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Primary Care Epidemiology

Non-steroids anti-inflammatory drugs and risk of peritonsillar abscess in pharyngitis: a French longitudinal study in primary care†

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Abstract

Background. The safety of non-steroids anti-inflammatory drugs (NSAIDs) in the context of pharyngitis is doubtful with contradictory results in the literature.
Objective. To evaluate the risk of peritonsillar abscess (PTA) associated to NSAIDs consumption during a pharyngitis episode observed in primary care.
Method. A retrospective cohort study using Observatory of General Medicine Datalink from 1995 to 2010. All patients consulting a GP from the Datalink network for pharyngitis have been included. The occurrence of a PTA in the 15 days following the consultation for pharyngitis was matched. The association between PTA and prescriptions of NSAIDs was studied via an adjusted logistic regression model.
Results. During the study period, 105 802 cases of pharyngitis and 48 cases of PTA following a pharyngitis were reported, concerning respectively 67 765 and 47 patients. In the multivariate analysis, the risk of PTA was associated positively with a NSAIDs prescription (OR = 2.9, 95% CI = 1.6–5.2). Other factors associated with PTA occurrence were the prescription of corticosteroids (OR = 3.1, 95% CI = 1.3–7.6) and an age between 20 and 40 years (OR = 5.7, 95% CI = 2.5–13.0). The prescription of antibiotics was not significantly associated with PTA ($P = 0.7$).
Conclusion. Prescription of NSAIDs in pharyngitis may increase the risk of PTA. This study encourages considering cautiously the balance between benefits and harms before prescription of NSAIDs for pharyngitis.

Key words. Common illnesses, ear, nose and throat (ENT, otolaryngology), infectious diseases, pharmacology/drug reactions, primary care, upper respiratory infections/common cold/bronchitis.

Introduction

Pharyngitis is a common pathology with 15 million consultations each year in the USA (4.7/100 inhabitants per year) and 9 million in France (13.6/100 inhabitants per year) (1,2). Pharyngitis is mostly diagnosed in primary care (74% in USA) (3). Symptoms are dominated by fever associated with odynophagia, sometimes intense.

One of the complications of pharyngitis is the peritonsillar abscess (PTA)—an inflammation often suppurative of the tonsil lodge, concerning 0.1–0.3% of cases, appearing within 15 days after pharyngitis (4–6). In 10% of cases, PTA may be inaugural (5–7).

Several risk factors for PTA have been found in the literature such as active smoke (4,8), age between 21 and 40 years (4,9) and being a male (4,8). A higher but not significant frequency of PTA during winter and spring has also been found in one study (9). To date, immunodeficiency situations (diabetes, cancer, etc.) have not been found as risk factors for PTA (5), but only few studies have investigated them (4,8,9).

In most cases, pharyngitis imposes symptomatic treatment only (2,10). Paracetamol is commonly used as part of pharyngitis to relieve pain and fever (11,12). When paracetamol is insufficient, non-steroidal anti-inflammatory drugs (NSAIDs) can provide additional benefits. Several studies recognize the superiority of NSAIDs over paracetamol for the management of these symptoms (13–17).

Yet, there are some doubts about the safety of NSAIDs in the context of pharyngitis. Several studies show contradictory results on the possible link between NSAID use in pharyngitis and the occurrence of PTA (6–9,18).

This uncertainty about the safety of NSAIDs leads to different recommendations varying between countries. In the USA and in the UK, it is recommended to treat pharyngitis—including group A streptococcus (1)—using NSAIDs for better symptom relief (1,19,20). In France, it is recommended to not use NSAIDs in pharyngitis because of the risk of complications, though these recommendations are based on a low level of evidence (expert advice) (2,5,21).

The objective of this study was to evaluate the risk of PTA associated to NSAIDs consumption during pharyngitis observed in primary care practice.

Methods

Data

A primary-care network of >120 French GPs all members of the 'Observatory of General Medicine' (OMG) routinely collected exhaustive data of their daily activity (22) in particular diagnosis and drug prescriptions for every consultation. Between 1995 and 2010, >6 million consultations involving ~690 000 patients were recorded (23). This representative database (23,24) was designed and managed by the French Society of General Medicine (SFMG). Participation of GPs was based on volunteering: data were not restricted to GPs who met diagnosis coding quality thresholds.

