

Prophylaxis of Infective Endocarditis: A Cross Sectional Survey among Physician Members of the Portuguese Society of Cardiology

Estudo Transversal sobre Profilaxia da Endocardite Infeciosa: Inquérito a Médicos da Sociedade Portuguesa de Cardiologia



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ABSTRACT

Introduction: In the last decade, the downgrading of indications for antibiotic prophylaxis for infective endocarditis caused an uncertain impact on the incidence of this condition. Since no data is available on the practice of infective endocarditis prophylaxis in Portugal, we aimed to characterize the pattern of antibiotic use for infective endocarditis prophylaxis and the compliance/awareness of scientific guidelines among physician members of the Portuguese Society of Cardiology.

Material and Methods: A cross sectional observational study was conducted. An online self-completed questionnaire with 12 items on infective endocarditis prophylaxis was sent to 1330 physicians, specialists and residents, members of the Portuguese Society of Cardiology. In addition, descriptive statistical analysis was performed.

Results: Two hundred and fifty-three valid questionnaires were responded. Eighty-seven per cent of respondents were cardiologists (specialists or residents), mostly between 30 and 40 years old (26.7%) and 50 to 80 years old (44.3%). The majority (83.0%) follow the European scientific guidelines. Still, 61.0% had or may have had doubts regarding prophylaxis of infective endocarditis in certain patients. Variable adherence to scientific guidelines was noted. Further scientific evidence was required by 60.6% of respondents.

Conclusion: Infective endocarditis prophylaxis was generally guided by European scientific guidelines among physicians of the Portuguese Society of Cardiology. There was, however, an evident discrepancy between the guidelines and real-world perception of the risk of infective endocarditis. This highlights the sensed gap in accessing more robust scientific evidence.

Keywords: Antibiotic Prophylaxis; Endocarditis; Portugal; Surveys and Questionnaires

RESUMO

Introdução: Na última década, a restrição das indicações para a profilaxia antibiótica na endocardite infecciosa teve um impacto incerto na incidência desta condição. Uma vez que não existem dados sobre a prática da profilaxia da endocardite infecciosa em Portugal, procurámos caracterizar o padrão de utilização antibiótica para a profilaxia da endocardite infecciosa e a conformidade/sensibilização das orientações científicas entre médicos, membros da Sociedade Portuguesa de Cardiologia.

Material e Métodos: Foi realizado um estudo observacional transversal. Um questionário online de autopreenchimento com 12 itens sobre profilaxia da endocardite infecciosa foi enviado a 1330 médicos, especialistas e internos, sócios da Sociedade Portuguesa de Cardiologia. Foi realizada uma análise estatística descritiva.

Resultados: Foram validados 253 questionários respondidos. Oitenta e sete por cento dos inquiridos eram cardiologistas (especialistas ou internos), a maioria entre os 30 e os 40 anos (26,7%) e os 50 e 80 anos (44,3%). A maior parte (83,0%) segue as orientações científicas europeias. Ainda assim, 61,0% admitiu ter ou poder ter dúvidas sobre a profilaxia da endocardite infecciosa em determinados doentes. Verificou-se uma adesão variável às orientações científicas. A necessidade de mais evidência científica foi defendida por 60,6% dos respondedores.

Conclusão: Entre médicos da Sociedade Portuguesa de Cardiologia, a profilaxia da endocardite infecciosa foi geralmente orientada pelas orientações científicas europeias. Existiu, no entanto, uma evidente discrepância entre as orientações e a perceção do risco de endocardite infecciosa na prática clínica. Isto reforça a necessidade de acesso a dados científicos mais robustos.

Palavras-chave: Endocardite; Inquéritos e Questionários; Portugal; Profilaxia Antibiótica

INTRODUCTION

Despite tremendous medical advances, the management of infective endocarditis (IE) is clinically challenging and carries a substantial rate of morbidity and mortality worldwide.¹ Its crude incidence ranges from 1.5 to 11.6 cases per 100 000 people.² Moreover, in-hospital mortality rate affects nearly one-fifth of patients as documented in international registries such as the International Collaboration Endocarditis Cohort³ or the recently published EURO-endo⁴ (18% and 17%, respectively).

Approximately a century ago, the role of bacteremia leading to IE in patients with preexistent valve disease was demonstrated.⁵ In addition, SD Elliot⁶ demonstrated that transient bacteremia occurring following a dental infection or trauma could lead to subacute IE. Moreover, the concept of prevention through oral treatment emerged. In 1970, Hilson⁷ defended the use of chemoprophylaxis for patients with increased susceptibility to endocarditis, citing Kelson and White who, in 1945, estimated a risk of endocarditis of 1 in 500 after dental extraction.

