



A RETROSPECTIVE CLINICAL EVALUATION OF THE RUBRICS USING LIKELIHOOD RATIO IN CASES WITH GOOD THERAPEUTIC RESPONSE TO ARSENIC ALBUM

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ABSTRACT

Repertory and M.M in Homoeopathic science comprises of numerous rubrics indicating a medicine but the question remains to which rubrics the physician must rely upon of being exact indication of a specific medicine. To answer this, evaluation of the symptoms by implication of Likelihood Ratio (LR) has been initiated as a measure of justification to bring into light the indicators of a specific medicine. This Retrospective observational study was attempted to validate rubrics of Arsenic Albm. 1 rubric, sneezing constant (LR+ 9.0, p=0.636) could be upgraded to Bold typeface, 5 rubrics (anxiety health about, vomit, appetite diminished diarrhea, stool odor offensive) were analogous to the existing typeface in Kent's Repertory, 7 rubrics [discharge watery (LR+3.65, p=0.656), coryza (LR+2.7, p=0.653), nausea (LR+ 2.85, p=0.643), Weakness in general (LR+2.20, p =0.685), Abdomen pain burning (LR+ 4.19, p=0.695), Rectum pain burning (LR+ 2.85, P=0.643) and Sleep disturbed (LR+ 2.16, P=0.684) the typeface could be downgraded, 4 rubrics [company desire for (LR+ 1.13, p=0.648) and urethra pain burning (LR+1.29, p=0.673), irritability (LR+0.68, p=0.537) and weeping tearful mood (LR+ 0.57, p=0.648) remains doubtful. The higher the LR+ relating to p-value, assurance increases for exception and adding entries into repertory

KEYWORDS : Homoeopathy, Arsenic Album, Likelihood Ratio, Retrospective Study.

INTRODUCTION

Evidence – based medicine¹ is a challenge for the future years of homoeopathy, within which we are further inspecting for evidence of effectiveness of the homoeopathic treatment which indeed could be done through clinical evaluation of the symptoms.² Prescriptions in clinical practice in the Homoeopathic Science depend on the spotting of suggestive signs and symptoms the patient presents. Although the knowledge regarding the symptoms which are marked to be indicators of a medicine are present in an unorganized and in a vague pattern³, presence of such massive amount of information makes the reliability questionable.

The complication is about the complexity regarding the selection of homoeopathic medicine, which depends over the co-occurrence of various symptoms. A symptom begins to be more important if few other symptoms are also available. There is a divergence between, making a choice of a medicine during consultation and justifying the same choice afterwards.

Clinical verification refers to curing of a proving symptom within a patient⁴.

Clinical evaluation indicates process of reviewing and confirming the symptoms that were already documented and noted in the literature of the homoeopathic science as the proving symptoms and the cases cured. If the documented symptoms are further seen in the cases which give a good therapeutic response to the relative medicine, this assures the pertinence of that symptom in association to that medicine. Clinical evaluation is the process which can further validate the fundamental principles on which homoeopathy is based upon; moreover the results obtained could be implemented for betterment and improvisation of daily clinical practice³.

Likelihood Ratio is one such modern epidemiological tool and also a modern Bayesian translation of the expression as “characteristic”, “peculiar” or “keynote” symptoms in homoeopathy⁵. If the symptom is peculiar, the prevalence is lower and LR will be high⁶.

The basic vindication behind this effort undertaken is quite easy and clear. For a symptom to be considered as a characteristic of a specific given medicine. Here the prevalence of that symptom must be higher within the patients responding well to it as compared to the remnant patients. The LR of the symptom must be > 1. If the prevalence of the symptom is lesser than 1 in that specific medicine than in the remainder of the patients, the symptom won't indicate to that medicine prescription⁷. In the present retrospective study, an attempt is made to verify and evaluate allocated symptoms of the medicine – Arsenic Album. LR calculation will enable accuracy based on evidences that are empirical instead of mere assumptions⁸.