Diagnosis of consultations was encoded by GPs using a thesaurus validated in France: the Dictionary of Consultation Results (25). This dictionary gathers the consultation results (CR) i.e. diagnoses and syndromic tables observed at least once a year by a GP on average. There are currently 278 CR in the Dictionary of Consultation Results (26). Each CR is associated with one code or more of the International Classification of Diseases (10th Revision, Clinical Modifications) and contains mandatory criteria to homogenize the CR between doctors. 'Pharyngitis' and 'PTA' CR are detailed in Supplementary Material. Criteria for 'PTA' didn't change during the study's period. Criteria for pharyngitis didn't change between 1995 and 2005. In 2005, the criteria for 'pharyngitis' were detailed by adding the subcriterion 'no characteristic nasal discharge'.

All consultations with a CR coded 'Pharyngitis' were included in the study. There were no exclusion criteria. For each included pharyngitis consultation, occurrence of PTA for the same patient was researched in the 15 days following the consultation. In case of multiple consultations for 'Pharyngitis' by the same patient during a 15 days period, only the last consultation date was conserved, which incorporated the full prescriptions list of the previous consultations. PTA without prior pharyngitis was not included.

The variables extracted from the database were date of consultation, sex, age, presence of diabetes or cancer in the year preceding the consultation and prescriptions of AINS (by using ATC code 'M01A'), corticoid or antibiotics.

Statistical analysis

This study was a retrospective cohort study

A logistic regression model was used to study the relationship between prescription of NSAIDs during pharyngitis and the occurrence of PTA. Because some patients consulted several times for pharyngitis during the study period, we used a generalized estimation equations technique, in order to obtain robust SEs of parameters estimates. For the multivariate analysis, we selected independent variables with a P value of <0.20 in univariate analysis, and we retained variables by progressive elimination (stepwise backward).

Because we suspected that age may not have a linear effect on the occurrence of PTA, three classes were used: 0–19, 20–39, 40 years and over, to be comparable with the other studies found in the literature (4,8,9).

Ethic

The use of OMG database for scientific research has been authorized by the National Commission of Informatics and Civil Liberties [Commission Nationale de l'Informatique et des Libertés (CNIL)] (agreement n = 311 668). Patient's consent for the collection and use of their consultation data for scientific research was also collected (23).

Results

Descriptive analysis

During the following period, 124 GPs participated allowing the identification of 105 866 pharyngitis, only 64 pharyngitis had missing data for analysis (0.07% of datas) and were excluded. 105 802 pharyngitis were analysed. Among these consultations, 48 were followed by PTA within 15 days of pharyngitis (0.04%). These concerned 67 765 patients, of which 47 had a PTA. Among patients, 48 637 (71.8%) had a single consultation for pharyngitis, 10 857 (16.0%) had two consultations and 8271 (12.2%) had three or more consultations.

Descriptive analysis of consultations is reported in Table 1. Among the studied consultations, 22% lead to a NSAIDs prescription (n = 23 404), 5% to a corticoids prescription (n = 4979) and 59% to an antibiotic prescription (n = 62 802). Penicillins accounted for 60% of antibiotics prescribed (n = 37 501).

The mean age was 25 years for patients with pharyngitis (interquartile range (IQR) = [8; 37]) and 31 years for patients with PTA (IQR = [21; 39]). Patients with pharyngitis were aged from 0 to 109 years and those with PTA from 7 to 58 years. No PTA were found for patients with diabetes or cancer during the study.

Statistical analysis

Univariate analysis

In the univariate analysis, the occurrence of PTA was significantly associated prescription of a NSAIDs (OR = 2.6 [1.4; 4.5], P = 0.001) and prescription of corticosteroids (OR = 2.9 [1.2; 6.9], P = 0.014)

(Table 2). It was also associated with age group ($P < 0.001$) with the highest OR for patients between 20 and 39 years old (OR = 5.9 [2.6; 13.6]). We did not find associations between PTA and antibiotic prescription, sex or consultation period.

