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Medical papers related to keywords of vaccine and vaccination in KoreaMed database, Korea (1962-2012)

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Purpose: To describe the present status and changing patterns of medical papers related to keywords of vaccine and vaccination published in Korea over the last 50 years, and provide basic data for future studies.

Materials and Methods: 185,603 papers are registered in the medical database KoreaMed, which is run by Korean Association of Medical Journal Editors. Among these papers, a search with the keywords vaccine or vaccination revealed a total of 1,089 articles which were published on vaccine and/or vaccination during the period of September 2, 1962 to April 30, 2012. Our study endeavors to analyze these 1,089 articles.

Results: Only one article published with the keywords vaccine and/or vaccination was published in the 1960s, and the number of journals steadily increased starting from the 1970s (24 articles) to 2 times, 10 times, 20 times in the 1980s, 1990s, and the 2000s (585 articles), respectively. The articles were classified into reviews (20.2%), original articles with clinical study (40.7%), original articles with experimental study (24.6%), and case reports (8.2%). The review articles mainly dealt with an overview. The original articles with clinical study were on epidemiology, effect and immunogenicity, clinical trial. Original articles with experimental study were mainly comprised of complication and overview. Articles on vaccine, pathogen or disease topics were mostly microorganisms such as bacteria or viruses, and studies on anti-cancer vaccines or vaccines of specific diseases were sparse.

Conclusion: The above data reflects the clinical uses of vaccines in Korea and the history of vaccine studies. The number of vaccine-related articles is increasing rapidly since the first article was published in 1962. This implies that with the increase of studies of clinical trials, clinical uses and results and analyses of the results, articles relating to basic studies are also on the rise. We intend these findings to be of use to researchers in this active and expanding field.

Keywords: Medical papers, Journals, Vaccines, Vaccination, KoreaMed, Medline, PubMed

Introduction

Numerous science and engineering papers are published daily. According to the report of Science and Engineering Indicators 2010 of the U.S. National Science Foundation [1,2], the article counts from a set of journals covered by Science Citation Index (SCI) and Social Science Citation Index (SSCI) [3] during the period between 1995 to 2007, reaches a count of 2.55 million articles, 3.6 times the count of Japan with 0.7 million articles. The leading five countries in order are the U.S., Japan, England, Germany, France with Korea in 14th place with 143 thousand articles and a count rapidly

increasing since 1993.

In 2009, the SCI article count of all documented articles on all sciences worldwide is 1.41 million with Korea's count being 42 thousand (2.9%), and the count of research papers excluding meeting abstracts worldwide is 1.11 million with Korea's count 37 thousand (3.3%). The number of medical papers registered up to April, 2012 at the medical database KoreaMed [4] run by Korean Association of Medical Journal Editors (KAMJE) is 185,603 in 188 different medical journals. Also the number of journals in this database is increasing rapidly each year.

Among the increasing Science and Engineering papers, how many are related to the keywords "vaccine and vaccination"? This is the essence of our study. Since analyzing the current trend of all overseas articles is difficult due to the sheer volume, we decided to analyze the trend in Korea through KoreaMed. With the papers registered in KoreaMed from January 1, 1962 to April 30, 2012 we analyzed the number and propotion of medical papers related to keywords of vaccine and vaccination, and classified them according to the article types. We also tried to establish characteristics of medical papers related to the keywords vaccine and vaccination published in the last 50 years by analyzing the subjects of the original articles, the subjects' age, study topic, and microorganism or vaccine lists. Therefore, our purpose is to grasp the current state of vaccine-related studies in Korea and provide information for further studies.

Materials and Methods

The medical database KoreaMed [4], managed by KAMJE was founded and started registering journals on December 31, 1996. Currently 185,603 papers in 188 types of medical journals are registered up to April 30, 2012. There was a total of 1,089 articles related to vaccine and/or vaccination when searched with the keywords vaccine or vaccination. These were articles published from, September 2, 1962 to April 30, 2012. The following categories were analyzed regarding these 1,089 articles (Table 1).

The categories are as follows: 1) the types of articles (review articles, original articles, case reports), 2) the subjects of the original articles (clinical study, *in vitro* and *in vivo* experimental study), 3) the age of the subjects (children, adults, children+adults, animals, laboratory, others), 4) the topics (overview, epidemiology, effect, diagnosis, prevention, etiology and pathogenesis, characteristics, manifestations, treatment, clinical trials, complication, immunogenicity, others), 5) microorganism or vaccine lists.