MATERIALS AND METHOD

A Retrospective assessment of Likelihood Ratio for rubrics allocated to Arsenic Album was performed. Mind : anxiety health about , irritability , company desire for , weeping tearful mood , Nose : coryza , sneezing constant , discharge watery , Abdomen : pain burning . Stomach : appetite diminished , vomit , nausea , Rectum : pain burning , diarrhea . stool : offensive , Urethra : pain burning , Sleep : disturbed , Generalities : Weakness .

All the records of the patient included in the study were taken from various OPD's in Bharati Vidyapeeth Homoeopathic hospital, Pune between the years 2014 – 2018. All the cases were handled and examined by experienced Homoeopathic physicians working as teaching staff along with group of students assisting them. Inclusion of the cases were done on

the basis of patients within age group of 18 – 65 years, prescriptions with only single remedy were considered, all the cases whether acute or chronic were taken into contemplation, where in the acute cases outcome at the last follow-up recorded is considered and cases with minimum 2 follow-ups were considered in the chronic cases. Repertorisation was done through the RADAR 10 software, using the Kent's Repertory. The assessment of the cases and their follow ups has been done following the GHOS or ORIDL scale. The outcome of the cases were calculated by using the 9 point scale of the above mentioned⁹. If a symptom is **vigorously present**, the degree is considered to be "2", if the symptom is present in **mild form** its degree is considered to be "1", and "0" is considered if there is **absence** of the symptom.

The calculation of LR+ and LR- was done through 2 x 2 contingency table including a, b, c and d represented in table no 1.

- a: aggregate of patients with a symptom, with positive results from Arsenic
- b: remaining population with presence of symptom
- c: aggregate of patients, symptom-absent, still improved by Arsenic
- d: remaining population with absence of symptom

Table No 1

	Medicine worked	Rest	
Symptom present	a	b	a + b
Symptom absent	c	d	c + d
	a + c	b + d	a + b + c + d

In order to suggest addition or omission of a rubric for Arsenic Album, divergent cut off values are used. To add a rubric for Arsenic Album the value for LR>1.5 and p value must be >0.60 and for omitting a rubric LR<1 and p<0.40.

Statistical techniques & Data analysis

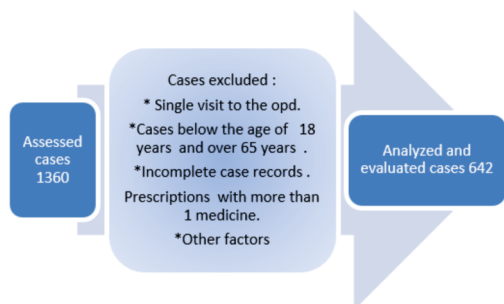
The comparison was conducted among 2 groups – Patients with positive response (improved and cured) to Arsenic Album and the remaining population (Patients who did not respond to Arsenic Album and also the patients who were prescribed with other medicine).

For all the 17 rubrics which were verified: the Prevalence, LR + with 95% Confidence Interval and LR - with 95% Confidence Interval were calculated. All the calculations were attempted with the help of MS Excel and MEDCALC (medcalc.org). For the calculation of p-value (area under the curve) was further calculated through STATA15

RESULTS

Assessed records: in the data recorded the mean age were 31.16 with standard deviation 11.62, and range 18 – 65 along with standard error of mean 0.4588. From 1360 records just 642 records were evaluated and 718 cases were discarded for multiple reasons as displayed in figure 1.

Figure 1
Assessed case records



Characteristics of the patient:

Case records of the patients were taken from year 2014 – 2018. case taking with Anamnesis was done by the physicians (teachers) in the Bharati Vidyapeeth homoeopathic hospital, Pune. Arsenic Album was frequently prescribed to the male (167) population than the female population (113). Good therapeutic response was recorded in 483 cases for the given treatment inclusive of all medicines, whereas out of 280 cases of Arsenic Album magnificent therapeutic response was recorded in 243 cases. Depicted in table no 2.