Multivariate analysis

In the multivariate analysis, the occurrence of PTA was significantly associated with prescription of NSAIDs (adjusted odds ratio (aOR) = 2.9, 95% CI = 1.6–5.2, $P < 0.001$) (Table 2). Corticoids prescription are also positively associated with occurrence of PTA (aOR = 3.1, 95% CI = 1.3–7.6, $P = 0.011$), as age over 20 years with the highest value for the age group 20–39 years (aOR = 5.7, 95% CI = 2.5–13.0, $P < 0.001$).

Discussion

By using a large database about consultations in primary care, we were able to study the association between NSAIDs prescription during pharyngitis and the risk of PTA occurrence in primary care. Our results confirm that patients with a NSAIDs or corticosteroids prescriptions or those aged between 20 years and over were associated with an increased risk of PTA after pharyngitis. These results

Table 1. Descriptive statistics of consultation for pharyngitis and PTA following a pharyngitis, Observatory of General Medicine, 1995–2010, France

	Pharyngitis consultation		PTA following a pharyngitis consultation	
	Number	%	Number	%
Gender				
Males	46 507	44.0	21	43.8
Females	59 295	56.0	27	56.2
Age (years)				
≤19	48 843	46.2	7	14.6
20–39	34 513	32.6	29	60.4
≥40	22 446	21.2	12	25.0
Treatments				
NSAIDs	23 163	21.9	20	41.7
Corticoids	4945	4.7	6	12.5
Antibiotics	62 168	58.8	27	56.3
Of which penicillins	37 118	59.7	20	41.7
Of which macrolides	14 523	23.3	5	10.4
Of which cephalosporins	9246	14.9	2	4.2
Of which others	1281	2.1	0	0.0
Associated disease				
Diabetes	1205	1.1	0	0.0
Cancer	155	0.1	0	0.0
Consultation period				
January–March	27 623	26.1	16	33.3
April–June	28 386	26.8	9	18.8
July–September	22 438	21.2	8	16.7
October–December	27 355	25.9	15	31.3

Table 2. Determinants of PTA occurrence following a pharyngitis consultation, Observatory of General Medicine, 1995–2010, France

	PTA following a pharyngitis consultation univariate analysis		PTA following a pharyngitis consultation multivariate analysis	
	OR (95% CI)	*P* value	aOR (95% CI)	*P* value
Gender female	1.01 (0.57–1.78)	0.978		
Age				
≤19 years	*Ref*	**<0.001**	*Ref*	**<0.001**
20–39 years	5.94 (2.60–13.56)		5.66 (2.46–12.99)	
≥40 years	3.78 (1.49–9.61)		3.81 (1.49–9.78)	
NSAIDs prescription	2.55 (1.44–4.52)	**0.001**	2.86 (1.58–5.17)	**0.001**
Corticoids prescription	2.93 (1.24–6.88)	**0.014**	3.14 (1.29–7.64)	**0.011**
Antibiotics prescription	0.90 (0.51–1.59)	0.723	–	–
Trimester			–	–
January–March	*Ref*	0.336		
April–June	0.49 (0.21–1.14)			
July–September	0.69 (0.31–1.56)			
October–December	0.95 (0.47–1.91)			

P-values <0.05 are indicated in bold.

suggest that NSAIDs or corticosteroids prescriptions may have increased the risk of PTA after pharyngitis. We did not find associations between occurrence of PTA and sex, consultation period or antibiotics prescription.

Strengths and limitations

A major strength of our study was the large database used, which listed >6 million consultations, enabling a retrospective cohort study. The use of a retrospective cohort was necessary because of the very low incidence of PTA. Another strength of this study is that GPs of the OMG are representative of French doctors (23,24), at the only exception of those in the rural sector being underrepresented (27). Patient characteristics (age, sex) do not significantly differ from those of the French population (27). CR between physicians was homogenized with the use of the Dictionary of Consultation Results, also limiting the risk of diagnostic error and misclassification bias.

However, this study has some limitations. Because of its retrospective nature, some variables have not been collected, such as smoking or the result of a rapid diagnostic test of Group A β-hemolytic streptococcus (GAS), searching for antibodies anti-GAS. This test, achievable in 5 minutes in ambulatory care, was used to confirm or not the presence of a GAS. This detection would have been interesting, as several authors consider that PTA is a specific complication of GAS (2), whereas several studies find multibacterial PTA, sometimes without GAS (7–9,28–30). We only had access to ATC codes, and information on the name of prescribed NSAIDs was not available. An NSAID agent-based analysis could have been informative as well: if all PTA had taken place with ibuprofen, this would have provided additional interesting information. Nevertheless, a large meta-analysis of the Cochrane library didn't show significant difference in terms of adverse event profile between the different NSAIDs (31).

