SPIROMETRY FOR SCREENING ELIGIBILITY E-CIGARETTE STUDIES; IS IT USEFUL OR NOT?

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Background: Emerging claims with regards to electronic cigarette's (e-cigarette) usefulness to defer COPD (chronic obstructive pulmonary disease) and other smoking related diseases has launched a wave of clinical research. The basis of this increase in e-cigarette research is the hypothesis that the diminished combustion of product (i.e., smoke) is considered one of the key factors on which e-cigarette producers claim pulmonary improvement with their use.

In the clinic, spirometry has become the dominant and only tool for viably accessing pulmonary function critical to understanding whether this new form of smoking is truly less harmful to the lungs or not. As part of controlled clinical research, the initial need is to eliminate subjects who already have severe or advanced lung disease. This exclusion ensures that the study endpoint outcome of "switchability" to an e-cigarette is not unduly impacted by the inclusion of subjects with advanced pulmonary small airway destruction. Thus, spirometry has become the mainstay for evaluating any lung physiological damage or improvements in clinical studies which evaluate the benefits of changing product types.

Method: Screening was performed on subjects for potentially enrolling in clinical research trials. The Flow-to-Volume curves (FVC) are the most commonly used index with their predictive values included in screening activities. FVC, FEV1 and FEV1/FVC ratios are the first assessments for eligibility and may rule out reversible airway disease as well as obstructive patterns by evaluation of pre- and post-bronchodilator measurements. Exclusion criteria in the pre-bronchodilator was FEV1/FVC ratio <0.7 and FEV1 <50% in one study for subjects with a longer history of smoking; whereas, in another study with a higher number of younger smokers the same FEV1/FVC ratio of <0.7 is used but with a more restrictive FEV1 <80%. All included a post-bronchodilator FEV1/FVC ratio < 0.75 and the FEV1 increases no more than 12% or 200 ml.

Results: In two ongoing studies, all of which had rigorous phone pre-screening requirements, failure rates have been low in these asymptomatic smokers, yet several subjects were still found to have airway disease that would have significantly altered the data outcome. In the one study requiring an FEV1 not <50%; there were 150 subjects screened, 89 failures for other reasons and another 8 spirometry failure subjects with advancing COPD. In the second more restrictive study for younger smoking age participants, there was an FEV1 requirement not <80%; with 94 screened, 37 failures for other reasons and still 4 spirometry failures, 2 of which had reversible airway disease, the other 2 with advancing COPD. While literature review does not indicated significant changes in FEV1, FVC or the FEV1/FVC ratio in smokers who have switched to e-cigarettes or quit, the FEF25-75% has shown to be a good biomarker for steady improvement over time, and may be the indicator of choice to follow as it defines small airway disease and its changes.

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Conclusion: Obstructive lung disease indicates a loss of elastic recoil and airway radial support resulting in pressure dependent collapse. The FEF25-75% with its indication of this small airway disease may be the best indicator of improvement in response to any treatment option; be that bronchodilators, smoking cessation or possibly switching to e-cigarettes. The change to e-cigarettes would not necessarily affect any benefit or measurable pulmonary function in those subjects suffering from irreversible airway disease; still, its use is clear in screening and measuring outcomes in clinical trials for smokers with limited disease state.

Spirometry is a useful tool in clinical research as a rapid functional test requiring modest operator experience; in return subjects with obstructive lung disease and even those with reversible airway patterns are eliminated from study inclusion which could potentially bias study conclusions.

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