

Global Trends of Botulinum Toxin Literature: A Bibliometric Analysis of Botulinum Toxin Publications Between 1975 and 2017

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Abstract

Background: Botulinum toxin has been effectively used cosmetically and therapeutically for the last decades in a wide range of medical conditions. Although bibliometrics has been a popular and growing study area in recent years, medical literature lacks studies evaluating published botulinum toxin literature. **Objective:** The goal of our study was to evaluate bibliometric features and to perform a detailed trend analysis in the medical literature related to botulinum toxin. **Materials and Methods:** We analyzed all the published documents including the keywords “botulinum toxin” and “botulinum neurotoxin” and commercial brand names of botulinum toxin products between 1975 and 2017. We performed a detailed bibliometric and scientometric assessment in this field. **Results:** A total of 24,948 articles were retrieved from four databases provided by Web of Science, and most of which were original articles (76.19%). The United States ranked first and dominated literature with 8,729 documents (34.29%) followed by the United Kingdom, Germany, and Italy (14.61%, 11.18%, and 5.5%, respectively). The United Kingdom was detected to be the most productive country with the highest productivity (55.09) followed Switzerland, Denmark, and Germany (47.7, 34.01, and 33.98, respectively). The most studied area was neurology (56.1%) and University of California System was the most productive institution. We noted no correlation between publication number and citations by year. **Conclusion:** We found that all top 10 authors and institutions were from developed countries. Physician from developing and the least-developed countries should be supported to carry out novel studies on botulinum toxin.

Keywords: Bibliometrics, botulinum toxin, botulinum neurotoxin, publication analysis, scientometrics, trend analysis

INTRODUCTION

Botulinum neurotoxin (BoNT) as the most potent biological toxin has been effectively used both therapeutically and cosmetically for a wide range of disorders in various of medical conditions.^[1] Bibliometrics is the evaluation of scientific literature in a certain field in an all-inclusive manner.^[2] Although there has been a rising popularity of bibliometric and scientometric assessment of the scientific data, the medical literature lacks a study investigating bibliometric features of the articles related to BoNT. In this study, we aimed to perform a detailed bibliometric evaluation of botulinum toxin literature and generated a trend analysis in this popular area.

SUBJECTS AND METHODS

All the documents published between 1975 and 2017 including “*botulinum toxin*” and “*botulinum neurotoxin*,” and commercial brand names of BoNT products such as “*botox*,” “*dysport*,” and “*xeomin*” were analyzed in this study. All data used in our study were retrieved from four databases (Web of Science Core Collection, Russian Science Citation Index, SciELO Citation Index, and Korean Journal Database) provided by Web of Science (WoS) (Thomson Reuters, New York). All articles

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published in 2018 were excluded. Articles published from Wales, England, Scotland, and Northern Ireland were evaluated under the United Kingdom main title. The “China” main heading was used for the articles from People’s Republic of China and the mainland of China. Documents from Germany, West Germany, East Germany, and Federal Republic of Germany were united under “Germany” main heading. We performed statistical analyses using SPSS (version 22.0, SPSS Inc., Chicago, IL; licensed for Hitit University, Çorum, Turkey). Spearman’s correlation coefficient analysis was used to investigate a possible correlation between publication numbers and citations of the literature. A value of $P < 0.05$ was accepted as statistically significant. We created infographics revealing world distribution density of botulinum toxin literature using GunnMap free software and Microsoft Excel (Microsoft Corporation, Redmond, Washington).^[3] We created bibliometric network maps showing the most used keywords, and relationships and connection of the countries and the institutions. Bibliometric network visualization maps were generated by using VOSviewer resource freeware (Centre for Science and Technology Studies, Leiden University, Leiden, The Netherlands) in our study.^[4]

RESULTS

Total number of publications

As we searched four databases, a total of 24,948 documents were found and 82.43% of which was in the WoS Core Collection. It was noted that 5,688 items were open access. Most of the documents were original articles ($n = 19,009$; 76.19%). Other most published document types were abstracts, reviews, and meeting reports (17.88%, 17.44%, and 14.4%, respectively) [Table 1]. The United States was the leading country in the literature with 8,729 items (34.29%) followed by the United Kingdom, Germany, and Italy (14.61%, 11.18%, and 5.5%, respectively) [Figure 1]. All top 10 countries ranked by total publication number were developed countries [Figure 2].

