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Translational Healthcare Can Prevent Ambulatory Diagnostic Failures

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Abstract

Translational medicine, viz. translational healthcare, aims to obtain the best evidence base for improving the health of individuals and to utilize it in specific clinical settings in the community for diagnosis, intervention, policies and education. Diagnostic failures comprise a significant and costly fraction of all healthcare failures in the U.S. and globally with devastating consequences for all stakeholders. One timely and critical question for the continued evolution and establishment of translational healthcare nationally and internationally relates to the role translational healthcare can play in preventing diagnostic failures. Here, we present two clinical situations in dentistry, which have profound and significant systemic sequelae, to exemplify the extent to which the clinical dental sciences are intertwined with the clinical medical sciences. In one case (Ludwig angina cellulitis), the best evidence base obtained through translational effectiveness is discussed as key to preventing diagnostic failures; in the other (disorders of the temporomandibular joint), translational research holds promise as the critical factor in preventing diagnostic failures. Taken together, the case is made that preventable adverse events in healthcare do occur, among which failed diagnoses and misdiagnoses, which can cause serious bodily and financial harm to the patients and stakeholders. Research tools proffered by translational healthcare, if judiciously utilized in the context of GRADE and DECIDE, can serve to prevent ambulatory diagnostic failures. Operationally, we propose that the role of translational healthcare in preventing diagnostic failures must be articulated along the three distinct inter-related domains of (1) engagement of the stakeholders, (2) dissemination and (3) increased health literacy of the best evidence base.

Keywords: Translational science in medicine and healthcare; Diagnostic failures in ambulatory healthcare; Ludwig angina cellulitis; Temporomandibular joint disorders; GRADE and DECIDE for evidence-based decisions; Health literacy; Stakeholders; Tele-healthcare

Introduction

Translational medicine improves the health of individuals and the community by "translating" the Best Evidence Base (BEB) into diagnostic tools, medicines, procedures, policies and education. The Institute of Medicine's Clinical Research Roundtable has identified a translational block (TB1) for obtaining and testing basic research findings in a clinical setting, and another translational block (TB2) for utilizing the best evidence base for interventions in standard clinical practice. The National Institutes of Health characterized translational research in medicine, and healthcare in general, as the process of going from the patient to the research bench, and back to the patient. In a similar vein, the Agency for Healthcare Research and Quality defined the process of translational effectiveness as obtaining and utilizing BEB in specific clinical settings. Translational research and effectiveness represent two distinct facets of one and the same construct of translational science, which begins with, is sustained by and ultimately defines and characterizes the patient-clinician encounter. Modern contemporary healthcare is patient-centered, effectiveness-focused and evidence-based, and by necessity and definition translational in nature. Translational science in healthcare, and specifically translational medicine, is now best defined and characterized as a four -tier process simply rendered as: (1) Tier one (T1 = translational phase 1) initiates TB1, the process from the patient-clinician encounter to the bench to the patient to the community of stakeholders, and usually requires preclinical studies from participant observations and case control studies, to *in vitro* and animal experiments, and observational cross-sectional and cohort studies to eventually phase 0, 1 and 2 clinical trials; (2) T2 expands the discovery phase by means of study designs with larger patient populations, such as cohort observational and phase 3 and 4 clinical trials, observational studies; (3) T3 launches TB2, the translational effectiveness-oriented stage of the process, and seeks to establish whether or not certain treatments or practices works in specific clinical settings and (4) T4 identifies and characterizes the optimal existing standard operating procedures, viz., the best practices for reaching clinicians, patients and all stakeholders with a nationwide policy concerning treatment X or strategy Y - that is to say, of translating BEB on treatment X or strategy Y into widely disseminated evidence-based revisions of clinical practice guidelines, while optimizing stakeholder health literacy and engagement [1,2].

One important question for translational medicine relates to what role translational research and translational effectiveness play preventing diagnostic failures. A number of studies going back to the early 1990's support the claim that diagnostic failure comprises a significant and costly fraction of all medical failures and have devastating consequences for patients, families, and health care professionals. The prevalence of ambulatory diagnostic failure is difficult to determine for many reasons, including varying definitions and study methods with their strengths and weaknesses, and variations in problem manifestations of selected diseases across patients and time. The level of coordinated diagnostic activity across multiple episodes of care, and the delayed consequences of upstream diagnostic failures on downstream patient outcomes are complicating factors. On average, estimates suggest that diagnosis is wrong in up to 20% of the cases – one in five! – and perhaps higher in certain specialty areas. Diagnostic errors may affect as many as 12 million U.S. adults every year, with serious potentially harmful and costly consequences. Global estimates are even more staggering. Diagnostic failures delay appropriate treatment, lead to disability, and can be ultimately fatal. They carry an unavoidable high financial cost-burden for healthcare organizations and patients alike.

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It is timely and critical that we define and characterize the benefit the translational science modalities can bring to the serious problem of diagnostic failures, in order to outline and validate methodologies and operational protocols to prevent harmful and costly health outcomes. The decentralized organization of ambulatory care substantially increases the risk of preventable adverse events and diagnostic failures. Case in point is general dentistry care. Preventable adverse events and diagnostic failures in the ambulatory general dentistry setting can range from exposure to infectious agents, abuse or under-utilization of antibiotics and other pharmaceuticals with consequential systemic adverse effects, to subluxation of the temporomandibular joint, and other related unique challenges and barriers to ensuring patient safety.