Available data on NSAIDs, corticosteroids and antibiotics are prescribing data. Patients may not have followed the prescribing procedures (doses, intervals between two catches or total treatment time). On the other hand, some patients may have consumed NSAIDs although without prescription. This is because in France (as in other countries), some of these treatments may be issue over-the-counter: each year, several million boxes of ibuprofen are sold in France without medical prescription (11).

Moreover, patients may have consulted other doctors for their pharyngitis or PTA and consultations would not be recorded in the database. The intensity of the symptoms experienced during PTA (fever, trismus, alteration of the general state) could conduct the patients to consult directly in emergency departments. The missed cases bias should be an explanation of our low rate of PTA (4,32,33). This could also conduct to underestimate the risk of PTA under NSAIDs.

The last limitation was due to the non-interventional nature of the study. Patients suffering from pharyngitis were not randomized for NSAIDs prescription. This could result to an indication bias: NSAIDs could be more prescribed for the most painful patients. We didn't find evidence in the literature that pain intensity was a risk factor of PTA, but this is an assumption that cannot be excluded. In this hypothesis, the risk of PTA under NSAIDs could have been over estimated. Indeed, the causal link between NSAIDs prescription and PTA could not be definitively proved by our analysis, but this study, however, reflected the actual practices in primary care.

Comparison with existing literature

These results are consistent with some other published studies. However, when studying the association between NSAIDs and PTA during pharyngitis, the majority of studies focused only on patients suffering from PTA (6,9,18,30). Only one another case-control study was reported, where non-prescription of NSAIDs was associated with PTA (8). In this study, controls where patients suffered from sore throat, not only pharyngitis (8). This makes difficult to compare this result to ours. The risk of PTA could be lesser for a nasopharyngitis than for pharyngitis. Patients with nasopharyngitis could receive more NSAIDs than those with pharyngitis and so decrease the risk of PTA in the treated group. To explain an increased risk of PTA under NSAIDs, several mechanisms have been proposed: alteration of the immune response by decreasing degranulation of the neutrophil cells (34) up to agranulocytosis (35) and/or delayed diagnosis by reduction of symptomatology (36).

NSAIDs exposure rates varied widely among studies, ranging from rates <10% (7) to 80%, sometimes with confusion between NSAIDs and corticosteroids (6,8,9,18,30). The role of corticosteroids was also suspected in the literature, mainly because of their immunomodulatory properties (37).

Several studies found similar results to ours concerning the lack of protection of antibiotics in the appearance of PTA (4,6,7,9,30,38). However, a meta-analysis found a modest protective effect of antibiotics but for all sore throats confounded (39). Several hypotheses have been put forward to explain these results: a greater frequency of antibiotic treatments in patients most at risk of complications (38), a co-prescription antibiotics—NSAIDs (30) or the rapid development of PTA, 2–3 days after the first symptoms of pharyngitis, leaving no time for antibiotic therapy to be effective (4).

As in our study, the average age of patients with PTA in the literature ranged between 27 and 32 years (4,7–9,18,30,40,41) and mainly concerned the age group 20–40 years (4,8,9). Contrary to our study, a Swedish one found a considerably higher incidence of PTA among the 14–21 years old age group than older age groups (42) but studied both PTA and peritonsillar cellulitis. The risk of PTA could be very low before 14 years old and be higher after 14 years old. In our study, we only had seven PTA for patients aged 0–20 years old. We would have an important lack of power if this age group was split to confirm this interpretation. The absence of PTA in patients aged 60 years and older in our data can be explained by the low incidence of pharyngitis at these age (6.13%), confirmed in other studies (7,9,30).

The predominance of PTA among males (55–65% of PTA) has been already reported (6,8,9,29,30,40,41) and could be explained by tobacco exposition that is a risk factor for PTA (4,5,8). Smoking is more prevalent with men, with consumption peaking between 20 and 40 years (43). There is no clear explanation for the increased risk of PTA by smoking.