Productivity

We calculated a productivity score for each country publishing academic documents. We measured the score with a formula published previously in the literature (total production number of country/population \times 1,000,000). The United Kingdom ranked first with the highest productivity score (55.09) followed by Switzerland, Denmark, and Germany (47.7, 34.01, and 33.98, respectively). The United States which ranked 1 in literature (34.29%) with the total publication number was 8 in this ranking [Figure 3].

Research areas, authors, journals, and institutions

Neurology, pharmacology, and biochemistry were found to be the most studied areas in the literature related to

BoNT (56.51%, 56.12%, and 47.16%) [Table 2]. Aktories was detected to be the most productive author with 235 articles (0.94%) followed by Jankovic and Dressler (0.69% and 0.65%) [Table 3]. All top 10 authors were from developed countries. University of California System was noted to be the most productive institution with 708 items (3%). All institutions were from developed countries [Table 4]. *Movement Disorders* was the leading journal in botulinum toxin literature and covered 3.34% of all documents followed by *Neurology* and *Toxicon* (2.08% and 1.99%, respectively) [Table 5].

Progression of publications and citations and the correlations

We performed a citation analysis of the last decade of BoNT literature. In the last decade, a total of 9,555 articles were published in this field. H-index of botulinum toxin literature was measured to be 83. Documents published in BoNT literature were cited 83,376 times (48,233 times without self-citations) in total between 2008 and 2017. Average citations per item was measured to 8.73 times. Peak year for citations was 2017 ($n = 17,496$) [Figure 4]. We detected no correlation between publication number and citation number by year ($P = 0.232$). The most cited article in this field was found to be titled “Recommendations for the pharmacological management of neuropathic pain: an overview and literature update” by Dworkin *et al.*^[5] published in *Mayo Clinic Proceedings* cited 592 times (average citations per year: 65.78) [Table 6].

Table 1: Document types in scientific literature related to botulinum toxin published between 1975 and 2017

Document type	Number ^a	% ^a
Original article	19,009	76.19
Abstract	4,461	17.88
Review	4,352	17.44
Meeting	3,592	14.4
Case Report	1,859	7.45
Clinical Trial	1,692	6.78
Letter	1,258	5.04
Editorial	1,025	4.11
News	98	0.39
Correction	95	0.38
Book	75	0.3
Reference Material	68	0.27
Biography	19	0.08
Bibliography	8	0.03
Report	7	0.03
Retracted Publication	5	0.02
Retraction	4	0.02
Other	8,352	33.48
Total	24,948	100

^aTotal number may exceed the number of the publications in this field and total percentages may exceed 100% because certain items were included in more than one category

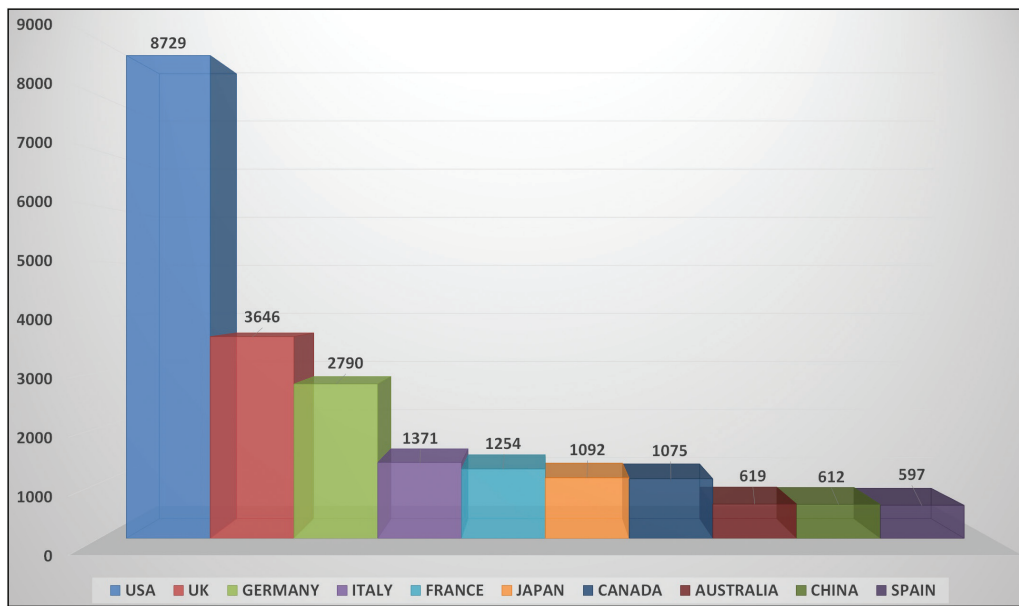


Figure 1: Top 10 countries publishing botulinum toxin publications by total number of documents