Methodological Rationale

Infection of the teeth or other surrounding oral structures may present as abscesses, or mandibular (parapharyngeal) or maxillary (paraparotidal) cellulitis (e.g., Ludwig angina, *angina maligna*, *morbus strangularis*). Abscesses and cellulitis may represent a spectrum of the same process in which bacterial infection of the tonsils and pharynx spreads to the surrounding soft tissues. Infection is virtually always unilateral and involves multiple bacteria: Streptococcus and Staphylococcus are the most frequent aerobic pathogens, and Bacteroides is the predominant anaerobic pathogen. In general, Bacteroides are resistant to a wide variety of antibiotics - β-lactams, aminoglycosides, and recently many species have acquired resistance to erythromycin and tetracycline. This high level of antibiotic resistance has prompted concerns that Bacteroides species may become a reservoir for resistance in other, more highly pathogenic bacterial strains, and complicate treatment.

Typically, abscesses present as localized cavities lined by fibrous connective tissue that contains exudate, which are treated by surgical intervention often augmented by an antibiotic regimen. Dental abscesses can be either endodontic or periodontal. Root canal therapy treats endodontic abscesses by removing diseased nerve tissue and replacing it with purified gutta-percha or related materials. Periodontal abscesses involve the alveolus of the teeth and the tissues holding the teeth in place, and are most often treated with surgical extraction of the tooth involved. Peritonsillar abscesses are acute pharyngeal infections that require needle aspiration, broad-spectrum antibiotics, drainage, hydration, analgesics, and, in extreme cases, tonsillectomy.

Cellulitis is a bacterial infection that spreads under the skin, affects the dermis and subcutaneous fat, and manifests as a rapidly spreading area of redness, warmth and swelling. The borders of the affected area are generally not sharp, but painful. Lymphatic vessels can be involved. Dental infections account for approximately 80% of cases of facial cellulitis, including Ludwig angina. Facial cellulitis is a fascial infection with bilateral involvement of the submandibular, sublingual and submental maxillary spaces, or the parotid mandibular spaces. External signs include bilateral lower facial edema around the mandible and upper neck, or conversely in the periorbital area. Intravenous antibiotics are the most common and effective treatment for facial cellulitis, which subsides, usually, within 48 h, with hydration and high-dose penicillin, or 1st-generation cephalosporin or clindamycin. Culture-directed antibiotics are prescribed for 10 days, during which time patients are under in-patient hospital care. A breathing tube must be inserted to restore breathing, or an emergency tracheostomy performed in acute Ludwig angina (i.e., pharyngeal cellulitis). If not treated promptly, cellulitis brings on septic shock, and can be lethal. By contrast, abscesses are incised and drained, or more simply drained by needle aspiration, under local anesthesia in an out-patient setting. Rarely do patients need hospitalization for parenteral antibiotics, IV hydration, and airway monitoring, and if so for a short duration of 3-5 days.

Misdiagnosis cellulitis is a significant life-threatening situation. Depending on the statistics, diagnostic failure of cellulitis may range from 5% to 75% (!), which reveals a frightening gap in knowledge. This situation may be due in part to the fact that peritonsillar abscesses are difficult to distinguish from cellulitis because they share several of the symptoms: severe sore throat, trismus, "hot potato" voice, and uvular deviation. Symptomatology can exacerbate into dysphagia, fever, otalgia, asymmetric cervical adenopathy, drooling, severe halitosis, tonsillar erythema and swelling, exudates, confusion or other mental/cognitive changes, neck pain, swelling and discoloration, weakness, fatigue, or excess tiredness. Cellulitis manifests as a diffuse, hard, erythematous swelling resulting from the spread of microorganisms through the soft-tissue fascia. But, the tonsillar swelling in abscesses appears more as a discrete bulge, with deviation of the soft palate and uvula and pronounced trismus. Ultrasonography and contrast-enhanced Computerized Tomography (ce-CT) scan of the neck can distinguish between a serious abscess and life-threatening cellulitis. ce-CT should be used to confirm the diagnosis when the physical examination is difficult or the diagnosis is in doubt. Case in point, the best evidence base to date suggests that the combination of ce-CT and clinical exam has an accuracy rate of 89% with a sensitivity rate of 95% for the differential diagnosis of Ludwig angina cellulitis and paratonsillar and parapharyngeal abscesses. Moreover, several clinically relevant predictors, which aid in avoiding diagnostic failures of Ludwig angina cellulitis, among which anterior visceral space involvement (odds ratio: 54.44; CI^{95}: 5.80- 511.22), diabetes mellitus (odds ratio: 17.46; CI^{95}: 2.10- 145.29), and bilateral submandibular swelling (odds ratio: 10.67; CI^{95}: 2.73-41.75) [3].