Results

Number of medical papers by searching the keywords vaccine and/or vaccination in KoreaMed database (September 2, 1962 to April 30, 2012)

185,603 articles were registered in KoreaMed until the end of April in 2012. When searched with the keyword vaccine or vaccination separately, 670 articles were found on vaccine and 700 articles were found on vaccination. A more specific research revealed 389 articles found only in the vaccine keyword search, 419 articles found only in the vaccination keyword search, and 281 articles appeared in both searches. Thus, the total number of articles relating to vaccine and/or vaccination is 1,089. This comprises 0.58% of the total 185,693 articles (Table 1).

Number of medical papers by searching vaccine and or vaccination and minor keywords in KoreaMed database (September 2, 1962 to April 30, 2012)

The distribution of articles when the keywords vaccine and/

Table 1. Number of medical papers by searching the keywords vaccine and/or vaccination in KoreaMed[a] database (September 2, 1962-April 30, 2012)

Category	No.
No. of medical journals in KoreaMed database	188
No. of medical papers (abstract) in KoreaMed database (A)	185,603
No. of medical papers (abstract) with keywords of "vaccine" in KoreaMed database	670
No. of medical papers (abstract) with keywords of "vaccination" in KoreaMed database	700
No. of medical papers (abstract) with keywords of "vaccine and/or vaccination" in KoreaMed database (B)	1,089
(B)/(A) (%)	0.58

[a]KoreaMed: KoreaMed search system provides access not only to the KoreaMed database of bibliographic information but also medical journal information, is established by the Korean Association of Medical Journal Editors (http://www.koreamed.org).

or vaccination and various minor keywords were searched is organized in Table 2. The minor keywords, in conjunction with major keywords vaccine and/or vaccination, included the following with the numbers representing the count of articles; study (311), infection (215), virus (189), research (180), clinical (183), control (174), immunization (171), children (160), antibody (149), cell (147), immune (140), prevention (135), human (134), immunology (129), response (126), development (118), protein (111), review (111), analysis (106), antigen (103).

Article count on vaccine and/or vaccination published yearly

After 1962, the number of articles about vaccine and/or vaccination being published in a decade is mounting up. One ar-

Table 2. Number of medical papers by searching vaccine and/or vaccination and minor keywords in KoreaMed[a] database (September 2, 1962-April 30, 2012)

Keywords	No.	Keywords	No.	Keywords	No.	Keywords	No.
Acceptability	1	Detection	27	Infection	215	Purification	50
Accuracy	7	Development	118	Inflammatory	14	Rash	4
Activated	12	Diarrhea	16	Injection	39	Reaction	67
Active	36	Distribution	34	Intramuscular	10	Receptor	11
Adult	95	DNA	82	Investigation	24	Recommendation	21
Adverse reaction	12	Dose	69	Investigator	2	Research	188
Analysis	106	Effect	87	Isolation	30	Response	126
Animal	60	Efficacy	92	Knowledge	20	Review	111
Antibody	149	Enzyme	47	Live-attenuated	28	RNA	23
Anti-cancer	6	Epidemiology	69	Manifestation	8	Safety	70
Antigen	103	Etiology	8	Measurement	6	Schedule	33
Anti-tumor	13	Expression	57	Mechanism	15	Sequence	40
Application	14	Factor	33	Monitor	4	Sero-conversion	37
Bacteria	21	Fever	55	Need	49	Sero-epidemiology	6
Cancer	93	Follow up	29	Novel	25	Serology	2
Case	64	Genetics	56	Oral	35	Serotype	27
Case report	34	Genotype	12	Organism	6	Surveillance	15
Cell	147	Guideline	11	Outbreak	26	Shock	12
Characteristics	32	Health care	23	Parasite	8	Side effect	6
Children	160	Heterogeneity	3	Passive	6	Site	39
Classification	9	Host	31	Past	32	Status	53
Clinical	183	Human	134	Pathogenesis	11	Storage	5
Clinical trial	39	Identification	18	Pattern	22	Strategy	27
Cloning	13	Immune	140	PCR	46	Structure	8
Cohort	4	Immunity	98	Peptide	20	Study	311
Colony	17	Immunization	171	Post-marketing	1	Survival	28
Combination	17	Immunoassay	13	Potency	4	Therapy	1
Combined	17	Immunogenecity	10	Practice	18	Toxicity	6
Complication	19	Immunology	129	Prediction	2	Trans-cutaneous	2
Concept	5	Immunotherapy	32	Prevalence	46	Treatment	93
Content	4	Impact	13	Prevention	135	Trial	51
Control	174	*In vitro*	29	Production	53	Tumor	63
Cost	21	*In vivo*	32	Prophylaxis	2	Update	7
Coverage	31	Inactivated	44	Prospects	3	Validity	4
Current issue	1	Incidence	75	Protection	60	Viral	106
Cytotoxic	28	Indication	4	Protective effect	16	Virus	189
Defense	2	Industry	7	Protein	111	Volunteer	1

