A REVIEW

Biosensors: The advanced molecular probes - A meta-analysis over a decade
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Abstract

Aim of the Study: To statistically demonstrate the enhanced specificity and sensitivity of Biosensors over other comparative investigative procedures for detection of oral pre-cancer over a decade.

Materials and Methods: Study sample included a review of research articles, based on databases from the Cochrane collaboration having a definite randomized control trial, on various investigative procedures for oral pre-cancer lesions and conditions and oral cancer itself over the past decade. This included literature on toluidine blue, Lugol’s iodine, Vizilite, Velscope, Colposcopy, and Biosensors - The mainstay of the intended study. The literature was assessed, analyzed, and studied; the comparison was made based on the various P values between various techniques on one side and biosensors on the other in terms of sensitivity and specificity. A meta-analysis of all the modalities including the above-mentioned parameters was carried out and advantages and disadvantages documented and compared with those of Biosensors to demonstrate the title of the study.

Result: Compared to the 100% sensitivity and specificity of biosensors, the sensitivity, and specificity of vital staining techniques were found to be, respectively, 95% and 81%, whereas the sensitivity and specificity of visual aids were found to be, respectively, 86% and 78%.

Conclusion: Biosensors definitely came up as the best diagnostic aids and investigative procedures at hand compared to all others existing or tried so far.

Keywords:
Biosensors, meta-analysis, randomized control trials, sensitivity, specificity

Introduction

Oral cancers, as all of us are aware are one of the most dreadful significant human maladies in our history. The alarming epidemiological data of various cancers of the human body, including the oral cancers ranking 6th among all, have been disheartening in the literature existing so far. It is estimated that there are almost three lakh cases of oral cancer reported worldwide in literature to claim numerous lives annually.[1,2] This malady has been an enigma not only to the patient but also the professional (oral surgeon and oncologist) because cancer is not a disease of a patient alone, but an entire family (physically, psychologically, and socioeconomically).[3-6]

Presently, cancers are being diagnosed very late usually at the untreatable stages, thereby increasing the morbidity and mortality rates and bringing down the survival rate drastically.[5,7] Hence, in the present scenario, an onus for early diagnosis probably at the molecular or biomolecular level before the genotypic conversion takes place, lays the preamble for combating this deadly disease.

The complexity and diversity of cancer etiology and various investigative procedure have posed many hurdles in meeting the challenge of early diagnoses of cancer thereby to improve the prognosis.[9,11] Among the many early diagnostic tools for the same, a newer biosensor technology has shown the potential to provide fast and accurate results in picking up these gene-conversions at the molecular level thus enhancing the prognostic outcome. It has claimed a sensitivity and specificity of 100%.[1,4,6,7]

Hence, the present study aims to evaluate the literature for various investigative procedures, to compare their efficacy (dependent on P values) in terms of specificity and sensitivity index, through a meta-analysis with those of biosensors, thus evaluating whether “Biosensors” are indeed a new wave in early stage cancer diagnostics, which could definitely herald a new era in the field of oral oncology diagnosis and treatment planning.[12-14]
Materials and Methods

Various researches and studies have documented that the Biosensors to be 100% sensitive and specific. With this fact in mind, a literature-based meta-analysis was carried out to fulfill the aim of this study. With the Cochrane collaboration taken as a source for authenticated scientific research data, 188 articles were selected having undergone a randomized control trial. Out of these, the articles were screened, and finally, 88 articles were selected which met the criterion for meta-analysis. There were three groups which were included in our study, viz.;

Group-1: Biosensors
Group-2: Vital staining techniques (Lugol’s iodine, toluidine blue, etc.)
Group-3: Visual AIDS (Colposcopy, Vizilite, etc.)

Group-1: Diagnostic kit and the mode of working of biosensors

The kit consists of silicon or a photonic crystal mounted on a glass slide [Figure 1]. The preamble lies in the detection of biomolecules such as the proteins. A drop of blood is pooled onto the silicon or photonic crystal following which the protein content of the blood is extracted and gets bound to the antibody dot present on the crystals thus exposing the entire panel of proteins on the screen. Then, the proteins pertaining to oral cancer (interleukin-8, alpha-fetoproteins) are segregated or sorted out and then a chemical solution with a fluorescent tag is added to it. If the protein contains antibodies, it will fluoresce on the application of light amplification by stimulated emission thus demonstrating the presence of dysplasia or malignancy in the body. This procedure claims 100% sensitivity because these biomolecules of oncoproteins can be picked up very early in the processes of oncogenesis.

Group-2: Vital staining techniques

These are the metachromatic vital dyes which bind to the tissues with rapid cell division and to the areas with DNA changes. This binding leads to the staining of those tissues which are abnormal in comparison to the surrounding normal tissues. As molecular and genetic analyzes are not carried out routinely, biopsies are the investigative modalities of choice having a characteristic feature of highlighting the mucosal lesions, thus assisting the physicians in better analyzing the surgical margins.

Graph-3: Visual AIDS

Various visualization modalities are being made into use as adjuncts to the normal routine visual and tactile oral examination. It is normally believed that the tissues undergoing abnormal metabolic and structural changes having varying absorbance and reflectance scales when exposed to different forms of energy and light. When acetic acid is applied to the sites of epithelial proliferation where the nuclear structures are altered, these sites reflect low energy blue-white light emitted with the generation of acetowhite changes. This indicates the dysplastic changes in that particular site.

Meta-analysis was performed using well-defined specific software, the one used in this study was comprehensive meta-analysis VS software.

Results

Meta-analysis is a technique of combining the results of many studies in a rigorous and systemic manner to allow us to better assess the prevalence rates of different types of gambling and determine which intervention has the best evidence regarding its effectiveness. A meta-analysis of all the modalities including the above-mentioned parameters was carried out, and advantages and disadvantages were documented and compared with those of Biosensors to demonstrate the title of the study. The sensitivity [Graph 1]
and specificity [Graph 2] of the vital staining techniques were statistically found to be 95% and 81%, respectively, whereas the sensitivity [Graph 3] and specificity [Graph 4] of the visual aids were found to be 86% and 83%, respectively. Finally, when all the three groups of the study were taken into consideration together, Biosensors proved to be the best among all with 100% sensitivity [Graph 5] and specificity [Graph 6] followed by the vital staining techniques and then the visual aids as diagnostic modalities for early detection of pre-cancer and cancer.

The meta-analysis graphical representations are depicted after the reference section later in this article.

**Discussion**

Biosensors work on the principle that the tumors or the cancerous cells elaborate specific oncoproteins which can circulate through the bloodstream and can be picked up even at minute concentrations. These oncoproteins are characteristic and are called BIOSENSORS. Biosensor devices are specially designed to detect biological entities by converting biomolecular signals into electrical signals which are further analyzed. This technology has the potential to provide fast and accurate detection which are reliable in, imaging of cancerous cells, monitoring angiogenesis and cancer metastasis.

Staining techniques and other visual aids have been used routinely as early diagnostic tools to pick up potentially malignant disorders. The concept and technology are based on genetic and morphological changes, i.e., changes which have already caused oncoconversion.

Therefore, the difference between the above three groups is that the Biosensors pick up early biochemical oncoconversions, whereas other two groups pick up functional and morphological conversions. In terms of oncoconversions, biosensors prove to
be the most significant of all and the same has been proven by our meta-analysis results.

**Conclusion**

The development of biosensors is probably one of the most promising ways to solve some of the problems concerning the increasing need to develop highly sensitive, fast, and economic methods of analysis in the early detection of cancers. In this regard, biosensors come up as the best weapons of choice in the future of the fight against oral cancers.

**References**