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Since then, several regimens have been proposed for the prevention of IE in susceptible patients. Scientific guidelines⁸ include previous history of IE, prosthetic or repaired cardiac valves, cyanotic congenital heart disease and any repaired congenital heart disease for up to six months after repair or lifelong prophylaxis in residual shunt or regurgitation as high-risk cardiac conditions. The downgrading of antibiotic indications for endocarditis prevention in 2007 in the USA⁹ and in 2009 in Europe⁹ has, nonetheless, led to heterogeneous compliance by physicians, as shown by Chambers *et al.*¹⁰ And this downgrading has not been adopted by several scientific societies, such as in Brazil or in Latin America. These still consider that native valve disease (such as aortic bicuspid valve or mitral valve prolapse) is a high risk situation and maintain antibiotic use before genitourinary or gastrointestinal procedures involving mucosa in high risk patients.¹¹

Several electronic surveys conducted in Spain¹² or France¹³ with dentists revealed that their knowledge of cardiac conditions and antibiotic side effects was inadequate.

The impact of this downgrading in antibiotic prophylaxis on the incidence of IE is still inconsistent¹⁴ even though it has been shown in Germany¹⁵ or in England.¹⁶ In Portugal, no study has analyzed this impact on local or national incidence.^{17,18} Nevertheless, an increasing trend was noted in the incidence of IE in Portugal in the last decade and the in hospital all-cause mortality rate affects one fifth of patients hospitalized with infective endocarditis.¹⁷ The compliance of physicians with guidelines needs to be considered for quality and standard of care and assessment. No study has evaluated the pattern of antibiotic prophylaxis for IE among Portuguese physicians. Surveys are an essential tool to gather information on the attitudes and practice of care delivery among physicians.¹⁹

Therefore, we aimed to assess acceptance and compliance with scientific guidelines regarding IE prophylaxis among physician members of the Portuguese Society of Cardiology.

MATERIAL AND METHODS

Study design

A cross sectional descriptive study was carried out between the 8th February and the 28th February 2021, in a partnership between the Valvular Heart Diseases Working Group (Portuguese Society of Cardiology) and the Faculty of Medicine of the University of Lisbon.

After reviewing the most recent scientific guidelines^{8,20} regarding antibiotic use in IE prevention, a 12 item questionnaire in Portuguese was developed (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17379/Appendix_01.pdf). All 12 questions were closed questions with an area in the end of the questionnaire for personal comments.

The questions regarding antibiotic prophylaxis in IE included data on 1) personal/professional background (age, specialty, year of medical degree), 2) international scientific guidelines and national/institutional guideline recommendations, 3) identification of high-risk conditions, 4) identification of high-risk procedures and 5) risk assessment and choice of antibiotics during dental procedures.

The questionnaire was planned to take less than five minutes to answer. All answers were anonymous. We gathered all quantitative and qualitative data for analysis. The questionnaire was active for three weeks and a reminder email was sent one week before the final date.

Sample

All physician members of the Portuguese Society of Cardiology (a total of 1330) were invited to participate in this online questionnaire, sent via email.

Statistical analysis

We performed a standard descriptive analysis of the results obtained from a convenience sample.

Continuous variables were presented as mean \pm standard deviation and categorical variables were expressed as frequencies and percentages. Missing values were excluded from analyses (we performed an available data analysis).

The data were analyzed using Excel 365 for Windows software.

Ethics

The Ethics Committee of the University of Lisbon Academic Centre study approved the study (reference number 349/19). All respondents gave their informed consent.

RESULTS

Of the 1330 invitations to physicians to participate in this survey, 255 questionnaires were returned, corresponding to a 19% response rate. However, two questionnaires contained no answers and were excluded. Most physicians were cardiologists and 60% of the participants were between 40 and 80 years old (Table 1); 93.3% reported regularly following patients with heart valve disease.

Compliance with scientific guidelines in IE prophylaxis

Nearly 83% of the respondents regularly followed the European Society of Cardiology scientific guidelines for IE prophylaxis (Fig. 1A). One quarter of physicians had institutional guidelines for IE prophylaxis (Fig. 1B).

Thirty nine percent of the respondents had no doubts regarding IE prevention (Fig. 2).