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ticle in the 1960s (0.1%), 24 in 1970s (2.2%), 46 in 1980s (4.2%), 242 in 1990s (22.2%), 585 in the 2000s (53.8%), 191 from 2010 to April, 2012 (27.5%) were published. There is a significant rise in numbers especially since the 1980s onwards. With the 1970s as a reference point, there was a two-fold rise in the 1980s, 10-fold rise in the 1990s, and a 20-fold rise in the 2000s. This was evidence that showed the correlation to the historical background in the usage of vaccines and/or vaccinations (Table 3).

Table 3. Article count on vaccine and/or vaccination published yearly in KoreaMed[a] database (September 2, 1962-April 30, 2012)

Years	No. of papers	%	Cumulative %
1962-1969	1	0.1	0.1
1970-1979	24	2.2	2.3
1980-1989	46	4.2	6.5
1990-1999	242	22.2	28.7
2000-2009	585	53.8	82.5
2010-Apr 2012	191	27.5	100.0
Total	1,089	100.0	100.0

[a]KoreaMed: KoreaMed search system provides access not only to the KoreaMed database of bibliographic information but also medical journal information, is established by the Korean Association of Medical Journal Editors (KAMJE) (http://www.koreamed.org).

Characteristics of the articles

Types of articles

The total of 1,089 articles were comprised of 220 review articles (20.2%), 780 original articles (71.6%), and 89 case reports (8.2%). Of the 780 original articles, there were 512 (65.4%), 268 (34.4%) articles of clinical study and articles of experimental study, respectively. Of the 268 articles on experimental study, *in vivo* and *in vitro* took up 122 (45.5%) and 146 (54.5%) each. The original articles with clinical study covered the widest range (Table 4).

Contents of the articles

The 1,089 articles containing review articles, original articles, and case reports were classified into different categories by their contents; 24.4% were overviews, 11.7% of epidemiology, 25.3% of effect and immunogenicity, 1.9% of diagnosis, 0.6% of prevention, 10.1% of etiology and pathogenesis, 2.0% of characteristics, 2.5% of manifestations, 3.0% of treatments,

Table 4. Characteristics of the articles

Characteristics	Review articles (n=220)	Original articles (n=780)				Case reports (n=89)	Total (%)
		Clinical (n=512)	Experimental (n=268)		Sub-total		
			In vivo (n=122)	*In vitro* (n=146)			
Contents of the articles							
Overview	175	62	1	1	64	27	266 (24.4)
Epidemiology	18	106	1	2	109	0	127 (11.7)
Effect and immunogenecity	10	131	76	57	264	2	276 (25.3)
Diagnosis	1	8	2	9	19	1	21 (1.9)
Prevention	2	3	1	0	4	1	7 (0.6)
Etiology and pathogenesis	1	17	31	61	109	0	110 (10.1)
Characteristics	1	9	2	10	21	0	22 (2.0)
Manifestation	3	23	0	0	23	1	27 (2.5)
Treatment	6	13	7	5	25	2	33 (3.0)
Clinical trial	1	124	0	0	124	0	125 (11.5)
Complication	2	16	1	1	18	55	75 (6.9)
Total	220	512	122	146	780	89	1,089 (100.0)
Subjects of the articles							
Children	23	225	0	0	225	56	304 (27.9)
Adut	65	168	0	0	168	25	258 (23.7)
Children+adult	103	102	0	0	102	2	207 (19.0)
Animal	5	0	122	0	122	0	127 (11.7)
Experimental	19	11	0	146	157	0	176 (16.2)
Other	5	6	0	0	6	6	17 (1.6)
Total	220	512	122	146	780	89	1,089 (100.0)

11.5% of clinical trials, 6.9% of complications.

Most of the reviews were overviews (175/220) while original articles with clinical study were mostly composed of epidemiology, effect and immunogenicity, and clinical trials. Original articles with experimental study were mainly composed of effect and immunogenicity, and etiology and pathogenesis while case reports were mostly complications and overviews (Table 4).

Subjects of the articles

The subjects of the 1,089 articles were divided into children (27.9%), adults (23.7%), children and adults (19.0%), animals (11.7%), laboratory experiments (16.2%), others (1.6%). The review articles and original articles with clinical study usually dealt with humans (children, adults, or both), while original articles with experimental study mostly dealt with animals in *in vivo* studies, and laboratory data in *in vitro* studies (Table 4).