Seasonality was not highlighted in our study. This was mentioned in only two studies (9,41), but with a non-significant effect on the risk of PTA.

The delay between the first oropharyngeal symptoms and the appearance of peritonsillar phlegmon is poorly understood. A study estimates it to 4 days with extremes ranging from 1 to 15 days (6).

Because PTA is an infectious complication, immunosuppression may be a risk factor. The only data available in our database for immunosuppression were the presence of cancer or diabetes. However, the absence of patients with diabetes or cancer suffering from PTA did not allow us to explore this hypothesis. The few

studies investigating this subject have also found very low numbers of PTA in these populations, thus preventing an conclusion to be drawn (4,8,9).

In our study, the frequency of consultations for PTA after a consultation for pharyngitis in primary care (0.04%) was lower than the frequency of PTA found in the literature: 0.1% in a French hospital study and 0.1–0.2% in two English studies carried out on an outpatient basis (4,33,38). This could be explained by the missed case bias, but also because the other studies took into account all the PTAs preceded or not by a consultation for pharyngitis (4,38). Furthermore, contrarily to the other French study, we did not considered consultations in hospital emergency departments (7,9,30).

This study took into account only patients consulting their GP for pharyngitis, so it cannot be generalized to all sore throat or to all patients with pharyngitis who self-medicate.

Implication for research and practice

This study showed that the prescription of NSAIDs in pharyngitis is independently associated with a higher risk of PTA. This result encourages careful consideration of the balance between benefits and harms before prescription of NSAIDs for pharyngitis, especially for patients aged 20–39 who appear to be at highest risk of PTA. These results, however, should be moderated because the risk of PTA remains low despite the prescription of NSAIDs. Yet, the potential severity of PTA should impose vigilance against any preventable risk factor. It seems important to explain the benefit-risk balance of NSAIDs to patients before any prescription or non-prescription, as NSAIDs are available over-the-counter. In order to determinate at best the risk factors for PTA and prove causal links, a randomized prospective study would be ideal. Yet, the low incidence of PTA makes such study difficult to conduct in practice. A national database in general practice with standardization of the results of consultation would at least refine these results.

Supplementary material

Supplementary material is available at *Family Practice* online.

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Declaration

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Conflict of interest: none.

