Dry eye Disease During COVID-19 : Need for Investment Into Research to Develop Solutions?

Komal Shah[1], Deepika Singhal[2], Ashka Patel[3], Binita Gadhavi[4], Jay Karan[5], Abhay Gaidhane[6], Deepak B Saxena[7]

[1]Assistant Professor, Indian Institute of Public Health, Gandhinagar, Gujrat, [2]Professor and Head, Department of Ophthalmology, [3]Junior Resident, Department of Ophthalmology,[4]Senior Resident, Department of Ophthalmology, GMERS Medical College and Hospital, Sola, Ahmedabad, [5]Associate Professor, All India Institute of Medical Sciences, Jodhpur, [6]Professor, Department of Community Medicine, Director, School of Epidemiology and Public Health, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, [7]Professor, Indian Institute of Public Health Gandhinagar, Adjunct Faculty Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical, Sciences, Sawangi (M), Wardha.

Abstract

Purpose: To review the Clinical Trial Registry of India (CTRI) for clinical trials registered for the interventions for the treatment of dry eye disease.

Methods: CTRI was manually searched by using the different key words related to the dry eye. Trials registered after 2009 were included in the analysis. All the parameters like type of interventions, phase of trial, sample size etc of the each trial were extracted in the predesigned proforma. Descriptive statistics was reported in the form of frequency and percentages.

Results: Total 35 trials were registered since 2010. Majority were phase 4 trials (Post Marketing Surveillance). More than half of the registered trials were related to the ayurvedic products. Most frequent allopathic intervention was lubricant and most frequently used comparator was Carboxy Methyl Cellulose. Range of sample size in different trials was 30-300.

Conclusion: A good number of trials related to the ayurvedic drugs are registered for dry eye. There is a need for similar research efforts for allopathic interventions.

Key words: *COVID-19 , Dry Eye Disease, Research*

Introduction

Coronavirus disease (COVID-19) emerged in December 2019 in China and became pandemic situation worldwide within no time. COVID-19 pandemic has affected more than 215 countries across the globe and many of these countries faced a complete lockdown[1,2]. Various sectors including routine on job work , academic teaching, field work has come to an stand still due rapid and complete shutdown of all activities [3]. This had led to increase in scree time and potentially might cascade to outbreak of Dry eye disease.

Dry Eye Disease (DED), as the nomenclature suggests is a condition characterized by dryness of eyes that may lead to tear film instability, hyperosmolarity, chronic inflammation and neurosensory abnormalities ultimately causing damage to ocular surface [4]. In contrast to earlier belief, the disease is no longer limited to old age population and has started precipitating in

Corresponding Author:
Deepak B Saxena
Professor, Indian Institute of Public Health Gandhinagar Adjunct Faculty Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha.
Email: ddeepak72@iiphg.org

early life years of an individual [5]. Premature occurrence of DED is often associated with compromised quality of life. In India the reported prevalence of DED ranges from 5 to 35% and is often influence by environmental conditions, life style factors and geographic locations [6, 7]. However, there may be substantial gap in terms of claimed prevalence of the condition as significant heterogeneity exist between the methods of diagnosis and there may be an underestimation of the disease due to undiagnosed asymptomatic patients [8]. This is partly contributed by the complex and unknown pathophysiology and epidemiology of the disease, subjective symptoms and poor correlation between the discomfort experienced by the patients with the objective clinical scales [9]. Mores with pandemic of COVID-19, this constantly evolving definition of the disease might become a public health challenge with reference to its classification, its management and relevance to local context.

With this complex nature of the disease and associated clinical burden, periodic update of the treatment strategies are essential. In last decade several newer treatment agents have emerged with promising results globally [10]. However, the landscape assessment of the trials registered from developing countries especially India has not been undertaken yet. Clinical trials forms the main source of evidence-based medicine and hence the backbone of clinical practice. With increase in screen time and possible outbreak of DED, present paper aims to provide a recent update on the clinical trials registered from India to address DED during last decade to understand if there is any need to foster the research on DED.

Methods

We accessed the clinical trial registry (http://ctri.nic.in/Clinicaltrials/login.php-last access on February 2020) using the search terms “dry eye” or “ocular surface”. The present communication is limited to trials registered after 2009 and investigating the effect of drugs on DED only. The trials studying effect of surgical or any other intervention were excluded from the review.

Results

A total of thirty-five trials were registered since the year 2010 and were at different stages of development (table 1). Majority (28%) of the trials were at post marketing surveillance phase (phase 4) and Efficacy trials phase 2 (28%). Very few registered trials were in Efficacy (phase 1) and Multi-centric efficacy phase (phase 3). Though the number of registered interventions for treating DED from India were substantial and comparable with global trends, majority of the trials assessed efficacy of Ayurvedic formulations (66%) (Table 2). Twelve trials (34%) were clinical drug trials where the most frequent category was involving lubricants. It was also observed that around 17% registered ayurvedic formulation trials were retrospective in nature. The sample size in individual trial ranged from 30 to 300. Eight of the registered trials have used Carboxy Methyl Cellulose as comparator , while 10 trials had no drug as comparator.

Table 1 : Overview of the Clinical trials addressing Dry eye disease

Total number of registered drug trials during 2010-2019	35
Range of sample size	30-300
Phases of trials	
Phase I Phase II Phase III Phase IV Others	2 (6%) 10 (28%) 2 (6%) 10 (28%) 5 (14%)
Retrospectively registered trials	6 (17%)
Synthetic drugs trials	12 (34%)
Ayurvedic drug trials	23 (66%)

Discussion

This study was designed with the aim of evaluating different clinical trials registered in Clinical Trials Registry of India (CTRI). Present evidence synthesis clearly indicates that reasonably good amount of clinical studies are initiated by Indian investigators and also registered to address DED. The review suggests an increasing interest of the Ayurvedic preparation for Dry Eye. India is recognised hub for use of ayurvedic medications with apparently broad spectrum of therapeutic potencies, similar registered trails with Ayurvedic formulations is an expected finding [11,12,13]. It also suggest that researchers are looking forward to evaluate age old ayurvedic formulations through well designed, rigorous clinical trial methodologies[14,15]. With an increasing penetration of mobiles, net and digital innovations, DED needs to be considered as a serious challenge for ophthalmic morbidity[16,17]. There is also urgent need for an advocacy effort towards willingness of the policy makers, clinicians and researchers to identify DED as a public health threat. Lastly a careful follow up for disseminations of these trial results culminating into scientific publication should also be advocated to substantiate findings further. Post COVID-19 pandemic and increased screen time as new normal, there is need to foster and invest into research for novel molecules as DED might create a big potential market looking for need of solutions.

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Ethical Approval: Obtained from Institutional Ethical Committee, DMIMS, Wardha

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