more chance to be observed repeatedly. So these symptoms and medicines are over-represented in the repertory.

Research methods

Symptoms in homeopathy have so far never been systematically and prospectively assessed. We started the first assessment in June 2004 regarding the six symptoms mentioned in table 1. One of the criteria for these specific symptoms was that they were not known as so-called keynotes for the same medicine. This way we hoped to prevent interrelation of the symptoms. The project will end December 2007. This is a multi centre (10 practices) research including all consecutive patients older than two years. All six symptoms were checked in all new patients. All prescribed medicines were recorded and results related to each medicine was monitored during the treatment. Participating doctors receive feedback on their results during consensus meetings twice a year. Data were entered in different computer programs for practice management, but the exported data were all in the same format. They were analysed and LR's were calculated in Excel spreadsheets. Pivot tables were inspected visually for possibly interrelated medicines. Some correlation matrices were calculated using the Vassar stats website (<http://faculty.vassar.edu/lowry/VassarStats.html>). Confidence intervals were calculated using the program CIA of BMJ (log method).

Results after 32 months

In February 2007, after 32 months, 3367 patients were included and 3246 prescriptions evaluated. Some of the results are shown in appendix 1. Compared to the existing repertory we can now make more reliable estimates about the LRs of various symptoms for a number of medicines. But this outcome has still to be interpreted carefully because numbers vary strongly among medicines. The number of cases responding well to some medicines is given in table 2.

Medicine	N=
Anacardium (anac.)	11
Argentum nitricum (arg-n)	29
Calcarea carbonica (calc.)	64
Causticum (caust)	38
Cocculus (cocc)	10
Conium (con.)	14
Gelsemium (gels.)	10
Ignatia (ign.)	23
Natrium muriaticum (nat-m.)	129
Phosphoricum acidum (ph-ac.)	19
Sepia (sep.)	76
Veratrum album (verat.)	5

Table 2: The number of cases responding well to some specific medicines.

For these medicines and for the assessed symptoms we made a table like table 1, but based on calculated LRs (Table 3). A blank in this table indicates that there was no patient responding well to this medicine with the symptom present. In bold type are entries that have either not one in their 95% Confidence Interval, or are unlikely to have the LR significantly above 1. In the first case they should be included as an indication for the medicine; in the second case they should be excluded. These entries can be used to estimate the accuracy of the existing repertory by comparing table 3 with table 1. The other entries are rather uncertain, but still based on a more reliable procedure than the original entries in the repertory.

Symptom nr.	Symptom										Prevalence
1.	Diarrhoea after anticipation										4.3%
2.	Fear of death										3.9%
3.	Grinding teeth during sleep										5.5%
4.	Herpes lips										4.8%
5.	Sensitive to injustice										9.8%
6.	Loquacity										6.7%
	anac	verat	cocc	gels	con	ph-ac	arg-n	sep	ign	caust	calc
1.	2.12	-	2.33	14.49	1.84	7.61	9.45	0.91	1.01	1.23	1.84
2.	13.11	10.42	2.58	2.58	3.71	-	1.78	1.72	2.25	0.67	1.21
3.	-	3.65	3.67	-	2.62	1.93	1.90	1.70	2.40	0.48	0.85
4.	1.92	-	-	2.11	1.60	1.11	-	2.28	-	1.67	0.33
5.	4.69	-	4.12	1.02	-	1.62	-	0.94	2.69	4.17	0.96
6.	2.75	9.13	-	-	-	-	0.52	1.60	0.65	1.19	0.46
total LR	688.2	347.2	90.9	80.5	28.6	26.4	16.6	9.1	9.5	4.0	0.3

Table 3: The same symptoms as in table 1, but arranged according to outcome of LR assessment

This table based on LR shows similarities to table 1, but also definite differences. About 25 of the 48 entries of table 1 do not correspond with the assessed LR data in table 3. We see that frequently prescribed medicines, like *Sepia* and *Calcarea*, show the most striking differences with the original repertory. We also see less frequently prescribed medicines emerging in this outcome, like *Anacardium*, *Cocculus* and *Conium*. If we compare table 1 with table 3 we see that about half of our findings do not correspond with the existing repertory. This estimation depend partly on subjective cut-off values for entries in either plain, italics or bold type, but is rather conservative. We considered LR=1.20 not as contradictory to an existing (plain) entry, although it is not likely to be indicative for a medicine.