Clinically, it is a challenge to discriminate between the two most prevalent internal derangements of the temporomandibular joint: anterior disc displacement with reduction, and symptomatic hypermobility. Both show clicking on opening and closing (reciprocal clicking), but there is a difference in timing of their opening and closing clicks. Unfortunately, it is not always feasible and practical to use this difference in timing clinically to distinguish between the two internal derangements, because it is the amount of mouth opening at the time of the clicking that is clinically notable, not the condylar translation. Two other criteria are the 5-mm difference in mouth opening at the time of the opening and closing clicks, and the detection of joint sounds on protrusion or laterotrusion in case of non-reciprocal clicking. The broad nature of these criteria leads to a significant risk of diagnostic failure [4,5]. Improved diagnosis by means of detailed translational research protocols (e.g., characterization of molecular profile of synovial inflammation - *viz*., by translational research protocols - is therefore timely and critical [6,7].

Discussion

These two examples exemplify diagnostic failures that are not uncommon in ambulatory general dentistry care, and that have substantial and serious risks – both health risks and financial risks – for patients and stakeholders. Both clinical situations, while arising in clinical dentistry, have profound systemic consequences that inform medicine. In the instance, of Ludwig angina, it was suggested that translational effectiveness evidence is now mounting for preventing diagnostic failures. In the case of TMJ disorders, it was indicated that translational research evidence was necessary to help avoid diagnostic failures. Taken together, they make the case that preventable adverse events in healthcare do occur, among which failed diagnoses and

misdiagnoses that can cause serious harm to patients and stakeholders. Research tools proffered by translational medicine, and more broadly translational healthcare, to garner the Best Evidence Base (BEB), must be judiciously use in clinical care to prevent ambulatory diagnostic failures.

Conclusion

The Grading of Recommendations Assessment, Development and Evaluation (GRADE), and its expanded form (Ex -GRADE) [8], provides an approach to grading quality of the best evidence base and the strength of clinical recommendations to ensure failure-less diagnosis. In a related vein, the Diagnostic Enhancement of Confidence by an International Distributed Environment (DECIDE) is an international endeavor, originally launched by the EU for Alzheimer's disease diagnosis and treatment, which now has been expanded to provide a vast set of tools for improved decision-making and dissemination of the best evidence base. Further revision of both the GRADE (and Ex-GRADE) and the DECIDE protocols will inform translational healthcare for preventing ambulatory diagnostic failures, and optimize BEB utilization in ambulatory clinical settings.

This bold objective is attainable as we develop new and improved means of engaging stakeholders [9] in healthcare, from diagnosis to clinical decision-making for treatment. This effort requires sustained dissemination of BEB by tele-healthcare and other web-based modalities [10] in a concerted effort at improving the health literacy of the patients, caregivers and stakeholders [10,11].

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References

1. Chiappelli F (2014) Fundamentals of Evidence-based Health Care and Translational Science. Springer–Verlag, Heidelberg.
2. Chiappelli F (2015) Comparative Effectiveness Research (CER): New Methods, Challenges and Health Implications. NovaScience Publisher Inc Hauppauge, NY.
3. Boscolo-Rizzo P, Da Mosto MC (2009) Submandibular space infection: a potentially lethal infection. Int J Infect Dis 13: 327-33.
4. Naeije M, Kalaykova S, Visscher CM, Lobbezoo F (2009). Evaluation of the Research Diagnostic Criteria for Temporomandibular Disorders for the recognition of an anterior disc displacement with reduction. Journal of Orofacial Pain. 23:303-11.
5. Hegab A (2015) Temporomandibular Joint Internal Derangement: What We Missed? J Dent Health Oral Disord Ther 2: 33
6. Barkhordarian A, Ajaj R, Ramchandani MH, Demerjian G, Chiappelli F et al. (2011) Osteoimmunopathology in HIV/AIDS: A Translational Evidence-Based Perspective. Patholog Res Int
7. Demerjian GG, Sims AB, Stack BC (2011) Proteomic signature of Temporomandibular Joint Disorders (TMD): Toward diagnostically predictive biomarkers. Bioinformation 5: 282-84.
8. Phi L, Ajaj R, Ramchandani MH, Brant XM, Chiappelli F (2012) Expanding the Grading of Recommendations Assessment, Development, and Evaluation (Ex-GRADE) for Evidence-Based Clinical Recommendations: Validation Study. Open Dent J. 6: 31-40.
9. Barkhordarian B, Demerjian G, Jan A, Du A, Chiappelli F et al. (2015) Stakeholder Engagement Analysis - A Bioethics Dilemma in Patient-Targeted Intervention: Patients with Temporomandibular Joint Disorders. J Transl Med 13: 15.
10. Barkhordarian A, Ramchandani MH, Dousti M, Kelly-Gleason L, Chiappelli F (2012) Disseminating the best available evidence: New challenges in public reporting of health care. Bioinformation.8:293-95.
11. Moura Jde A, Costa BC, de Faria RM, Soares TF, Chiappelli F et al. (2013) Improving communication skill training in patient centered medical practice for enhancing rational use of laboratory tests: The core of bioinformation for leveraging stakeholder engagement in regulatory science. Bioinformation. 9: 718-20.