A PUBMED Survey of Bladder Extrophy Publications - Main Topic: Animal Research

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Background/Purpose: “Researching of research” give the investigators a vision what is done in a special subject of medicine, opens new horizons and give the chance to see the spectrum of science in an enlarged picture. This study aimed to collect and investigate the data in regard to bladder extrophy and mainly focusing on animal research, based on PUBMED and investigate it in a technical and medical point of view.

Materials & Methods: We did a PUBMED search using keywords related to bladder extrophy and related disorders. We investigated only the abstracts for collecting data in regard to find out: 1. Distribution of research articles among countries, institutions, among years, the published journal, authorship details, 2. Type of investigation, 3. The related subtopics, 4. The usage of research animals.

Results: Ten subject related keywords were used and 6281 related articles were found. From these only 3313 bladder extrophy related publications and 249 (7.5%) of these were experimental research and the majority of these articles were published in the last two decades. In 87.2% of the articles were in English language, in 68 different journals from 897 investigators. The sub topics were augmentation, use of matrix, animal models, substitution and diversion. Among the 24 countries and 219 institutions, US was the leading country with 93 articles followed by Japan with 20 articles. Urology journals were leading followed by Pediatric Surgery journals in regard to publishing specialties. Rat was used mostly (36.6%) followed by dog (27.7%) and pig (15.8%) in animal research.

Conclusion: The data showed an increase of animal research based articles in the last two decades, mainly published in English and in English speaking countries and institutions (US is the leading country). These articles were published mainly in Urology journals. The specialties publishing the research are Urology, pediatric surgery, surgery, pediatrics and urology departments or cooperation of these. The rat is the main animal used for research followed by dog, pig, rabbit and lambs.

Index Word: Bladder extrophy, Experimental Animal Models.

INTRODUCTION

“Researching of research” give the investigators a vision what is done in a special subject of medicine, opens new horizons and give the chance to see the spectrum of science in an enlarged picture.

Medical literature surveys can be done in many ways. Library based searches are the classical way to do it but in the last decade, increasing use of internet resources and databases gave the investigators the opportunity to research the medical literature in a very quick and versatile way. Depending on the subject chosen these investigations gives the researchers the opportunity to see the...
published scientific material, which is very helpful to
other researchers to improve their perspective in their
field.
The main topic “bladder extrophy and the animal
research” is chosen for this investigation aims to
investigate the tendency and the related published
work on this subject using internet resource PUBMED.

PATIENTS AND METHODS

A PUBMED search using keywords related to bladder
extrophy and related disorders were done at
September 2008. These searched keywords and
publications were:
1- Bladder extrophy = 1886 - MESH
2- Bladder augmentation = 1283 – Non MESH
3- Extrophy vesica = 71 - Non MESH
4- Ureterosigmoidostomy = 625 – Non MESH
5- Colonic conduit = 410 – Conduit MESH
6- Cloacal extrophy = 288 – Cloaca MESH
7- Epispadias = 695 - MESH
8- Gastrocystoplasty = 135 – Non MESH
9- Enterocystoplasty = 437 – Non MESH
10- Bladder neck reconstruction = 451 - Bladder neck
MESH

Some of these keywords were chosen from MESH and
the remaining were from common pediatric urology
practice (synonyms and thesaurus) to be able to reach
the related subjects for bladder extrophy.

We then studied only the abstracts of the collected
data to find the following parameters:
1. Distribution of research articles among countries,
institutions, years, publishing journal, and authorship
details.
2. Type of investigation
3. The related subtopics
4. The usage of research animals

RESULTS

Ten subject related keywords were used and 6281
related articles were found. Excluding duplications
and non topic related papers yielded 3313 papers
remained for investigation, from which 249 (7.5%)
were animal research. Probably depending on the
early years failed documentation in 25 articles (10%)
in the animal research group no abstracts were
present or no data was found in this regard in the
abstracts, are excluded from study (29 in totals) and
the data represents of total 220 articles. The
publication distribution through years is summarized
in Table 1. The majority of animal research articles
were published in the last two decades.

Animal research details:
Articles published in English represented 87.2% of
the total, they were published in 68 different journals
from 897 investigators (3.6 author / publication),
being 17 (6.8%) in vitro studies.

Authorship:
From the 897 investigators, 713 (79.5%) had only one
publication and 184 (20.5%) more than one. The most
common authors were with:
Kropp BP / Rink RC: 14 (5.6%) publications.
Tanagho EA: 9 (3.6%) publications.
Dahiya R : 8 (3.2%) publications.
Badyak SF / Mitchell ME: 7 (2.8%) publications:
Atala A / Gonzales R / Nunes LS / Dewan PA: 6
(2.4%) publications.
Lin HK / Baskin LS / Kaminodo S / Lane GJ /
Manivel JC: 5 (2.0%) publications.