Vaccine, pathogen, or disease topics

The types of vaccines, pathogens, and diseases chosen as topics in review articles, original articles with clinical study, original articles with experimental study (*in vivo* and *in vitro*), and case reports are shown in Table 5. There was a wide variation in the vaccines chosen as the topic among the review articles, clinical studies, experimental studies, and case reports. The review articles, clinical studies, and case reports mostly dealt with vaccines currently in use while experimental studies included a wider range of topics.

Table 5. Vaccine, pathogen, and disease topics in frequency

Review articles
HPV, Hepatitis B virus, Influenza, Hepatitis A virus, Varicella zoster virus, Rotavirus, BCG tuberculosis, MMR, Small pox, AIDS, Hib., Non-specific, *Strptococcus pneumoniae*, DNA vaccine, RS virus, EB virus, Ocular vaccination, Adenovirus, DTP, AngQb, Hepatitis C virus, *Helicobacter pylori*, Cancer, AGI infection, *Toxoplasma gondi*, Norovirus, Meningococcal, Coccidia virus, Chicken pox, Rabies, Others
Original articles with clinical study
Hepatitis B virus, Influenza, Hepatitis A virus, BCG, tuberculosis, HPV, *Streptococcal pneumonia*, DPT, D, T, P, Td, Hantann virus, Tuberculosis, Rotavirus, Varicellar zoster virus, MMR, M, M, R, Hib., CpG oligodeoxynucleotide, ADEM, Japanese encephalitis virus, Dendritic cell, Enterovirus, *Plasmodium falciparum, Plasmodium vivax*, Yellow fever, Small pox, Non specific, Varicella, Meningococcal, Mouse and human type of CpG, Hog cholera virus, *Neisseria meningitis*, RS virus, *Saccharomyces cerevisiae*, Hematopoietic stem cell, Rabbit papilloma, Rabies, *H. pylori, Mycoplasma pneumoniae, Porphyromonas gingivalis*, HIV, DNA, *Shigella sonnei,* New castle disease, Dendritic cell, *Salmonella typhi*, Anti-tumor, *Pseudomonas aeruginosa*, Combined Hepa-DTP vaccine, Leptospires virus, Others
Original articles with experimental study (in vivo)
Influenza virus, BCG, Tb., Dendritic cell, DPT, D, T, P, IBDV, Hepatitis B virus, *Cryptosporidium baileyi*, Entero virus, Anticancer, HIV Type I, New castle disease, *Sarcocystitis ovi-canis, Leishmania amazonensis*, Murine toxoplasmosis, CpG oligodeoxynucleotide, *Neospora caninum, Acanthamoeba culbertsoni, Schistosoma mansoni, Actinobacillus pleuropneumoniae, Hyalomma dromedarii,* Transgenic carrot, CIITA gene, Plasmid DNA vaccine, *Plasmodium chabaudi adami, Vibrio vulnificus, Francisella tularensis, Bacculo virus, Photobacterium damselae,* HPV, RS virus, Infectious bursal disease virus, Baculo virus, *S. pneumoniae*, GnRH based, HSV, *Porphyromonas gingivalis, Theileria sergenti*, Hepatitis A virus, Leptospira virus, Rotavirus, Recombinant vaccine, Poliomyelitis vaccine, Hantann virus, *Fasciola gigantica,* Baculo-based vaccine, *Coccidiosis protozoa, Salmonella enteritidis, Brucella abortus,* Hepatitis C virus, DNA virus, 5-aza-2'-deoxycytidine (ADC), Hog cholera virus, Hantann virus vaccine, Varicella zoster virus, Others
Original articles with experimental study (in vitro)
Dendritic cell, BCG, Tb, Other Mycobacterium, Hepatitis B virus, HSV, Influenza virus, Anti-tumor, New castle disease virus, RS virus, *H. pylori, Porphyromonas gingivalis, Vibrio vulnificus, Leishmania promastigotes,* Japanese encephalitis virus, *Bordetella bronchiseptica,* Varicella zoster viurs, *Salmonella typhi*, Entero virus, Dengue fever, HPV, Herpes virus, Swine fever virus, *Plasmodium berghei*, Rabies, *Clostridium difficle, Pasteurella multocida,* Glioma, Bovine corona virus, HER 2 neu, *Clonorchis sinensis,* Sarcocystis, Bursal disease virus, *Actinomyce temcomitans,* HGM-CSF, Hepatitis C virus, Rota virus, *Photobacterium damselae,* Hib., Allogeneic-DC Vaccine, NK cell, Polio virus, *Actinobacillus pleuropneumoniae*, Porcine respiratory syndrome virus, HID virus, *Toxoplasma gondii,* Bovine mastitis, *Theileria sergenti, Escherichia coli, Shigellar sonnei,* Hantann virus, Pertussis, HFRS, *Bacillus anthracis,* MMR, Pseudorabies virus, *Boophilus annulatus,* Others
Case report
BCG, Tuberculosis, Influenza, Herpes zoster virus, Hepatitis B virus, *Mycoplasma pneumonia*, MMR, M, M, R, Yellow fever, DTP, D, T, P, *Pesudomonas aeroginosae, Tetanus trismus,* Complement 9 deficiency, Cerebelitis, Hemorrhagic fever, Hepatitis A virus, ADEM, Rickettsia, Granulomatous disease, Encephalomyelitis, HID virus, Toxic epidermal necrolysis, *S. pneumoniae, Nisseria meningitis,* Kawasaki disease, *Perifolliculitis capitis,* Others