Table 2
characteristics of patients

N = 642	Arsenic Album Cases	Remaining medicines	Aggregate
Male	167	141	308
Female	113	221	334
Aggregate (n)	280	362	642

Prescriptions:

Thirty two various medicines were indicated in the recorded cases used for evaluation and analysis, there were such medicines which just prescribed once: Argentum Nitricum, Calcarea Sulph, Carbo Veg and Kali Carb. Whereas an effective therapeutic response was recorded in few frequently prescribed medicines: Lycopodium, Apis, Cantharis, Causticum, Graphitis, Kali Bi, Merc Sol, Petroleum, Puls, Staph, Sulphur, Thuja and Nux Vomica. Depicted in table 3.

Table No.3
Aggregate of caes in comparson with cases responding to medicines.

Medicines	Total No. of Case	Cases responding to the medicines
Arsenic Album	280	243
Allium Cepa	3	1
Apis Mellifica	4	0
Argentum Nitricum	1	1
Belladonna	12	9
Bryonia Alba	18	13
Calcarea Carb	6	3
Calcarea Sulph	1	1
Cantharis	19	16
Carbo Veg	1	1
Causticum	10	8
Dulcamara	7	7
Graphitis	6	5
Hepar sulph	2	1
Ignatia	7	4
Kali Bi.	4	3
Kali Carb	1	1
Lachesis	9	7
Lycopodium	24	15
Merc. Sol.	11	10
Natrum Mur.	52	25
Nitric Acid	4	3
Nux. Vom.	30	20
Petroleum	5	4
Phosphorus	10	5
Pulsatilla	37	24
Rhus Tox	19	15
Sepia	22	10
Silicea	7	5
Staph.	7	7
Sulphur	20	13
Thuja	3	3
Total	642	483

Significantly majority of the patients suffered from ailments of Gastrointestinal System, Respiratory System and

Multisystem, where remarkable results were found after the prescription of Arsenic Album (table 4)

Table No. 4
Complaints and System involvement with response to Arsenic Album and remaining population

SYSTEM INVOLVED AND COMPLAINT S	Cases responding to Arsenic Album	Remaining population
Central Nervous System	9	49
Cardiovascular System	6	29
Musculoskeletal System	0	1
Gastrointestinal System	78	60
Endocrine System	0	1
Genitourinary System	3	6
Immune System	7	3
Integumentary	13	49
Psychological	4	2
Reproductive System	3	28
Respiratory System	66	42
Skeletal System	0	1
Urinary System	3	21
Vestibular System	0	1
Visual System	0	2
Multisystem Involvement	51	104
Total	243	399

Seventeen rubrics were considered for evaluating the type face of Arsenic Album as mentioned in the Kent's Repertory. For Sneezing constant, Arsenic Album is present in *italic* type face. Following what our assessment suggests, sneezing constant (LR+ 9.03, p= 0.636) Arsenic should be placed in **Bold** typeface as it higher than the cutoff value (LR+ > 6, p>0.60). Arsenic Album for the rubrics Vomit (LR+ 6.15, p =0.721), Diarrhea (LR+ 11, p= 0.684), Stool odor offensive (LR+ 6.15, p= .701) qualify for the **Bold** type face as they cross the cut off value (LR >6, p = 0.60) and also the rubrics

"Anxiety Health About" (LR+ 1.56, p =0.612) and "Appetite Diminished" (LR+ 2.15, p= 0.698) stands by the cutoff values (LR>1.5, P >0.60 for roman) which states presence of the medicine in roman type face. All the 5 rubrics with their respective and required values mentioned above for the medicine Arsenic Album justify the existing type faces in the Kent's Repertory.