Cardiac conditions and procedures considered for IE prophylaxis

Patients with cardiac valve prosthesis, prosthetic material used in valvuloplasty, cyanotic congenital cardiac disease and previous IE were among the most frequently conditions identified by responders as high-risk conditions for IE (Table 2). The previous history of rheumatic valve disease was identified in 29.4% of the answers.

Most physicians identified dental procedures as a condition that increased the risk of IE, followed by implantation of intracardiac devices. Permanent tattooing and body piercing raised more doubts than any other procedure regarding the recommendation for IE prophylaxis (Fig. 3).

Dental procedures and IE

From the total number of respondents, 60.6% defended that further scientific evidence was needed to demonstrate the benefit of antibiotic use in invasive dental procedures.

Dental invasive procedures were identified as being high risk for the risk of IE whereas brushing teeth or eating was perceived as low risk activities (Fig. 4A). Nearly 93% of physicians used amoxicillin for IE prevention during dental procedures (Fig. 4B).

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the current practice among physicians regarding IE prophylaxis in Portugal. In our study, applied to physicians who were members of the Portuguese Society of Cardiology, the European guidelines⁸ were the most followed and the identification of high-risk cardiac conditions and procedures was mostly in accordance with them. Nonetheless, previous rheumatic fever, the presence of native valve disease or intracardiac devices were substantially identified as being high-risk cardiac conditions for IE, thus conflicting with current indications. Also, 61% of responders had doubts regarding IE prophylaxis in certain patients. Lastly, further evidence regarding dental procedures and IE prophylaxis was warranted by a substantial proportion of physicians.

The accepted standard of care relies more and more often on scientific expert guidelines. Ethically, though, deviation from these recommendations may be feasible if they are fully discussed with patients to ensure informed consent²¹ and supported on scientific evidence.

From 2007 to 2009, several scientific societies^{9,22,23} limited the use of antibiotic indication in the prophylaxis of IE. The United Kingdom's (UK) National Institute for Health and Care Excellence (NICE) guidelines²² were the most restrictive, advising against all forms of antibiotic use for IE prophylaxis. These overall measures were justified by the lack of scientific evidence of the benefit associated with the risk of inefficient use of antibiotics concerning side effects and increased risk of resistance.⁸ Nevertheless, its impact has been controversial. A significant increase in the incidence of IE in England was noted by Dayer *et al*,²⁴ followed by similar findings in the Netherlands²⁵ and Germany.²⁵ Still, uncertainty persists²⁶ as significant heterogeneity between different studies and the follow-up period is still too short to allow drawing more permanent conclusions. Additionally, compliance can be challenging. Dayer *et al*¹⁰ concluded that 39% of cardiologists/cardiac surgeons did not adopt the most recent NICE guidelines.

Most physician members of the Portuguese Society of Cardiology accepted the 2015 European guidelines.⁸ Still, substantial conflict persists as many respondents expand IE prophylaxis use in cardiac conditions no longer considered high risk by the more recent guidelines, such as previous rheumatic fever, intracardiac devices or native valve disease carriers. Other studies have shown this heterogeneity. Grattan *et al*²⁷ concluded that among pediatric cardiologists, the 2007 American Heart Association guidelines⁹ led to a reduction of IE prophylaxis recommendations among low risk patients by 44.9% but unexpectedly a reduction of 9.3% among high risk patients as well. This was also shown by Pharis *et al*²⁸ in a study carried out among New Zealand, Canada, Australia and American pediatric and adult congenital cardiologists in 2008.

The same is true for high-risk procedures. Dental procedures were almost always considered a high-risk situation by this group of 253 physicians. Nonetheless, other procedures currently removed from scientific guidelines such as obstetric procedures, urologic and gastroenterological procedures in the absence of active infection were also identified as procedures where IE prophylaxis was recommended. Remarkably, body piercing and permanent tattooing were the procedures that raised a significant proportion of doubt among respondents. In 2008, Armstrong *et al*²⁹ collated all cases of IE related to body art and concluded that transient bacteraemia can arise. Despite the fact that no antibiotic use is currently recommended by European guidelines,⁸ education is crucial and in patients with high risk cardiac conditions and native valve disease these procedure should be discouraged.