HPV, human papillomavirus; BCG, Bacillus Calmette-Guérin; MMR, measles, mumps, and rubella; AIDS, acquired immunodeficiency syndrome; RS, Reed-Sternberg; EB, Epstein-Barr; DTP, diphtheria-tetanus-pertussis; AGI, acute gastrointestinal infection; Td, tetanus and diphtheria; Hib., *Haemophilus influenza* type B; ADEM, acute disseminated encephalomyelitis; HIV, human immunodeficiency virus; IBDV, infectious bursal disease virus; GnRH, gonadotropin releasing hormone; Tb., tuberculosis; HSV, herpes simplex virus; HGM-CSF, human granulocyte-macrophage colony-stimulating factor; NK, natural killer; HFRS, haemorrhagic fever with renal syndrome.

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Discussion

In Medline/PubMed baseline database [5,6], a database of biomedical papers managed by the US National Library of Medicine, approximately 23,000 articles are updated everyday and about 20 million records are contained up to the present May, 2012. Among these articles, 236 thousand articles are found in a search with keywords vaccine and/or vaccination, which is about 1.8% of the total. In the KoreaMed database [4], 1,089 articles were found from a total of 185,603 articles, constituting 0.58% of the total, roughly half the percentage of articles on "vaccine and/or vaccination" in the Medline/PubMed database. In short, compared to the publications on vaccine and/or vaccination worldwide, the publications in Korea are relatively less.

The utilization of vaccines for specific diseases started in the 1970s. Therefore with the start of 1 article on vaccine and/or vaccination published in the 1960s, and 24 in the 1970s, the number has doubled in the 1980s, increased 10-fold in the 1990s, and increased 20-fold to a total of 585 articles in the 2000s. This reflects the active proliferation of studies done on vaccines in Korea around that period. Also, the number is expected to increase even more in the 2010s. Deducing from the results above, the percentage of articles with the keywords "vaccine and/or vaccination" is expected to increase as well as the proportion on the topic of vaccine in biomedical studies and research.

When classified by their types, review articles took up 20.2%, original articles 71.6%, and case reports 8.2%. A more detailed categorization showed reviews, original articles with clinical study, original articles with experimental study, and case reports as 20.2%, 40.7%, 24.6%, 8.2%, respectively with original articles at the most. The original articles were further divided into clinical studies and experimental studies with the ratio of 2:1. The clinical studies and experimental studies in particular are on the rise, and articles with high academic value that provide data for clinical and basic studies were encouraged.

It is a matter of course that the contents of the articles differ according to the article types. The contents of review articles were mostly overview, and the contents of original articles with clinical study were epidemiology, effect and immunogenicity, and clinical trials. Case reports mostly contained complications and overviews, clinical studies had contents on effect and pharmacology, and experimental studies focused on basic research such as pathogenesis and immunologic analysis.

The vaccines, pathogens, or diseases that were the topics of these articles are most probably related to the period background. Thus, studies showed a tendency towards microorganisms such as bacteria and viruses while studies on anticancer vaccines or vaccines of particular diseases were sparse. The trend can be expected to include a wider range of topics such as vaccines dealing with miscellaneous diseases caused by other microorganisms or immunologic diseases, or anticancer vaccines instead of the invention of vaccines for known pathogens.

This study reflects well the historical background of vaccines research and their clinical usage in Korea. Ever since the first article on vaccines was published in 1962, the number of vaccine-related articles are increasing. This shows that research results on basic experiments are also rapidly increasing as well as studies on clinical trials, vaccine utilization, and analysis of the results. We intend these findings to be of use to researchers in this active and expanding field.

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