For Rubrics like discharge watery (LR+3.65, p= 0.656), coryza (LR+2.7, p =0.653), Nausea (LR+ 2.85, p=0.643), Weakness in general (LR+2.20, p=0.685), Abdomen pain burning (LR+ 4.19, p=0.695) Arsenic Album is present in **Bold** type face in Kents's Repertory, but as per our assessment Arsenic Album for Weakness, Nausea and Coryza must be downgraded to roman type face, and for the rubrics Abdomen pain burning & discharge watery it should be downgraded to *Italic* type face.

For the rubrics Rectum pain burning (LR+ 2.85, P= 0.643) and Sleep disturbed (LR+ 2.16, P= 0.684) Arsenic Album is present in *Italic* type face in Kent's Repertory, but after our evaluation Arsenic Album for both the rubrics must be downgraded into roman type face. Whereas for the rubrics "company desire for" (LR+ 1.13, p = 0.648) and urethra pain burning (LR+1.29, p=0.673) the typeface for existence of Arsenic Album is still doubt full, reason being LR > 1 but cutoff for p value is > 0.60, this can be an indicate roman typeface.

As the existing entries in the Kent's Repertory the type face assigned for Arsenic Album for the rubric irritability is *italic* and for weeping tearful mood it is roman, but after evaluation it was found that the chance for irritability is 54% (LR+0.68, p=0.537) and for the rubric weeping tearful mood is 65% (LR+ 0.57, p=0.648) could be added in Roman typeface but the value for LR does not fulfill the criterion for cut off values, whereas it is still doubtful. Rubrics for the medicine Arsenic Album with a,b,c,d, values for LR+ with 95%CI, LR- with 95% CI and p-value are given in the table no 5.

Table No. 5
Values of LR+ and LR- with 95%C.I along with relevant p-values

Rubric's of Arsenic Album	No. of cases present with this symptom	a	b	c	d	LR+	95% CI	LR-	95% CI	p-Value
Mind										
Anxiety Health About	n=41	20	21	223	378	1.56	0.86-2.82	0.97	0.93 - 1.01	0.612
Irritability	n=130	38	92	205	307	0.68	0.48-0.96	1.02	1.02-1.18	0.537
Company Desire For	n=44	18	26	226	372	1.13	0.63-.2.02	0.99	0.95-1.04	0.648
Weeping tearful Mood	n=46	5	41	239	357	0.57	0.08-0.50	1.09	1.05-1.13	0.564
Nose										
Coryza	n=80	50	30	193	369	2.74	1.79-4.18	0.86	0.08-0.92	0.653
Discharge watery	n=58	40	18	203	381	3.65	2.14-6.22	0.87	0.82-0.93	0.656
Sneezing Constant	n=13	11	2	232	397	9.03	2.02-40	0.96	0.93-0.99	0.636
Abdomen										
Pain Burning	n=19	13	6	190	433	4.69	1.81-12	0.95	0.91-0.99	0.6955
Stomach										
Appetite Diminished	n=133	71	62	132	377	2.5	1.84-3.33	0.76	0.68-0.84	0.698
Nausea	n=52	33	19	210	380	2.85	1.66-4.90	0.91	0.86-0.96	0.643
Vomiting	n=50	37	13	166	426	6.15	3.35-11	0.84	0.79-0.90	0.721
Rectum										
Pain Burning	n=29	15	14	188	425	2.32	1.14-4.71	0.96	0.92-1	0.685
Diarrhoea	n=41	34	7	169	432	11	4.74-23	0.85	0.79-0.90	0.684
Stool										
Odour, offensive	n=23	17	6	186	433	6.15	2.45-15	0.93	0.89-0.97	0.701
Urethra										
Pain Burning	n=24	9	15	195	423	1.29	0.57-2.89	0.99	0.96-1.02	0.673
Sleep										
Disturbed	n=94	47	47	156	392	2.16	1.50-3.13	0.86	0.79-0.93	0.684
Generalities										
Weakness	n=103	52	51	151	388	2.20	1.56-3.12	0.84	0.77-0.92	0.685

Expressing the relative incidence of the rubrics into the form of LR is the only correct and feasible method. After conversion of the LRs of the respective rubrics into typeface only we can approximate of what number of patients would respond well to the medicine underneath analysis. For Arsenic Album the same along with prevalence in terms of percentage has been depicted in table 6.