Still, the epidemiology of infective endocarditis is changing worldwide.⁴ Portugal is no exception. Patients hospitalized with IE in the last decade are older, have a higher burden of comorbidities such as arterial hypertension or diabetes

mellitus, or cancer. There is an increasing proportion of patients with cardiac implantable electronic devices (CIED) or cardiac valve prosthesis.¹⁷ Non-rheumatic valve disease is proportionally two-fold more frequent compared to rheumatic valve disease. Thornhill *et al*³⁰ also evaluated the impact of previous cardiac conditions on the risk of developing IE. Ultimately, in addition to the already known 'high risk' situations, other 'moderate risk' conditions such as congenital valve anomaly, hypertrophic cardiomyopathy, heart transplant, or left ventricle assist devices had a similar risk as some 'high risk' conditions. Contemporary risk stratification algorithms need to be revisited,^{30,31} allowing for a better definition of prevention strategies. This is probably why in our study and in Pharis *et al*²⁸ a significant proportion of physicians expressed doubts regarding antibiotic use in IE prophylaxis in certain patients, probably for fear of leaving some at risk by not prescribing.

Regarding dental procedures, most respondents in our study considered invasive dental procedures to represent a higher risk of IE when compared with typical daily activities such as eating or brushing teeth. In 1977, Everett *et al*³² reviewed bacteraemia occurring after several medical procedures and classified them almost always as short lived. However, the rate of post dental extraction bacteraemia was considered high (60% - 90%), which is substantially higher than with brushing teeth or dental flossing. Lockhart *et al*'s³³ 2008 study and a more recent meta-analysis by Cahill *et al*²⁶ concluded on the significant incidence of transient bacteraemia after tooth brushing. Still, transient bacteraemia is probably not the suitable surrogate for IE as it is more likely that low levels of bacteraemia occurring in most daily activities and medical procedures are insufficient to cause IE.³⁴ More robust and high-quality research is required, according to nearly two thirds of our responders.

Limitations

Firstly, a 19% response rate is considered low, which could partially implicate the impact of the presented results on the overall population of physicians dealing with valvular or congenital patients in Portugal. In fact, according to Abdulaziz K *et al*, physician surveys are characterized by a low response rate which can increase the presence of a nonresponse bias.¹⁹ Nevertheless, higher response rates do not seem to impact the nonresponse bias in physician surveys.³⁵ The input of other specialities would be valuable to ascertain, namely dentists, family physicians or gastroenterologists and should deserve further analysis. Secondly, no further characterization of the location of the leading clinical activity was requested due to the compelling requirement to maintain anonymity. This variable may, however, influence individual practice. Still, our study was not aimed at identifying why physicians have different practice patterns.

CONCLUSION

This survey is an initial effort to understand the practice of IE prophylaxis in Portugal. In this sample, IE prophylaxis is mostly guided by international scientific guidelines, mainly European. Nonetheless, there is some discrepancy regarding identifying high-risk cardiac conditions and procedures among professionals. Therefore, a substantial rate of uncertainty is assumed by most when deciding for certain patients and more scientific evidence is warranted. Interventions to promote continuous physician education should be considered, promoting a practice based on the best available evidence. Further studies should be conducted among other specialties outside of the scope of the Portuguese Society of Cardiology to take the complete national picture of IE prophylaxis practice.

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AUTHOR CONTRIBUTIONS

CSS: Data analysis, draft and critical review of the manuscript.

AGA, FJP: Data analysis, critical review and approval of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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Table 1 – Characteristics of physicians that participated in the questionnaire

| Medical Specialty | | |
|--|-----|-------|
| Cardiology | 190 | 74.5% |
| Resident - Cardiology | 30 | 11.8% |
| Internal Medicine | 4 | 1.6% |
| Resident - Internal Medicine | 0 | 0.00% |
| Cardiothoracic surgery | 9 | 3.5% |
| Resident - Cardiothoracic Surgery | 1 | 0.4% |
| Paediatric Cardiology | 16 | 6.3% |
| Family physician | 1 | 0.4% |
| Not mentioned | 4 | 1.6% |
| Age (year-old) | | |
| 20 to 30 | 26 | 10.2% |
| 30 to 40 | 68 | 26.7% |
| 40 to 50 | 41 | 16.1% |
| 50 to 80 | 113 | 44.3% |
| > 80 | 5 | 2.0% |
| Year of Medical graduation | | |
| 1960 - 1989 | 99 | 39.3% |
| 1990 - 1999 | 31 | 12.3% |
| 2000 - 2009 | 61 | 24.2% |
| 2010 - 2019 | 61 | 24.2% |
| Frequent evaluation of valve disease patients | | |
| Yes | 238 | 93.3% |
| No | 16 | 6.3% |

