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Research article

Development of Nasopharyngeal Secretion Collection Tool

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Abstract

Objective: To develop a device for collecting nasopharyngeal secretions and to test its effectiveness in laboratory. **Methods:** This research and development created prototype tool for collecting nasopharyngeal secretions through stakeholder brainstorming, and tool design and fabrication. Subsequently, the prototype was tested in laboratory for its efficacy and safety using a medical manikin model. **Result:** The developed apparatus was suitable for collecting nasopharyngeal secretions because it allowed access to nasopharynx, provided clear visualization of where the sample should be taken, and used suction with low pressure rather than swabbing. The instrument was tested for 1,000 times and was able to reach the nasopharynx region without touching the surrounding tissues. The apparatus had a 96.09% efficacy index with no evidence of apparatus penetration to surrounding area. **Conclusion**: Laboratory testing of the developed prototype is promising. The prototype could be further tested for its effectiveness and safety.

Keywords: collecting tube, COVID-19, nasal swab, secretion, screening test

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บทความวิจัย

การพัฒนาเครื่องมือเก็บสารคัดหลั่งจากโพรงจมูก

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บทคัดย่อ

วัตถุประสงค์: เพื่อพัฒนาอุปกรณ์สำหรับเก็บสารคัดหลั่งจากโพรงจมูกและทดสอบประสิทธิภาพของเครื่องมือในห้องปฏิบัติการ **วิธีการ:** การวิจัยและพัฒนานี้ได้สร้างเครื่องมือต้นแบบสำหรับการรวบรวมสารคัดหลั่งจากโพรงจมูกผ่านการระดมสมองของผู้มีส่วนได้ส่วนเสีย และการออกแบบและการผลิตเครื่องมือ ต่อจากนั้น ต้นแบบได้รับการทดสอบในห้องปฏิบัติการเพื่อประเมินประสิทธิภาพและความปลอดภัยโดยใช้หุ่นจำลอง **ผลการวิจัย:** เครื่องมือที่พัฒนาขึ้นนี้เหมาะสำหรับการรวบรวมสารคัดหลั่งจากช่องจมูก เนื่องจากทำให้เข้าถึงช่องจมูกได้ ทำให้เห็นได้ชัดเจนถึงตำแหน่งที่ควรเก็บตัวอย่าง และใช้การดูดด้วยแรงดันต่ำแทนการดูดซับในการเก็บตัวอย่าง เครื่องมือนี้ได้รับการทดสอบ 1,000 ครั้ง และพบว่าสามารถเข้าถึงบริเวณช่องจมูกโดยไม่ต้องสัมผัสเนื้อเยื่อรอบข้าง เครื่องมือมีดัชนีประสิทธิภาพร้อยละ 96.09 โดยไม่มีหลักฐานว่า อุปกรณ์เจาะทะลุไปยังบริเวณโดยรอบ **สรุป:** ผลการทดสอบในห้องปฏิบัติการของต้นแบบที่พัฒนาขึ้นนั้นมีแนวโน้มดี ดังนั้น สามารถนำต้นแบบไปทดสอบเพิ่มเติมในเรื่องประสิทธิภาพและความปลอดภัย

คำสำคัญ: หลอดเก็บสิ่งส่งตรวจ โควิด-19 ที่เก็บตัวอย่างจากจมูก สารคัดหลั่ง การตรวจคัดกรอง

Introduction

Nasopharyngeal secretions are collected for a variety of reasons, including disease diagnosis, microbial detection, allergen detection, and physiological examination of the nasopharynx and nasal cavity. (1-5) Currently, the collection of secretions in the nasal cavity plays a greater role in screening potential COVID-19 carriers during this pandemic. As a result, the antigen detection test performed with an antigen detection test kit (ATK) is widely used in early detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. (6-10)

Thai government, through the Ministry of Public Health, has recommended those exposed to or suspected of being exposed to the COVID-19 virus to conduct self-testing using ATK. (11) ATKs available in Thailand involve three distinct methods of secretion collection including nasal swab, nasopharyngeal swab, and saliva collection. (12)

