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Unusual Raise in Intraocular Pressure In A Glaucoma Patient - A Case Report On Suspected Adverse Drug Reaction To The Siddha Medicine *Nilavembu Kudineer*

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ABSTRACT

Nilavembu Kudineer is a commonly used Siddha medicine in Tamil Nadu available by prescription and over the counter for the treatment of fever and arthralgia; and it is widely used in the prevention and management of dengue and chikungunya fever. The bitter taste of *Nilavembu Kudineer* occasionally induces nausea and vomiting in some patients; except this, till date there is no recorded adverse drug reaction for the drug. In this case report, spontaneous reporting of an adverse drug reaction to *Nilavembu Kudineer* in a glaucoma patient is discussed. For three consecutive days, the patient found unusual increase in intraocular pressureimmediately after the intake of *Nilavembu Kudineer* in 'empty stomach'. There after the patient shifted the time of administration of *Nilavembu Kudineer* to 'after breakfast' and found no abnormality in intraocular pressure. During the time of adverse drug reaction, no other medicines were administered with *Nilavembu Kudineer* in 'empty stomach', which clearly exhibits a strong causal relationship between the adverse drug reaction and *Nilavembu Kudineer*. The case report indicates the need for more active surveillance of *Nilavembu Kudineer* by healthcare professionals for an improved understanding of the medicine.

KEY WORDS

Nilavembu Kudineer, Siddha medicine, case report, adverse drug reaction, increased intraocular pressure, glaucoma patient, spontaneous reporting

INTRODUCTION

In the clinical discipline 'pharmacovigilance', drug safety monitoring is an essential element for the effective use of medicines and for high quality medical care. It has the potential to inspire confidence and trust among patients and health professionals in medicines and contributes to raising standards of medical practice. Healthcare practitioners are in a position to make good use of their patients' positive and negative experiences of treatment to contribute to medical science and to an improved understanding of disease and of the medicines [1].

The poly-herbal Siddha medicine, "*Nilavembu Kudineer*" (NK) is a decoction prepared from the coarse powder made from nine herbal ingredients which is available in the markets of Tamil Nadu in the name of "*Nilavembu Kudineer Chooranam*". Since it offers promising results in fever and arthralgia, it is widely used in the prevention and management of dengue and chikungunya fever in Tamil Nadu[2], [3],[4]. It is also a commonly prescribed drug in the management of diabetes mellitus. Except nausea and vomiting in some patients due to the high level of bitterness in the medicine, till date there is no recorded adverse drug reaction (ADR) to NK. In this case report, spontaneous reporting of an ADR to NK in a glaucoma patient is discussed.

PATIENT INFORMATION

The patient is a 66-year old male presented with the complaint of pain in forehead, cough and low back ache. He is a known case of glaucoma for the past 3 years and getting treatment for the problem in a premiere government ophthalmic institute in New Delhi. He underwent three surgical procedures for the correction of glaucoma problem and at present he is on the allopathic medication 'brimonidine tartrate and timolol maleate ophthalmic solution' (one drop to be instilled in the affected eye twice daily, approximately 12 hours apart). He is also a case of type 2 diabetes mellitus since three years and his blood sugar levels are under proper control with an Ayurveda medicine in powder form(he didn't have a correct idea of the name of the medicine, the dose is 2 gm twice daily, after food).

Since the patient is suffered from cough and pain in forehead and a known diabetic, the drug *Nilavembu Kudineer Chooranam*5gm(to be prepared as NK decoction and taken in

empty stomach, once in a day, in the morning) was prescribed along with the chewable tablet *Thalisathy Vadagam* 500 mg (two tablets, as needed during cough) for 15 days.