Table 2 – Clinical conditions in which IE prophylaxis should be applied

| | | |
|---|-----|-------|
| Patients with cardiac valve prosthesis | 241 | 94.5% |
| Patients with prosthetic material used in cardiac valvuloplasty | 174 | 68.2% |
| Patients with history of rheumatic fever | 75 | 29.4% |
| Patients with cyanotic congenital cardiac disease | 228 | 89.4% |
| Patients with cardiac murmur or other evidence of native valve disease | 32 | 12.6% |
| Patients with intracoronary stent intracoronary or coronary-aortic bypass graft surgery | 6 | 2.4% |
| Patients with previous IE | 230 | 90.2% |
| Patients with intracardiac device (pacemaker/implantable cardioverter defibrillator) | 46 | 18.0% |
| All the options | 6 | 2.4% |
| None of the options | 4 | 1.6% |
| Other: | | |
| Bicuspid aortic valve | 3 | 1.2% |
| Recently implanted cardiac devices | 1 | 0.4% |
| Patients with residual lesions after congenital defect repair | 2 | 0.8% |
| Ventricular septal defect | 1 | 0.4% |
| Percutaneous or surgically repaired congenital cardiac condition within 6 months of procedure | 1 | 0.4% |

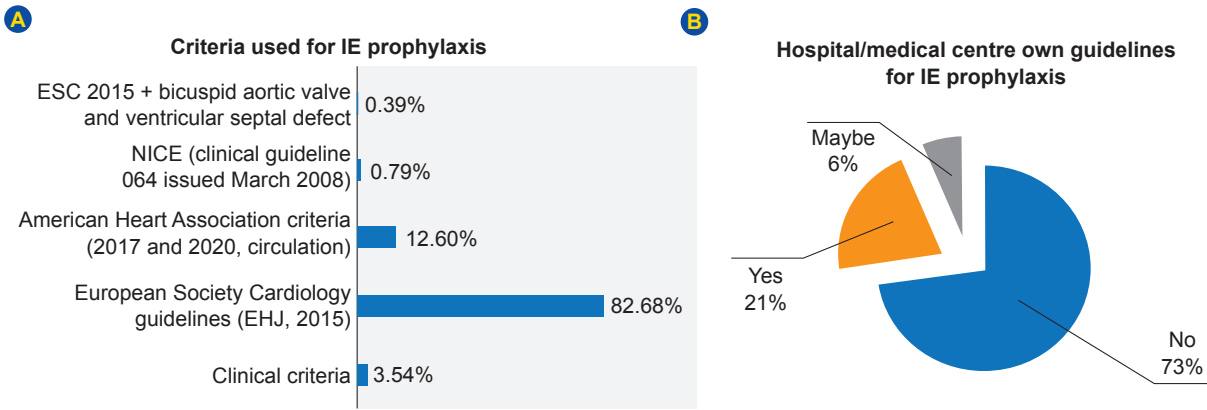


Figure 1 – (A) Usual criteria used by physicians for IE prophylaxis; (B) Institutional guidelines issued by medical institutions for antibiotic use in IE prevention.