These 15 authors had 1.6% of all publications and they
had a total of 108 out of the 249 animal research
publications (% 43.3). The most common 1st author
was Kropp BP with 6 (2.4%) publications. The most
common authorship in articles with only one author
belongs to Alberti C with 3 (1.2%) publications.

Journals:
From the 68 journals (3.6 publication / journal) the
most publication were done at:
J Urol (89 publications, 35.7%)
BJU Int (20 publications, 8.0%)
Urology (17 publications, 6.8%)
Urol Res (13 publications, 5.2%)
Br J Urol, J Pediatr Surg (10 publications 4.0%)

Articles published in the above journals represent
63.8% of the total animal research articles.

Country:
Among the 24 countries and 219 institutions, US was
the leading country with 94 articles (42.7%) followed
by Germany (20, 9%), Japan (17, 7.7%), Turkey (17,
7.7%) and Italy (9, 4%).
Institutions:


Japan: Juntendo uni: 4, Kobe University: 4, Shinshu Uni: 3.

Turkey: Cerrahpasa Medical Faculty: 4, Ankara SB Hospital: 3.

Germany: Aachen University: 4, R-Westfalishe Tech University: 3.

UK: Southampton University: 2, St James Uni: 2, Royal Free Collage: 2.

Canada: Toronto University: 5.

Brazil: San Paulo University: 4.

Italy: Parma University: 3.

Australia: Adelaide Hospital: 3.

Clinic:

Urology: 136 62.9%
Pediatric surgery: 30 13.8%
Surgery: 18 8.3%
Pediatric Urology: 14 6.4%
Biomedical: 13 6.0%
Nephrology: 5 2.3%
Others*: 17 8.0%
Collaborate work**: 16 7.4%

*: Pathology, Orthopedics, Pediatrics, Biochemistry, Plastic surgery, etc...
**: Included in above mentioned data

The most common sub topics were augmentation, use of matrix, animal models, substitution and diversion (Table 2).

Animals:

Rat was used mostly (36.6%) followed by dog (27.7%) and pig (15.8%)

From 249 publications, only 220 could be investigated in details due to lacking of information from abstracts.

Animals employed in the studies were:

Rat : 73+1 (36.6%) *

Dog : 55+1(27.7%) *
Pig : 32 (15.8%)
Rabbit : 18+2 (9.9%) *
Sheep : 8 (3.9%)
Mouse : 8 (3.9%)
Hamster : 2 (0.8%)
Sheep fetus : 3 (1.4%)
Rabbit fetus : 1+1 (0.9%)
Chicken fetus : 3 (1.4%)

* Research with multiple animals

The number of animals used in research (only represents the animals from 146 of 205 publications with exact data).

Dog : 42 publications total of 485
Rat : 50 publications total of 2883
Pig : 24 publications total of 298
Rabbit : 17 publications total of 368
Sheep : 7 publications total of 107
Mouse : 1 publications total of 20
Sheep fetus : 2 publications total of 35
Rabbit fetus : 1 publications total of 247
Chicken fetus : 2 publications total of 159

Table 1: Publication distribution among years (n=3313)

<table>
<thead>
<tr>
<th>Year</th>
<th>All</th>
<th>Animal Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>1800</td>
<td>5</td>
<td>None</td>
</tr>
<tr>
<td>1900-49</td>
<td>15</td>
<td>None</td>
</tr>
<tr>
<td>1950-59</td>
<td>191</td>
<td>5 (2.6%)</td>
</tr>
<tr>
<td>1960-69</td>
<td>256</td>
<td>6 (2.3%)</td>
</tr>
<tr>
<td>1970-79</td>
<td>401</td>
<td>9 (2.2%)</td>
</tr>
<tr>
<td>1980-89</td>
<td>529</td>
<td>21 (4%)</td>
</tr>
<tr>
<td>1990-99</td>
<td>1008</td>
<td>98 (9.7%)</td>
</tr>
<tr>
<td>2000-08</td>
<td>908</td>
<td>110 (12.1%)</td>
</tr>
</tbody>
</table>
Table 2: The distribution of subjects of animal research (n=249)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of Literature</td>
<td>11</td>
<td>4.4%</td>
</tr>
<tr>
<td>Augmentation</td>
<td>103</td>
<td>41.3%</td>
</tr>
<tr>
<td>Otoaugmentation</td>
<td>5</td>
<td>2.0%</td>
</tr>
<tr>
<td>Gastrocystoplasty</td>
<td>26</td>
<td>10.6%</td>
</tr>
<tr>
<td>Enterocystoplasty</td>
<td>59</td>
<td>23.6%</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Omentum</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Amnionic membrane</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Muscle/fascia</td>
<td>7</td>
<td>2.8%</td>
</tr>
<tr>
<td>Tissue expander</td>
<td>3</td>
<td>1.2%</td>
</tr>
<tr>
<td>Different type of matrix</td>
<td>74</td>
<td>29.7%</td>
</tr>
<tr>
<td>Bladder bioengineering</td>
<td>16</td>
<td>6.5%</td>
</tr>
<tr>
<td>Small bowel submucosa</td>
<td>24</td>
<td>9.7%</td>
</tr>
<tr>
<td>Acellular bladder</td>
<td>12</td>
<td>4.8%</td>
</tr>
<tr>
<td>Collagen</td>
<td>6</td>
<td>2.4%</td>
</tr>
<tr>
<td>Absorbable membrane</td>
<td>7</td>
<td>2.8%</td>
</tr>
<tr>
<td>Acellular membrane</td>
<td>5</td>
<td>2.0%</td>
</tr>
<tr>
<td>Synthetic materials</td>
<td>2</td>
<td>0.8%</td>
</tr>
<tr>
<td>Nanopolimer</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Gore-tex</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Overall extrophy</td>
<td>28</td>
<td>11.2%</td>
</tr>
<tr>
<td>Pubis repair</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Embryology/physiology</td>
<td>10</td>
<td>4.0%</td>
</tr>
<tr>
<td>Models</td>
<td>7</td>
<td>2.8%</td>
</tr>
<tr>
<td>Ca ++</td>
<td>9</td>
<td>3.6%</td>
</tr>
<tr>
<td>Monkey case report</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Bladder substitution</td>
<td>6</td>
<td>2.4%</td>
</tr>
<tr>
<td>Bladder transplantation</td>
<td>4</td>
<td>1.6%</td>
</tr>
<tr>
<td>Prefabricated bladder</td>
<td>2</td>
<td>0.8%</td>
</tr>
<tr>
<td>Urinary diversion</td>
<td>29</td>
<td>11.6%</td>
</tr>
<tr>
<td>Overall</td>
<td>12</td>
<td>4.9%</td>
</tr>
<tr>
<td>Ureterosigmoidostomy</td>
<td>17</td>
<td>6.9%</td>
</tr>
<tr>
<td>Bladder pacemaker</td>
<td>1</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