Correlation between symptoms

For the medicines *Anacardium*, *Cocculus*, *Gelsemium*, *Conium* and *Sepia* correlation matrices were calculated (appendix 2). We see some possible correlations between symptoms for *Anacardium*, *Cocculus* and *Conium*, but numbers are too small. There are no indications for correlation between symptoms for *Sepia*. The symptoms ‘diarrhoea from anticipation’ and ‘herpes lips’ could be related for *Anacardium*, therefore the combination of these two symptoms could be a stronger indication than expected from table 3. But visual inspection of the database showed that only one case (out of 11) was responsible for this correlation. Apart from *Anacardium* the correlation matrices give no other picture than table 3.

Several other medicines with a larger number of records were investigated for correlation between symptoms, but few correlations were found. There could be correlation between ‘diarrhoea after anticipation’ and ‘herpes lips’ for *Nux vomica* (3 out of 30 cases), and for ‘herpes lips’ and ‘sensitive to injustice’ for *Phosphoricum acidum* (2 out of 19 cases), see appendix 2.

Interpretation

Without experience in homeopathic practice one would easily prescribe *Anacardium*, based on table 3. A combined LR of these symptoms of 688 for *Anacardium* would elevate a prior-chance of 1% to a posterior-chance of 87%. But practice experience learns that all medicines in table 3 are still possible. Looking at the table an experienced homeopathic physician will intuitively scan all medicines and discard some of them because the ‘type’ of patient before him doesn’t fit the overall picture of the medicine. Even character is important. If the patient before him has no problems with self confidence or self-perception doubt will rise. The homeopathic doctor will ask supplemental questions, based on this table. If the patient then appears to have serious car-sickness and a character liable to be worried, preference will go to *Cocculus* (*cocc.*). In the end the overall picture is much more important than the symptoms chosen to make a table like table 3.

If you ask the homeopathic doctor about the main reasons for his final choice, he will come up with a different set of symptoms than after the first phase in the diagnostic process. If the chosen medicine is *Cocculus*, the worrying character will not appear in the first set of symptoms because this symptom is vague and it is hard to find the right repertory-rubric for this symptom. Possibly the patient did not mention the car-sickness because it was there all his life (recall bias). The number of variables is large and the whole set for each possible medicine cannot be overseen in the first part of the consultation.

Discussion

In our research we closely followed existing homeopathic practice trying to provide the method with a more scientific methodology. We showed that it is feasible to collect the prevalence of a limited number of symptoms in a large number of patients and also to collect a large number of evaluated prescriptions using appropriate software. We were able to reconstruct data that are relevant to homeopathic practice with simple tools.

Our results corresponded partly with the existing repertory, but there were also significant differences. As expected, the most prescribed medicines had the lowest accordance with the existing repertory. But there is no clear general rule as to how entries of frequently prescribed medicines could be corrected systematically.

We want to stress that this kind of research is not suited to prove the efficacy of the homeopathic method. The perception of symptoms and results is highly subjective. The doctors participating in this research should be fully aware that their own method becomes biased if they are not aware of the dangers of

selection and confirmation bias when evaluating symptoms and results. Results of experimental proof should improve if the main instruments are better.

Symptoms and results are not specified by using special (and time-consuming) interrogatories, leaving daily practice as it is. There is much vagueness involved in assessing symptoms and effects and this vagueness cannot be ruled out completely by consensus and feedback. The general idea however is that we use our best prescriptions to calculate LRs. The quality of our instrument (repertory) will then gradually move from poor towards better.