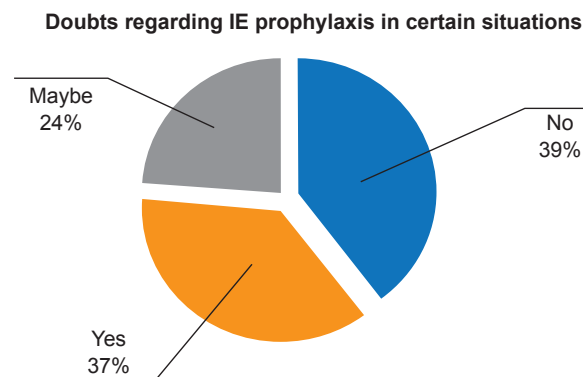


Figure 2 – Doubts regarding IE prophylaxis in clinical practice

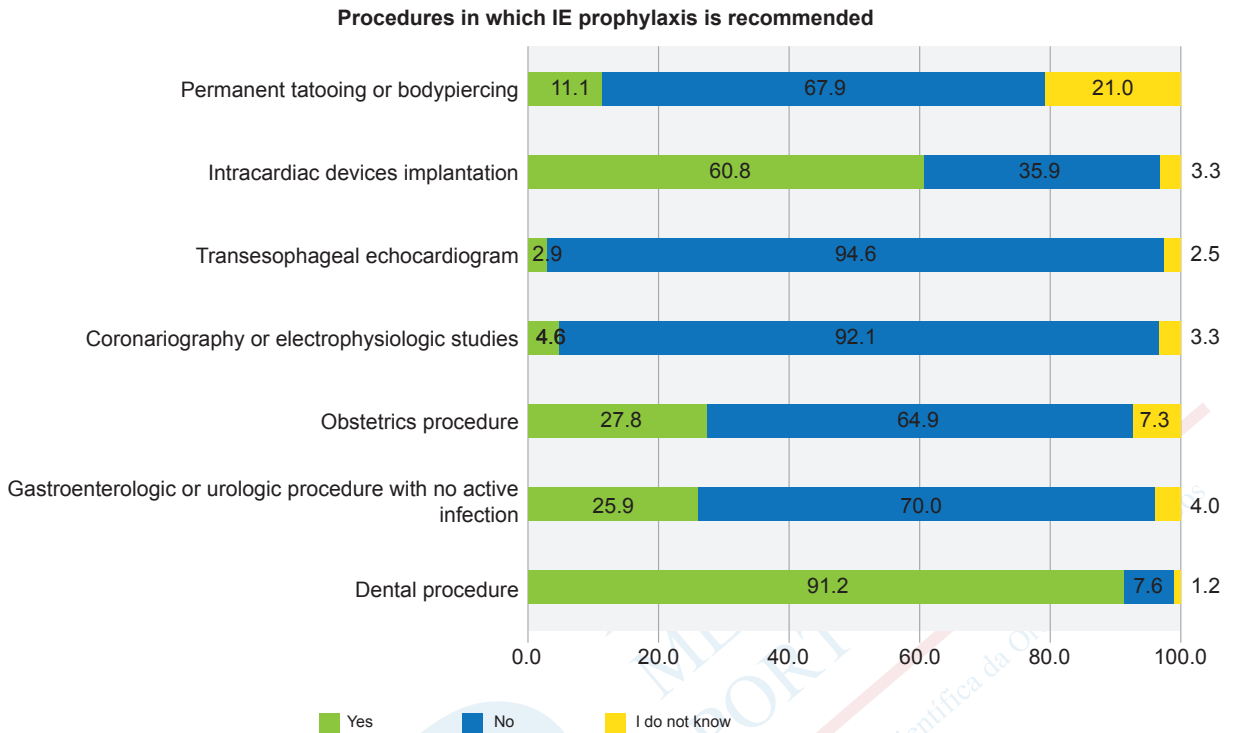
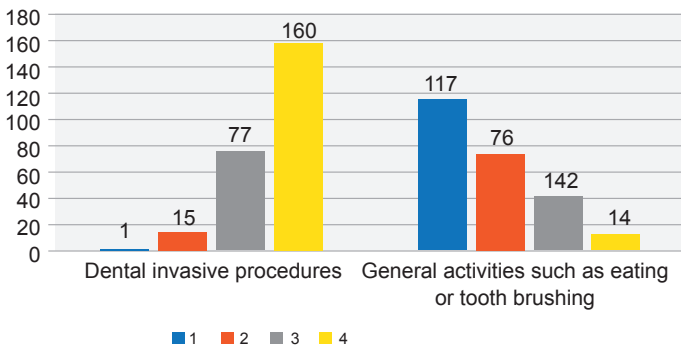


Figure 3 – IE prophylaxis recommendation in specific settings (%)

A

Contribution for the risk of IE



B

Antibiotic choice for dental invasive procedures

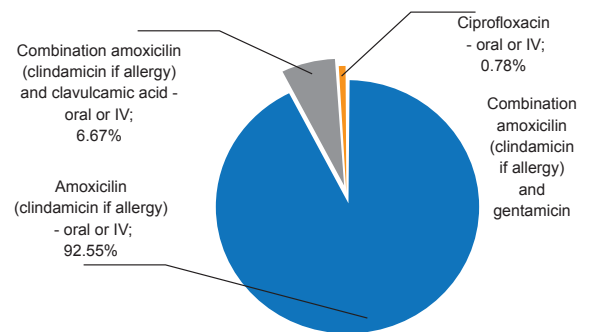


Figure 4 – (A) Perceived contribution that each of the following factors plays in the risk of developing infectious endocarditis (value of 1 to 4, being 1- no contribution and 4 - major contribution); (B) Antibiotic regimen (%) usually used in antibiotic prophylaxis in dental procedure.