References

1. Shulman ST, Bisno AL, Clegg HW *et al*. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2012; 55: 1279–82.
2. CMIT. UE6—n°146 : angine de l'adulte et de l'enfant et rhinopharyngites de l'enfant. http://www.infectiologie.com/UserFiles/File/formation/ecn-pilly/ecnpilly2016-ue6-146-web.pdf (accessed on 23 July 2017).
3. Schappert SM, Rechsteiner EA. Ambulatory Medical Care Utilization Estimates for 2006. 2008. http://www.lahealthaction.org/library/Ambulatory_Medical_Care.pdf (accessed on 8 February 2017).
4. Dunn N, Lane D, Everitt H, Little P. Use of antibiotics for sore throat and incidence of quinsy. *Br J Gen Pract* 2007; 57: 45–9.
5. Paganelli A, Khalfallah SA *et al*; de travail de la SFORL G. Recommandation de la SFORL sur les complications locorégionales des pharyngites. *Annales françaises d'Oto-rhino-laryngologie et de Pathologie Cervico-faciale*. 2014; 131: 211–16.
6. Pinaud V. Phlegmons péri-amygdaliens chez l'adulte épidémiologie de 34 observations nantaises. 2008. http://archive.bu.univ-nantes.fr/pollux/show.action?id=50b2cc5c-6456-4964-9a96-77290adc96ab (accessed on 11 July 2017).
7. Page C, Peltier J, Medard C, Celebi Z, Schmit JL, Strunski V. [Peritonsillar abscesses (quincy)]. *Ann Otolaryngol Chir Cervicofac* 2007; 124: 9–15.
8. Lepelletier D, Pinaud V, Le Conte P *et al*; for the French PTA Study Group. Is there an association between prior anti-inflammatory drug exposure and occurrence of peritonsillar abscess (PTA)? A national multicenter prospective observational case–control study. *Eur J Clin Microbiol Infect Dis* 2017; 36: 57–63.
9. Lepelletier D, Pinaud V, Le Conte P *et al*; for the French PTA Study Group. Peritonsillar abscess (PTA): clinical characteristics, microbiology, drug exposures and outcomes of a large multicenter cohort survey of 412 patients hospitalized in 13 French university hospitals. *Eur J Clin Microbiol Infect* 2016; 35: 867–73.
10. Revue Prescrire. Diagnostic et traitement des angines aigues 3ème partie. *Soulager les symptomes d'angines : d'abord un antalgiques et des moyens non médicamenteux* 2004; 24: 443–8.
11. ANSM. Analyse des ventes de médicaments en France en 2013. 2014. http://ansm.sante.fr/var/ansm_site/storage/original/application/3df7b99f8f4c9ee634a6a9b094624341.pdf (accessed on 27 November 2016).
12. Besnard M. Médecins généralistes, AINS et infections ORL : quelles pratiques ? Comparaison aux recommandations actuelle. 2013. http://dune.univ-angers.fr/fichiers/20076432/2013MCEM1664/fichier/1664F.pdf (accessed on 23 July 2017).
13. Pierce CA, Voss B. Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. *Ann Pharmacother* 2010; 44: 489–506.
14. Perrott DA, Piira T, Goodenough B, Champion GD. Efficacy and safety of acetaminophen vs ibuprofen for treating children's pain or fever: a meta-analysis. *Arch Pediatr Adolesc Med* 2004; 158: 521–6.
15. Bertin L, Pons G, d'Athis P *et al*. Randomized, double-blind, multicenter, controlled trial of ibuprofen versus acetaminophen (paracetamol) and placebo for treatment of symptoms of tonsillitis and pharyngitis in children. *J Pediatr* 1991; 119: 811–4.
16. Ruperto N, Carozzino L, Jamone R *et al*. A randomized, double-blind, placebo-controlled trial of paracetamol and ketoprofren lysine salt for pain control in children with pharyngotonsillitis cared by family pediatricians. *Ital J Pediatr* 2011; 37: 48.
17. Lala I, Leech P, Montgomery L, Bhagat K. Use of a simple pain model to evaluate analgesic activity of ibuprofen versus paracetamol. *East Afr Med J* 2000; 77: 504–7. http://www.ajol.info/index.php/eamj/article/view/46696 (accessed on 14 July 2017).
18. Feasson T. Phlegmons péri-amygdaliens : impact des anti-inflammatoires. 2015. http://bibnum.univ-lyon1.fr/nuxeo/nxfile/default/1abfca66-95e4-40a1-bff1-5ba3635e2fb2/blobholder:0/THm_2016_BELBAL_Karima.pdf (accessed on 11 January 2017).
19. Scottish Intercollegiate Guidelines Network (NHS). Management of Sore Throat and Indications for Tonsillectomy. 2010. http://www.sign.ac.uk/assets/sign117.pdf (accessed on 22 July 2017).
20. Chiappini E, Principi N, Mansi N, *et al*. Management of acute pharyngitis in children: summary of the Italian National Institute of Health Guidelines. *Clin Ther* 2012; 34: 1442–58.e2.
21. Azria R, Barry B, Bingen E *et al*. Antibiotic stewardship. *Médecine et Maladies Infectieuses* 2012; 42: 460–87.
22. Saint-Lary O, Boisnault P, Naiditch M *et al*. Performance scores in general practice: a comparison between the clinical versus medication-based approach to identify target populations. *PLoS ONE*. 2012; 7: e35721.
23. SFMG. Informations sur les données de l'Observatoire de la Médecine Générale). http://omg.sfmg.org/content/com/toutsuromg.pdf (accessed on 14 June 2017).