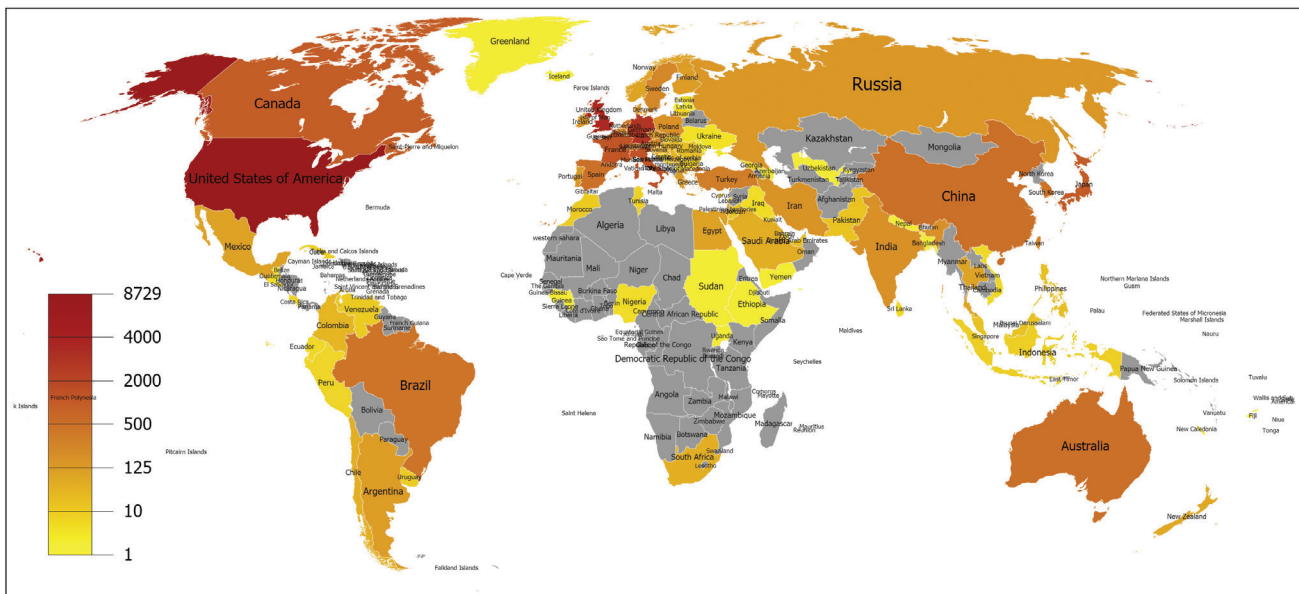


Figure 2: Global publication density on botulinum toxin between 1975 and 2017

Bibliometric network analyses

As we performed a detailed keyword analysis, we found that the most used keywords in this field were “*botulinum toxin*,” “*botulinum toxin type a*,” “*spasticity*,” and “*dystonia*.” We noted that the most used keywords were selected from neurological terms. We generated a bibliometric keyword network visualization map in which the keyword of “botulinum toxin” centered with the largest diameter and connected with the other keywords [Figure 5]. We created a connection network map of the countries producing documents in this area, and this bibliometric network revealed seven main centers including the United States, Germany, United Kingdom, Italy, Canada, France, and Japan.

Institutional bibliometric network showed connections between medical organizations and the companies producing commercial BoNT products [Figure 6].

Indian contribution to the literature

Although Indian population is equivalent to 17.71% of the total world population, it produced only 0.83% of all botulinum toxin literature ($n = 207$ articles). The most common document type was original article (64.368%) followed by review, letter, and meeting abstract (21.839%, 5.747%, and 4.598%, respectively). The most prolific Indian author was Dhaked from Biotechnology Division, Defence Research and Development Establishment,