Table No. 6
Expected and verified occurrence of the rubrics of Arsenic Album

Rubric	Prevalence (%)	Type	Present	Expected
Anxiety health about	6.38%	Roman	1.56	>1.5
Irritability	20.25%	<i>Italics</i>	0.68	>3
Company desire for	6%	Bold	1.13	>6
Weeping tearful mood	7.16%	Roman	0.57	>1.5
Coryza	12.46%	Bold	2.7	>6
Discharge watery	9.03%	Bold	3.65	>6
Sneezing constant	2.02%	<i>italics</i>	9.03	>3
Abdomen ,pain burning	3%	Bold	4.19	>6
Appetite diminished	20.71%	Roman	2.5	>1.5
Vomiting	8%	Bold	6.15	>6
Nausea	8%	Bold	2.85	>6
Rectum, pain burning	4.51%	<i>Italics</i>	2.32	>3
Diarrhea	6.4%	Bold	11	>6
Stool , odor offensive	3.5%	Bold	6.15	>6
Urethra, pain burning	4%	Bold	1.29	>6
Sleep , disturbed	15%	<i>Italics</i>	2.16	>3
Weakness	16%	Bold	2.20	>6

DISCUSSION:

Various weaknesses must be taken into consideration while taking into account the results of research undertaken. Various kinds of bias could influence the study and figures. While conducting a retrospective study, it becomes difficult to determine when the patient had an effective progression and hence it becomes more difficult to assign with the medicine and the treatment. Just because the symptom has been recorded in the case does not connote that the symptom was actually present in the patient and even the intensity isn't accurate or powerful enough so that it could be considered as a definitive indicator of that medicine. Few symptoms are left unnoticed or unrecorded by the physician. The inference corresponds to higher prevalence rather than with LR. High prevalence of a symptom could discard the medicine in absence of that symptom, whereas to confirm a medicine a LR of that symptom must be high.^[2]

According to our evaluation and assessment from the 17 rubrics under research , Arsenic Album for the rubric "sneezing constant " must be upgraded to Bold typeface while for 5 rubrics it was found to be relevant with its existing typeface in the Kent's Repertory . From 5 rubrics which were present in Bold type face in the repertory , 3 rubrics could be downgraded to roman whereas other two rubrics must be downgraded to *italics* . The values of LR+ for Bold typeface can be considered >4 or 5 and for plain or roman type face the values can be >1.3¹⁰ , keeping this into view Arsenic Album for the rubric "Abdomen pain burning" could be kept into the Bold typeface .2 such rubrics with LR+ > 1 but < 1.5 could be placed in roman typeface. For 2 other rubrics the entries are still doubtful and Arsenic could be placed in roman typeface .Other 2 rubric fail to cross the cutoff value for LR+ but they cross the cut off for p value , this again make the entries doubtful and could be further added to roman typeface.

Discrepancies were found between Kent's Repertory and our evaluated result , as in the earlier times the chance influence was not taken into account for adding and discarding entries

in a rubric .The shortcomings of the Repertories could be handled by adapting this methodology but this does not mean that it will solve every shortcoming, few may be solved by implication of LR and some might not .

CONCLUSION:

There are flaws in Kent's repertory, which can further be corrected and rectified by implication of the Likelihood Ratio. Physicians are well acquainted with the Main symptoms and the symptoms which indicate directly to Arsenic Album but this depends upon the prevalence of the symptom rather than the LR of the symptoms. Retrospective verification and assessment of symptom prevalence and LR in patients with good response can be a better way for selection of the symptoms for a prospective study.

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