DISCUSSION

We previously done PUBMED based medical research in different subjects and using this resource we obtained many interesting findings 6-8. In this study we focused on animal research on bladder extrophy, which describes the main highlights of the subject.

The hardest part of such a PUBMED research is to obtain reliable data from the abstracts as they don’t always include sufficient data for investigation. Free internet resources have limits in regard to reach the full text publication, the investigator have to reevaluate the reliable data obtained from the abstract itself and we done it this way.

Additionally, investigators usually do PUBMED search with MESH words but from the key words we used only are half were MESH keywords, thus you still get results, which shows that the authors still use non MESH keyword in there articles (2551 articles 40%). The necessity for increase on MESH keywords to reach more specific data, as is clearly seen here is out of the scope of this study. It’s also important to point that if the investigators use research and/or experimental as keyword, they can only reach a very limited number (only 53.85% of all experimental papers) of the here mentioned papers. This finding indirectly shows that the specific keywords (experimental & research) are not always included in papers as key words.

We noticed in the last two decades, the investigations in this area in total and that with the use of medicine related advanced technology the basic science research at cellular level are both increased.

Although there are many reports from all over the world, it is noticeable that some centers are specialized and produce more research in these subjects. This can be explained by the fact that the centers, which have the technology and information published more than the others 9. US is a leading country, and institutions from US dominated in all parameters in regard of the number, usage of advanced technology, authorship and publication.

Urology journals, clinics and authors also dominated in regard to the subject. Pediatric surgery comes in the second place; obviously the other specialties and basic science have limited interest just by being having co authorship only.

Although FELESA recommend usage of 3R Rule (Reduction, Refinement, Replacement) and use animals of low species in research, the tendency in this area seems to be usage of big animals such as dog, pig and rabbit. This can be explained that some surgical techniques are more easily done in these bigger animals and/or with the existence of previous animal models which proved to be efficient. Looking to the spectrum of subjects, it is clearly noticeable that the augmentation and related surgical techniques makes 41.3% of the papers. The second most common subject (29.7%) is use of different type of matrix, which also includes the bladder engineering, which is popular in the last decade and also represents the use of modern technology in bladder extrophy related research and these papers come from specific centers.

It is also a remarkable finding from the collected data that the research on the origin of the diseases represents only a small number compared to therapeutically approaches. Some could argue that the opposite dominance could be more beneficial.
We found among the experimental papers only 7 (2.8%) models of bladder extrophy, which shows actually a lack and need of new models in this area. The most used animal is rat followed by dog, rabbit and pig. The numbers and the necessity of the used animals are not aimed to discuss here.

CONCLUSION
Our data showed an increase of animal research based articles in the last two decades. These articles were published mainly in Urology journals and by urology departments followed by pediatric surgery. Increase in dedicated centers, use of modern technology, creating new models and investigating the origin of pathologies are, from our point of view, the most important factors which will affect the horizon of research in this area in the future and the pediatric surgeons should increase their contribution to this subject.

REFERENCES
2. Houston JD, Fiore DC. Online medical surveys: using the Internet as a research tool. MD Comput 15:116-120, 1998