Medical evidence indicates that tests with nasopharyngeal secretions have higher sensitivity in detecting SARS-CoV-2 infection, produce fewer false positive or negative results, and require fewer secretions than nasal swab and saliva specimens. (13-18) However, existing tools and collection methods, particularly nasopharyngeal swab, have limitation on effectiveness and may cause harm to the patient. (12) A cotton-tip swab with a long wooden or plastic handle

is mainly used to collect the specimen from nasopharyngeal area. The swab-tip is inserted into the nasal canal until it reaches the back of the nasopharynx. In terms of efficiency, although it is readily available and affordable, the swab-tips may rub against the nasal turbinates, resulting in an insufficient amount of secretions collected on the swab for examination. In terms of safety, any contact of the swab-tip to any part of the nasopharyngeal cavity may result in injury or inflammation, and in severe cases, may penetrate to the brain. This could lead to severe damage of tissue that is difficult to assess. (Figure 1) Therefore, an effective device for collecting nasopharyngeal secretion that is highly safe or non-invasive and capable of collecting enough secretions for examination is necessary.

Technology has advanced significantly in recent years, particularly in electronics and internet of things (IoT). (19,20) These technological advancements can be used to develop new medical innovations such as a nasopharyngeal secretion collection tool. Research question of this study was "What device is best for collecting nasopharyngeal secretions with high efficiency and safety?" the objectives of the study were 1) To design and fabricate an apparatus for collecting nasopharyngeal secretions, and 2) To evaluate effectiveness and safety of the newly developed instrument in laboratory.

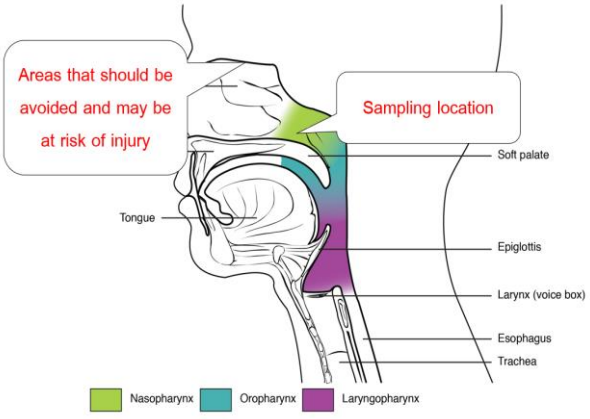

Figure 1. Anatomical structure of the nasopharyngeal cavity illustrating the optimal sampling location and areas that should be avoided to prevent tissue injury

Methods

The study consisted of three major phases including brainstorming among experts, product design and development, and laboratory testing. This study did not involve human subjects or animals, and was exempted for ethical consideration by the Naresuan University Institutional Review Board.

Brainstorming

The stakeholders participating in brainstorming to generate ideas on characteristics of ideal tools for nasopharyngeal secretion collection, included medical experts and product design specialists. Medical experts consisted of one otorhinolaryngologist, one anesthesiologist one pediatric pulmonologist and one pharmacist specializing in otolaryngology and larynx, with extensive experience on nasopharyngeal secretion collection or had been swabbed in the nasopharyngeal cavity. Product design specialists included one product designer and one mechanical engineer.

Brainstorming was conducted separately in each group of experts to ensure independent ideas were formed. The session took approximately 30-45 minutes and ended once the information was saturated. The following questions were presented in the brainstorming session: "What factors do you think contribute to the effectiveness of SARS-CoV-2 detection?" and "If you want to develop a tool to collect nasopharyngeal secretions, what features should it have and why?" During the brainstorming process, recall bias was minimized by asking the participants to recall the most recent experiences on nasopharyngeal secretion collection.

Each group of participants was responsible for distinct objectives. Medical experts emphasized on the objective on developing a tool with unique characteristics and achievable capabilities. They needed to decide where the secretions should be stored while considering the importance of efficacy and safety during secretion collection. Product designer group determined the tool's characteristics and mechanism of

operation, which must be compatible with the results from medical experts' brainstorming and must be economically viable for further development and commercialization.