For calculation of LRs we compared a relatively small population responding well to one medicine with a large rest-population, comprising patient who did not respond to the medicine and patients that did not use that specific medicine. This procedure is different from conventional diagnostic research, where the rest-population is smaller, i.e. the population put to the test, but with negative result (false negatives). Our assumption is that only a small number of patients will respond to one particular homeopathic medicine. There will be patients in the rest-population that could have responded well to the medicine, but to whom it was not prescribed (possible responders). Based on our assumption this number is relatively small compared to the rest-population. But the population of possible responders will not be much smaller or larger than the population that received the medicine but did not respond (non-responders). We therefore estimated that the error of comparing responders with non-responders would be greater than of comparing with the whole rest-population.

Prevalences of symptoms in this assessment are indicated to enable the practitioner to compare these results with his own estimations of his practice. LRs coming from this kind of research are only indications for the relative importance of the symptom for each medicine. Then there is the choice of threshold value. Every symptom could be present in all various degrees. Our values of LR are based on a mean in our population. If, however, a symptom is present in an extreme degree, the LR will be larger than in our assessment.

From a methodological point of view this research is flawed because it assessed LRs of six symptoms as if they were independent of each other. Correlation matrices (appendix 2) show that this is not always true, but for this set of symptoms it seems a small problem. We followed the existing methodology of the repertory regarding symptoms as independent entities. If we were to develop homeopathy from scratch we might prefer to assess one medicine and its corresponding symptoms. Multivariate analysis could then indicate the relation of each symptom regarding that medicine. The problem is that there are many symptoms corresponding to one medicine, sometimes more than 3,000. It seems not feasible to assess more than 10 symptoms in one investigation. It is possible that prevalences of symptoms are too low to perform multivariate analysis. We plan to investigate the possibility of multivariate analysis in the existing database at the end of the project. For a following project we are examining the possibility to assess symptoms regarding one medicine. We will also investigate other methods of assessing correlation, like principle components analysis.

Homeopathic methodology cannot be changed overnight, we don't even know how it should be improved. If we enrich the present repertory with LR data we make the present methodology more accurate. If we want to apply multivariate analysis the method changes substantially. We should evaluate if such changes are for the better. Changes like proposed here have considerable implications. For applying LR we need consensus about how this should be done. There are a number of subjective choices to be made, like when to enter or discard medicines in/from repertory rubrics. The outcome of multivariate analysis seems more appropriate for the materia medica, but how can we apply this in the repertory?

Is it feasible to improve the repertory this way? We estimate that this kind of research is most appropriate for symptoms with a prevalence in the general population of 2-15%. Many of those symptoms comprise a large number of entries and these entries are partly incorrect because of chance error. Symptoms with higher prevalence are not very interesting for homeopathic practice. Symptoms with lower prevalence demand larger populations and such symptoms correspond to smaller rubrics that can easily be interpreted intuitively. We estimate that there are about 600 repertory rubrics that could benefit strongly from this kind of assessment. Probably 100 assessments, each assessing six symptoms and lasting three years, are needed.

Appendix 1: LR assessment of some medicines regarding six homeopathic symptoms

Diarrhoea after anticipation

The symptom occurred in 145 out of 3367 patients, prevalence 4.3% (95% CI 3.7 to 5.1%).

		LR+	95% CI
total=	3367		
diarrhoea	n=145		
	am-c	5.87	1.75 to 19.71
	arg-n	9.45	5.76 to 15.49
	cimic	7.83	2.50 to 24.57
	gels	14.49	8.52 to 24.66
	ph-ac	7.61	3.85 to 15.04

Fear of death

Prevalence 3.9% (95% CI 3.3 to 4.6)

		LR+	95% CI
fear	n=131		
	acon	6.51	1.94 to 21.88
	anac	12.11	6.20 to 23.65
	ars	6.42	3.13 to 13.16
	con	3.71	1.02 to 13.55
	verat	10.42	3.52 to 30.91

Grinding teeth at night

Prevalence 5.5% (95% CI 4.7 to 6.3)

		LR+	95% CI
grinding	n=185		
	bell	5.47	2.59 to 11.59
	calc-p	4.08	1.19 to 13.96
	carc-c-c	4.59	1.37 to 15.37
	cocc	3.67	1.05 to 12.78
	merc	2.90	1.45 to 5.82