24. DREES. TABLEAU 11. NOMBRE D'ACTIVITÉS exercées par les médecins par spécialité, taille d'unité urbaine, tranche d'âge et sexe. 2016. http://www.data.drees.sante.gouv.fr/TableViewer/tableView.aspx?ReportId=3336 (accessed on 25 October 2018).
25. Ferru P, Kandel O. *Dictionnaire Des Résultats de Consultation (Dictionary of Consultation Results). Révision 2003–2004*. Paris: Société Française de Médecine Générale, 2004. http://www.sfmg.org/data/generateur/generateur_fiche/444/fichier_dr62_maj_drc_2004b314c.pdf (accessed on 29 June 2017).
26. SFMG. Dictionnaire des résultats de consultation en médecine générale. 2010. http://www.sfmg.org/data/generateur/generateur_fiche/749/fichier_drcc0d8b.pdf (accessed 18 July 2017).
27. Rosman S, Le Vaillant M, Pelletier-Fleury N. Gaining insight into benzodiazepine prescribing in General Practice in France: a data-based study. *BMC Fam Pract* 2011; 12: 28.
28. Haas H. Antibiothérapie probabiliste aux urgences dans les abcès de la tête et du cou de l'enfant. *Archives de Pédiatrie* 2008; 15: 495–7.
29. Tachibana T, Orita Y, Takao S *et al.* The role of bacteriological studies in the management of peritonsillar abscess. *Auris Nasus Larynx* 2016; 43: 648–53.
30. Demeslay J, De Bonnecaze G, Vairel B *et al.* Possible role of anti-inflammatory drugs in complications of pharyngitis. A retrospective analysis of 163 cases. *Eur Ann Otorhinolaryngol Head Neck Dis* 2014; 131: 299–303.
31. Kim SY, Chang Y-J, Cho HM, Hwang Y-W, Moon YS. Non-steroidal anti-inflammatory drugs for the common cold. In: JohnWiley & Sons, Ltd, ed. *The Cochrane Library*. Chichester, UK: John Wiley & Sons, Ltd, 2015. https://onlinelibrary-wiley-com.etna.bib.uvsq.fr/doi/10.1002/14651858.CD006362.pub4/abstract (accessed on 31 January 2016).
32. Peterson I, Johnson AM, Islam A *et al*. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. *BMJ* 2007; 335: 982.
33. Maugat S, Léon L, Vaux S. Augmentation de l'incidence des séjours hospitaliers pour infection ORL grave ? Analyse de la base PMSI nationale 2002–2010. http://www.infectiologie.com/UserFiles/File/medias/JNI/JNI13/posters/2013-JNI-P-03.pdf (accessed on 11 January 2017).
34. Kaplan HB, Edelson HS. Effects of Non-steroidal Anti-inflammatory Agents on Human Neutrophil Functions In Vitro and In Vivo. http://ac.els-cdn.com/0006295284902284/1-s2.0-0006295284902284-main.pdf?_tid=5d671c1a-d015-11e6-bf35-00000aab0f01&acdnat=1483270266_1fa8d53d39ee5c9dbc4b3e5ca13098d5 (accessed on 1 January 2017).
35. Services d'hématologie Lyon Sud et GH Edouard Herriot. Sang et métabolisme. http://lyon-sud.univ-lyon1.fr/servlet/com.univ.collaboratif.utils.LectureFichiergw?ID_FICHIER=1320397714254 (accessed on 1 January 2017).
36. Revue Prescrire. AINS : phlegmons, cellulites cervicales ? *Prescrire* 2014; 34: 516.
37. Coutinho AE, Chapman KE. The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights. *Mol Cell Endocrinol* 2011; 335: 2–13.
38. Petersen I, Johnson AM, Islam A, Duckworth G, Livermore DM, Hayward AC. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. *BMJ* 2007; 335: 982.
39. Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. In: The Cochrane Collaboration, ed. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd, 2013. http://doi.wiley.com/10.1002/14651858.CD000023.pub4 (accessed on 5 January 2017).
40. Windfuhr JP, Chen YS. Immediate abscess tonsillectomy—a safe procedure? *Auris Nasus Larynx* 2001; 28: 323–7.
41. Mazur E, Czerwińska E, Korona-Głowniak I, Grochowalska A, Kozioł-Montewka M. Epidemiology, clinical history and microbiology of peritonsillar abscess. *Eur J Clin Microbiol Infect Dis* 2015; 34: 549–54.
42. Risberg S, Engfeldt P, Hugosson S. Incidence of peritonsillar abscess and relationship to age and gender: retrospective study. *Scand J Infect Dis* 2008; 40: 792–6.
43. Beck F, Guignard R. Prevalence du tabagisme en France et comparaisons internationales. 2012. http://inpes.santepubliquefrance.fr/Barometres/barometre-sante-2010/pdf/prevalence-tabagisme.pdf (accessed on 1 May 2017).