After the completion of the fifteen days course, he came for follow up and informed that, in the initial three days, he felt an unusual increase in the intra-ocular pressure immediately after the intake of NK in 'empty stomach' in the morning. Thereafter he changed the time of intake of NK to 'after breakfast' and felt no abnormality in the intraocular pressure. So, he used to take the medicine 'after breakfast' for the rest of the days and there was no recurrence of the ADR. However *Nilavembu Kudineer Chooranam* was dropped in his next prescription considering the suspicion of the possible role of NK in increasing the intraocular pressure in the patient.

Discussion

Few ADRs were reported in respect of the single herb *Nilavembu* (*Andrographis paniculata* (Burm. f.) Wall. Ex Nees)[4], [5], [6].*Nilavembu* is one among the nine ingredients present in NK and it shares one ninth parts in the NK formulation. The discussed case report on suspected ADR to NK might be the first reported ADR to the poly-herbal formulation NK.

The history reveals that the ADR occurred immediately after the intake of NK in empty stomach in three consecutive mornings and during these days no other medicines were administered with *Nilavembu Kudineer*. Accordingly the patient himself changed the time of intake of NK into after breakfast, and found that there was no abnormality in the intraocular pressure when the medicine was taken after breakfast.

Through pharmacovigilance perspective, in this case report there is no recurrence of ADR, after partial 'de-challenging' i.e., withdrawal of the intake of the drug in 'empty stomach' in the morning and 're-challenging', i.e., intake of the drug again by the patient 'after breakfast'.

The positive de-challenge i.e. the ADR did not recur after withdrawal of the intake of the drug in 'empty stomach' and the negative re-challenge i.e. the ADRdid not recur after the drug was restartedby changing the time of administration to 'after breakfast', clearly exhibits a strong causal relationship between the ADR and the administration of the drug in empty stomach.

In re-challenging, generally a positive re-challenge i.e., the ADR recurring after restarting the drug, is most appropriately helpful in identifying the causal relationship

between the drug and ADR;butnegative re-challenge i.e., the ADR does not recur after the drug is restarted,is little challenging and confusing condition in establishing a causal relationship between the drug and ADR. In this case, the de-challenging and re-challenging were performed by the patient and especially the drug was re-challenged by changing the time of administration and the negative re-challenge favors here in establishing the causal relationship of ADR with the time of administration of NK.

Clinically, re-challenging is justifiable when the benefit of re-introduction of the drug to the patient outweighs the risk of recurrence of the reaction. In this case, the doctors dropped NK from the patient's next prescription, since the risk of recurrence of ADR to NK outweighs the trivial role of NK in the management of the presenting complaints of the patient.

Recommendation

The reported ADR is a spontaneous report revealed by the patient. Spontaneous reporting is basically the reporting of a suspected ADR on the initiative of the health professional, who becomes aware of the problem, or on the patient's initiative[7]. The spontaneous reporting system is especially helpful in the detection of adverse reactions that are specific or occur in a suggestive time-relationship with drug use[1]. In the discussed case report, occurrence of ADR and its time relationship with the administration of the drug NK in empty stomach was detected.Indicators of inappropriate drug use also can be obtained from spontaneous reports of ADR[1]. The reported ADR to NK indicates glaucoma patients as an "at-risk group" for the drug.

Although spontaneous reporting is the mainstay of passive surveillance, the information obtained is inherently limited and likely to be insufficient for regulatory and clinical decisions[1]. However, since glaucoma is the second leading cause of blindness worldwide[8], the suspected ADR to NK on increasing the intraocular pressure in a glaucoma patient, may be communicated to all the health professionals involved in the use/distribution of NK to make them cautious on administering NK in glaucoma patients and also to involve them in active surveillance of NK for addressing more safety concerns.

Conclusion

The discussed case report might be the first reported ADR to the poly-herbal formulation NK. In this case, NK is the probable cause for the unusual raise in intraocular pressure in the glaucoma patient. The reported ADR to NK indicates glaucoma patients as an "at-risk group" for the drug; it also stresses the need for more active surveillance on NK by healthcare professionals foran improved understanding of the medicine.

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