Herpes lips

Prevalence 4.8% (95% CI 4.1 to 5.5)

		LR+	95% CI
herpes	n=160		
	bry	4.72	1.38 to 16.19
	lyc	2.41	1.23 to 4.71
	nat-m	3.38	2.12 to 5.28
	sep	2.28	1.16 to 4.47
	staph	3.43	1.38 to 8.26

Sensitive to injustice

Prevalence 9.8% (95% CI 8.8 to 10.9)

		LR+	95% CI
injustice	n=330		
	anac	4.69	2.44 to 9.04
	bell	2.42	1.02 to 5.73
	carc	2.37	1.28 to 4.39
	carc-c-c	5.15	2.56 to 10.38
	caust	4.17	2.78 to 6.27
	cocc	4.12	1.92 to 8.86
	ign	2.69	1.34 to 5.40

Loquacity

Prevalence 6.7% (95% CI 5.8 to 7.6)

		LR+	95% CI
loquax	n=224		
	ambr	7.57	2.82 to 20.35
	hyos	6.10	2.83 to 13.18
	lach	5.20	3.08 to 8.76
	tarent	3.78	1.31 to 12.65
	verat	9.13	4.41 to 18.88

Appendix 2: Correlation matrices

Names of variables:

- V1 Diarrhoea from anticipation
- V2 Fear of death
- V3 Grinding teeth at night
- V4 Herpes lips
- V5 Sensitive to injustice
- V6 Loquacity

Anacardium

VassarStats: Correlation Matrix

Number of Variables = 6 Observations per variable = 11

r	V1	V2	V3	V4	V5	V6
V1	1	0.585	-0.14	0.886	0.188	0.283
V2		1	0.418	0.418	0.069	-0.028
V3			1	-0.1	-0.289	-0.14
V4				1	0.346	0.373
V5					1	0.485
V6						1

Cocculus

Number of Variables = 5 Observations per variable = 10

r	V1	V2	V3	V4	V5
V1	1	-0.207	0.872	-0.31	-0.329
V2		1	-0.156	-0.167	-0.318
V3			1	-0.234	-0.281
V4				1	0.053
V5					1

Gelsemium

Number of Variables = 6 Observations per variable = 10

r	V1	V2	V3	V4	V5	V6
V1	1	0.469	0.156	0.447	0.156	-0.5
V2		1	-0.22	0.116	-0.22	-0.234
V3			1	0.116	0.756	-0.234
V4				1	0.116	0
V5					1	0.156
V6						1

Conium

Number of Variables = 6 Observations per variable = 14

r	V1	V2	V3	V4	V5	V6
V1	1	-0.226	0.011	-0.226	0.147	0.614
V2		1	0.501	0.731	-0.405	-0.023
V3			1	0.017	-0.404	0.258
V4				1	-0.405	0.138
V5					1	-0.027
V6						1

Sepia

Number of Variables = 6 Observations per variable = 76

r	V1	V2	V3	V4	V5	V6
V1	1	0.218	0.128	0.308	0.009	-0.262
V2		1	-0.049	0.076	-0.101	-0.166
V3			1	0.012	-0.106	-0.114
V4				1	0.115	-0.207
V5					1	0.04
V6						1

Nux- vomica

Number of Variables = 6 Observations per variable = 30

r	V1	V2	V3	V4	V5	V6
V1	1	0.029	0.176	0.659	-0.012	0.227
V2		1	-0.064	-0.106	-0.107	0.141
V3			1	0.248	0.161	0
V4				1	0.156	0
V5					1	-0.059
V6						1

Phosphoricum acidum

Number of Variables = 6 Observations per variable = 19

r	V1	V2	V3	V4	V5	V6
V1	1	0.149	0.219	0.216	-0.177	-0.226
V2		1	-0.117	-0.081	-0.221	-0.076
V3			1	0.061	-0.077	-0.161
V4				1	0.619	-0.111
V5					1	0.288
V6						1