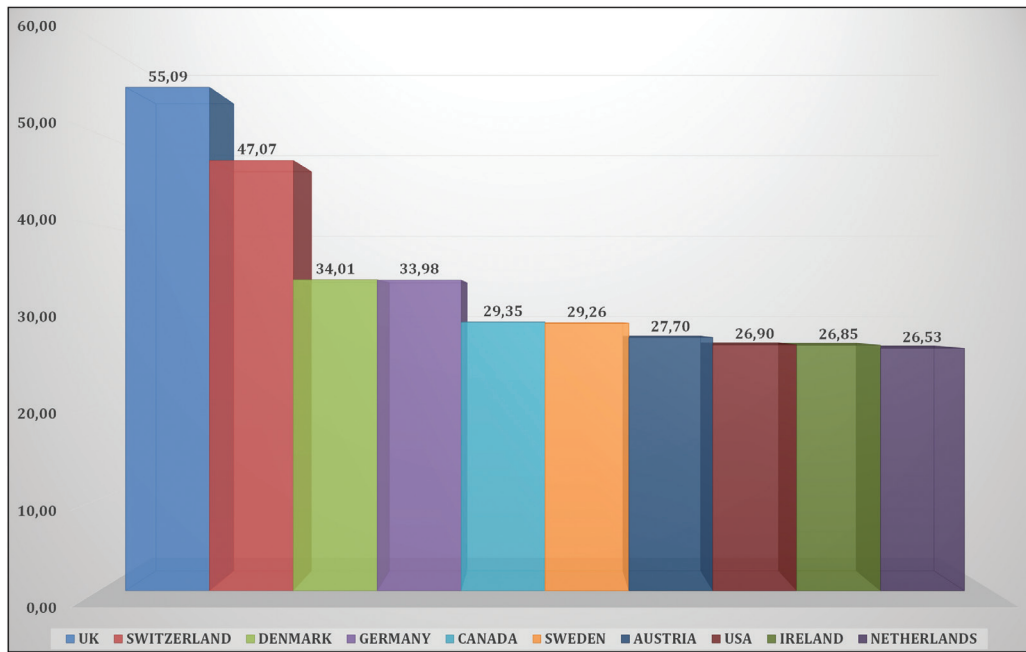


Figure 3: The most productive 10 countries on botulinum toxin literature between 1975 and 2017

Table 2: The first 10 research areas of the publications related to botulinum toxin

Research areas	Number of publications ^a	% ^a
Neurosciences/neurology	13,348	56.51
Pharmacology/pharmacy	13,256	56.12
Biochemistry/molecular biology	11,141	47.16
Toxicology	9,453	40.02
Surgery/plastic surgery	4,459	18.88
Physiology	3,705	15.68
Anatomy/morphology	3,644	15.43
Infectious diseases	3,406	14.42
Behavioral sciences	2,861	12.11
Geriatrics/gerontology	2,858	12.1

^aTotal number may exceed the number of the publications in this field, and total percentages may exceed 100% because certain items were included in more than one category

with 10 articles. Defence Research and Development Establishment was also the most productive institution of the Indian literature with 17 documents. *Annals of Indian Academy of Neurology* was the most productive source title with seven items. H-index of Indian literature was measured as 20 and total number of citations was 1760 (1719 without self-citations). The most cited manuscript was a review titled “Drooling in Parkinson’s disease: a review” written by Srivanitchapoom *et al.*^[6] published in 2014. This article has been cited 123 times in total.

DISCUSSION

Botulinum toxin serotypes inhibit neurotransmitter release from nerve terminals and prevent acetylcholine release at the neuromuscular junction. Seven different types of BoNT titled from BoNT A through BoNT G

Table 3: The first 10 authors by record count

Author	Institution	Country	Record count	% ^a
Aktories	University of Freiburg	Germany	235	0.94
Jankovic	Weill Cornell Medical School	United States	172	0.69
Dressler	Weill Cornell Medical School	Germany	161	0.65
Johnson	University of Wisconsin–Madison	United States	147	0.59
Kozaki	Osaka Prefecture University	Japan	139	0.56
Montecucco	University of Padua	Italy	131	0.53
Barth	University of Ulm	Germany	130	0.52
Popoff	Institute of Pasteur	France	127	0.51
Oguma	University of Tokyo	Japan	117	0.47
Bigalke	Toxogen	Germany	116	0.46

^aTotal documents published in homeopathy literature

have been identified so far. An eighth serotype named BoNT X has been reported more recently but no product of this serotype has been produced yet.^[7] Although *Clostridium botulinum* is the organism for the production of BoNT, some companies have been exploring the use of recombinant expression of *Escherichia coli*.^[8] Generated

infographic of institutional bibliometric map revealed a cooperative network of the companies producing publications in BoNT literature [Figure 6].