Information and measurement bias were reduced by recording and transcribing the discourse during brainstorming. Misclassification bias was minimized by asking each stakeholder examine the results from brainstorming as concluded by the researchers

Product design and development

Product designers and mechanical engineers conceptualized product specifications and established the working principle of the tool. Subsequently, they fabricated tools using materials that are safe for human tissue and having appropriate size to access the region for specimen collection. The device and fabrication process integrated industry-standard materials that are used in invasive medical devices and allowed mechanical and electronic experts to monitor and control each stage of the fabrication process.

Laboratory tests

Laboratory tests consist of performance testing and safety evaluation as follows:

Performance testing: The study employed a model replicating physical features of the human anatomy and was positioned for swabbing simulation to obtain secretions in the nasopharyngeal cavity. (Figure 2).

The developed prototype tool was tested for 1,000 replications in collecting secretions from a predetermined location behind the nasopharyngeal area, as determined by otolaryngologists. (Figure 2) The study calculated the volume of secretions collected and compared it with the volume of secretions instilled to the area by the researchers. The volume was measured with a single channel micropipette with a measuring tube size of 0.5-10µl. The tool was considered effective if the amount of secretions collected was sufficient for laboratory testing for SARS-CoV-2.

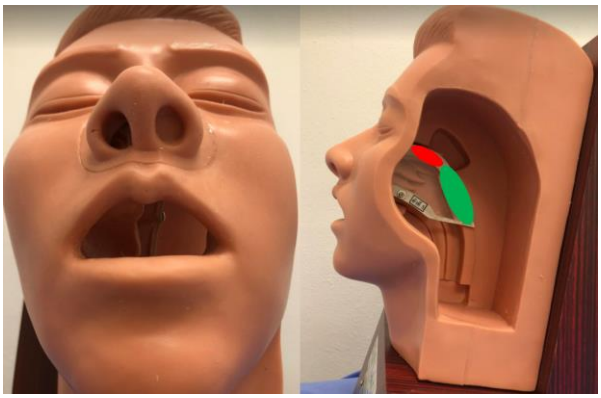

Figure 2. Medical model used in the efficacy testing procedure.

Note: Green area indicates the ideal location for collecting the specimens at the nasopharynx, while red area indicates an area potentially dangerous if contacted with any device

Safety test: One of the researchers observed, through the monitor during 1,000 times of performance testing, whether the tool contact with any area in the nasopharyngeal cavity that might cause injury. The tool was regarded as safe if it did not touch any area in the nasopharyngeal cavity that might cause injury.

Statistical analysis

Opinions from brainstorming session were organized and described into relevant information by a Thai language expert. Subsequently, the information obtained was conveyed to the designer of the tool. The volume of secretions collected was compared to that previously instilled into the model using t-test statistics. The instrument efficiency index was calculated using the formula: efficiency = secretion volume collected x 100 / secretion volume instilled into nasopharyngeal area. Proportion of tests with tool contacting with any areas in the nasopharyngeal cavity that might cause injury was employed as safety indicator.

Results

Features and functions of the tool

Three specific features and functions of the tools were derived from the study. First, the device

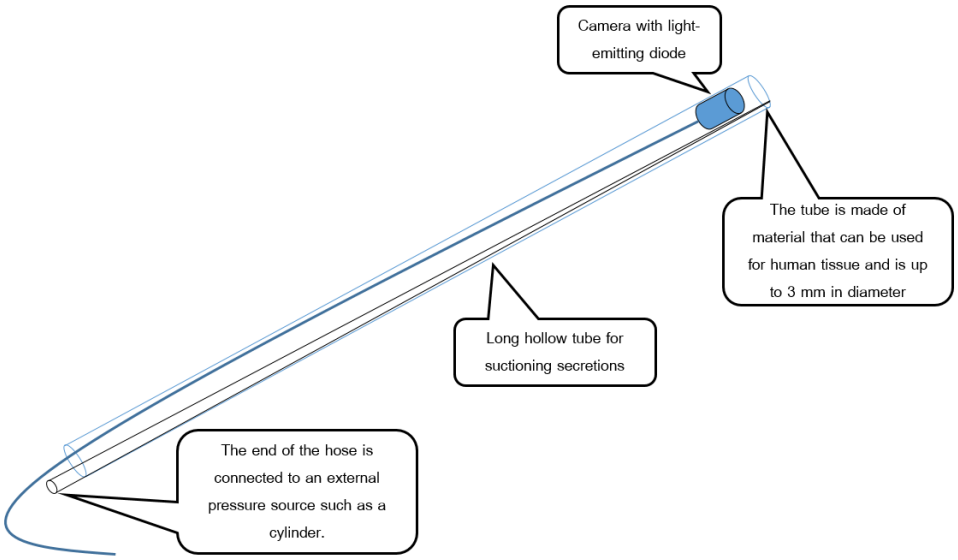

Figure 3. A prototype apparatus for collecting nasopharyngeal secretions.

Note: A signal cable is included to connect to the electronic device and provide a clearer view of the location for specimen collection. The end of the secretion suction hose is open-ended to connect to a pressure source.

should be made of small, soft and flexible material to ensure that the instrument does not cause pain when inserted into the nasal or nasopharyngeal cavity. Secondly, the tool could be inserted into the nasal cavity until the nasopharyngeal area is reached. Lastly, location for specimen collection should be visible and clearly displayed on any devices, such as a mobile phone, TV or computer, allowing individuals to perform the secretion collection by their own.

Specifications of the tool

The designed apparatus is cylindrical in shape, 8 cm. in length and 2-3 mm.in diameter. It is equipped with a camera, a light source, and a tube to collect the secretions. Volume of the tube equals to the cylinder's height x π x radius^2 (8 cm. x 3.14 x (0.3 cm.)^2 = 2.26 cm^3). External suction pressure is applied via the cylinder connection. (Figure 3)

Results from laboratory test

The apparatus was positioned in the nasopharyngeal cavity to allow visual observation of the simulated secretion sample during the 1,000 test repetitions. (Figure 4) Mean volume of secretions collected was 2.21±0.11 cm^3 or 96.09% of the volume of secretion instilled into the model (2.30 cm^3). Statistical test of the mean and instilled volume showed no significant differences. No contact of the tool to any surrounding tissues inside the nasal cavity was detected during the 1,000 test repetitions.

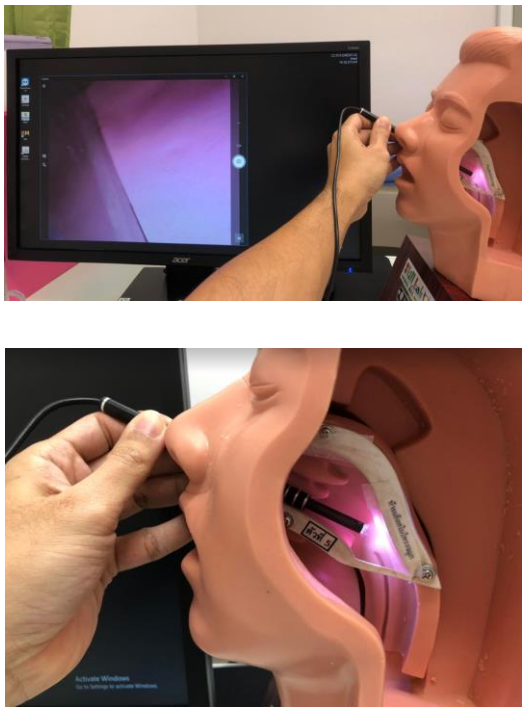

Figure 4. Illustration of a simulated secretion collection using the prototype instrument.