Bibliometrics is a novel and popular scientific field investigating academic literature and analyzing publication trends and patterns in a certain area.^[9] Although an expanding and high demand across the world has been reported in noninvasive cosmetic treatment solutions such as botulinum toxin, to the best of our knowledge, there has been no study investigating bibliometric features of botulinum toxin literature.^[10] Thus, the only limitation of our article was that there was no study to compare our results within the literature.

Today, the cosmetic use of BoNT has been reported to be the most common aesthetic procedure performed throughout the world.^[11] Current common aesthetic applications of BoNT include treatment of forehead wrinkles and glabellar, periorbital, perioral, and horizontal neck lines. In 2015, the members of American Society of Dermatologic Surgery (ASDS) performed approximately 10 million treatments and BoNT A was used in 1.8 million of which. The net revenue of BoNT A application in aesthetic indications reached \$199.4 million in 2016 and according to the American Society of Plastic Surgeons, a total of 15.4 million aesthetic procedures were performed during 2016 and in 7 million of which BoNT A was used.^[12] According to 2017 report of ASDS, nearly 12 million cosmetic procedures were performed and BoNT A was applied in 2.1 million of which.^[13] In the United States, three BoNT A formulations are available for aesthetic applications although specific aesthetic versions of BoNT A are on market in the European Union. BoNT B is also available for neurological conditions and it is not yet approved for aesthetic indications.^[14,15] Use of BoNT A has been rising for the last decades cosmetically and therapeutically, and the global market for BoNT A is estimated to reach approximately \$7.4 billion by 2024.^[10] Although the products of botulinum toxin are known to

Table 4: The top 10 institutions by number of publications in literature related to botulinum toxin

Organizations	Document number	%
University of California System (United States)	708	3
University of London (United Kingdom)	649	2.75
University College London (United Kingdom)	485	2.05
United States Department of Defense (United States)	416	1.76
University of Wisconsin System (United States)	398	1.68
University of Wisconsin Madison (United States)	393	1.66
United States Army (United States)	371	1.57
Harvard University (United States)	333	1.41
Hannover Medical School (Germany)	315	1.33
University of Toronto (Canada)	306	1.29

Table 5: The first 10 journal source according to the number of published documents

Journal name	Number of publications	%
<i>Movement Disorders</i>	789	3.34
<i>Neurology</i>	491	2.08
<i>Toxicon</i>	471	1.99
<i>Dermatologic Surgery</i>	353	1.49
<i>European Journal of Neurology</i>	331	1.4
<i>Journal of Urology</i>	319	1.35
<i>Journal of Biological Chemistry</i>	291	1.23
<i>Plastic and Reconstructive Surgery</i>	239	1.01
<i>Neurourology and Urodynamics</i>	232	0.98
<i>Journal of Neurology</i>	188	0.8

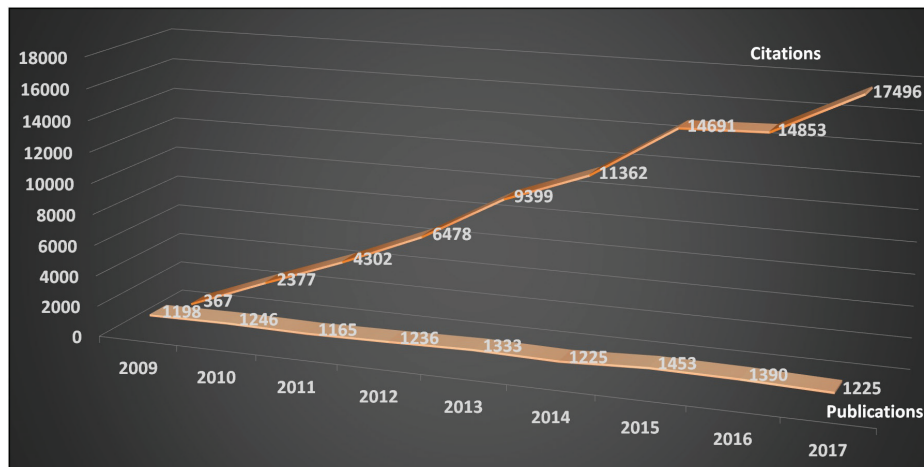


Figure 4: Total publication and citation numbers of botulinum toxin articles by year

Conflicts of interest

There are no conflicts of interest.

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