Discussion

Laboratory testing showed the reliability of the instruments to collect adequate specimens for testing, particularly those from nasopharynx, which is difficult to access and prone to cause tissue injury during the procedures. (1,2) Several studies revealed that ATK testing is an effective pre-screening tool prior to conducting confirmatory real-time polymerase chain reaction (RT-PCR) testing, which is the gold standard for diagnosing COVID-19. 3-8. Moreover, ATKs are readily available and inexpensive as compared to RT-PCR test, which is costly and conducted only in hospitals or laboratory facilities.

ATK testing has several limitations, particularly in terms of the result interpretation. A clinical study comparing test results of various brands of ATK to those of RT-PCR testing discovered that some brands produced inconsistent results, including false positives and negatives. (10,13) Numerous studies revealed discrepancies in results when secretions from nasopharynx, nasal cavity, and saliva were used, and these studies concluded that secretions from the nasopharyngeal cavity had the most consistent results with those from RT-PCR examination. (13-18)

In Thailand, there are no known brands of ATK that have been certified by Thai Food and Drug Administration that test nasopharyngeal secretions (Table 1). The situation prompted the proponents of this research to devise a prototype tool. (12) ATK is not the standard test for detecting the infection due to unreliable source of secretion which does not yield accurate results compared to those of RT-PCR that uses secretions from nasopharynx.

Table 1. Comparison of specific brands of ATK approved by Food and Drug Administration of Thailand (12)

	Brand and manufacturer	secretions used/equipment used to collect specimens
1.	standard Q COVID-19 Ag home test, SD Biosensor Inc. ,Korea.	nasal swab/ long cotton swab
2.	SARS-CoV-2 antigen self test nasal, SD Biosensor Inc., Korea.	nasal swab/ long cotton swab
3.	SARS-CoV-2 antigen rapid test kit (colloidal gold immunochromatography), Beijing Lepu Medical Technology Co., Ltd., P.R. China	nasal swab/ long cotton swab
4.	SARS-CoV-2 antigen test kit (GICA), Shenzhen Kisshealth Biotechnology Co., Ltd, P.R. China	nasal swab/ saliva/ long cotton swab
5.	Biosynex autotest antigenique COVID-19 Ag, Biosynex Swiss SA, Switzerland	nasal swab/ long cotton swab
6.	Panbio COVID-19 antigen self-test, Abbott Diagnostics, Korea Inc., Korea	nasal swab/ long cotton swab
7.	AnyLab COVID-19 Ag test kit, Z Biotech Inc., Korea	nasal swab/ long cotton swab
8.	PCL COVID19 Ag gold, PCL, Inc., Korea	nasal swab/ saliva/ long cotton swab
9.	SARS-CoV-2 antigen rapid test, ACRO BIOTECH, Inc., USA	nasal swab/ long cotton swab

Note: The table contains data on only 95 certified species. No ATK brands use specimens collected from nasopharynx (as of November 2, 2021).

The study developed the promising prototype for an effective and safe collection of nasopharyngeal secretions. In future research, the device should be tested on human subjects together with a variety of ATK brands to demonstrate that 1) Is nasopharynx the optimal location for specimen collection; and 2) which ATK brands produce results comparable to that from RT-PCR when nasopharyngeal secretions are used.

The strength of this research stems from real-world research questions and the integration of design techniques and technology that controls only the components that are required. This enables fabrication of tools to be as inexpensive as possible and increases likelihood of commercialization. Moreover, the tool is extremely safe because nasal and nasopharyngeal cavities are always visible through the camera during the specimen collection. This features significantly reduce the risk of damaging the surrounding tissues.

This study is subject to some limitations. First, the newly developed tool may cause irritation that may induce sneezing or coughing resulting in aerosols that potentially infect the medical personnel performing secretion collection. Second, the developed instruments are still prototypes and have only been subjected to preliminary laboratory testing. In the future, this medical device will be subjected to industry-standard testing and research on healthy volunteers prior to being used on actual patients.

Conclusion

The prototype device developed in this research has been proven in preliminary laboratory testing to be safe and effective in collecting secretions from nasopharyngeal region. The tools should be further tested for its effectiveness and safety.

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