Abstract: 2014 PBMI Annual Drug Benefit Conference

Las Vegas, USA (3-5 Feb 2014)

Poster Presentation

Topical Prescription Compounds for the Treatment of Neuropathic, Osteoarthritic, Oncologic and Other Complex Chronic Pain Syndromes: A Literature Review and Appraisal

Del Doherty, PharmD, MPH; A. J. Day, PharmD; Gus, Bassani, PharmD; Maria Carvalho, PharmD, PhD

PCCA, 9901 South Wilcrest Drive, Houston, TX 77099, USA

Background: The utilization of compounded prescription drugs has increased over the years and now represents approximately 1-5% of total prescriptions filled in the United States. Although the trend has remained relatively flat, primarily because of the growth of expensive biologics and other specialty medications in the market, some pharmacy benefits managers (PBMs) and health plans (HPs) have made a myriad of plan design, formulary and clinical decisions to manage the utilization and expenditure of prescription compounds. While some of these decisions are necessary, others have been detrimental to patients' outcomes. One of the most targeted therapeutic options is topical prescription compounds. These products commonly include Amitriptyline 2% -10%, Gabapentin 5%-10%, Imipramine 2% - 10%, Ketamine 5% - 10%, Ketoprofen 10%, and Lidocaine 1% - 10%, amongst others. These agents are typically used for serious pain conditions such as neuropathic, osteoarthritic, oncologic and other types of complex chronic pain syndromes. The clinical basis for using these products as optimal alternatives to systemic therapy for the treatment of pain is predicated on their mechanism of action and the receptors accessible from dermal application of these ingredients. Several studies including anecdotal reports, case reports or case series, cohort analyses and clinical trials have evaluated the efficacy and clinical impact of topical prescription compounds compared to traditional therapy for the treatment of pain. Some PBMs and HPs have based formulary and clinical decisions regarding topical prescription compounds on such studies which concluded that topical prescription compounds show no clinical superiority over manufactured traditional therapies and should, therefore, not be covered.

Objective: To conduct a literature review and appraisal of the key studies on the use of topical prescription compounds versus manufactured products for the treatment of neuropathic, osteoarthritic, oncologic and other complex pain syndromes in order to determine whether they meet the methodological rigor to influence a policy change.

Methods: A comprehensive review and appraisal of the literature on clinical efficacy of topical compounded products versus traditional therapy for the treatment of neuropathic, osteoarthritic, oncologic and other types of complex chronic pain syndromes.

Results and Discussion: After a thorough search process, 31 articles were found that met the search criteria. Of the 31 articles identified, 17 were case reports or case series, 8 were randomized placebo-controlled (2 double blind and cross-over) trials and 6 were cohort (3 retrospective and 3 prospective) studies. Among the 17 case reports or case series identified in this evaluation several hold no predictive value, are anecdotal in nature and could show no potential causal links. The case reports did not provide enough information for a critical appraisal of the evidence presented and were, therefore, excluded from the final analysis. Unlike case reports or case series, cohort studies are longitudinal in nature with a follow up of two or more patient groups in order to observe the outcome of interest. The 6 cohort studies identified in this analysis included a combined 143 participants (averaging 24 per study). In some instances there was no statistical basis for the conclusion, no data was presented to support the conclusion, the sample sizes were too small to produce statistically significant results and, at least in one case, the clinical protocol was questionable since patients were simultaneously receiving other topical products not included in the study. The most significant concern with the cohort studies was a high potential for selection bias which was not addressed by the authors, making the overall conclusion of these cohort studies questionable at best. There were 8 randomized placebo-controlled trials identified in this analysis, including a combined 460 participants (averaging 58 per study). Three of these trials, with an average of 100 participants, showed that patients had a favorable clinical outcome when treated with topical prescription compounds, the remaining five, with an average of 32 participants per trial, showed no improvement in pain outcome. A critical limitation of these trials was the small sample size. To address this, authors used crossover designs with a washout period. In at least one of the trials with a crossover design, the authors themselves question whether the duration of the washout period was adequate. There were also clinical concerns raised by the authors in some of the studies about dose optimization for selected treatments, and whether monotherapy represented optimal treatment in certain cases.

Conclusion: The results of this evaluation demonstrate the lack of evidence or clinical basis to support the decision by some PBMs and HPs to preclude or severely limit the coverage of topical compounds. The majority of the studies included in the final analysis had some methodological challenges and did not have a sample size with the power to show a difference in pain outcome. There is a need for more studies in this area with larger sample sizes, appropriate clinical design, and statistical rigor to address some of the important research questions around the use of topical prescription compounds. However, future studies should not only focus on clinical efficacy, but also on total cost and overall quality of care.

Click the QR to see more PCCA studies and reports.

Topical Prescription Compounds for the Treatment of Neuropathic, Osteoarthritic, Oncologic and Other Complex Chronic Pain Syndromes: A Literature Review and Appraisal

Del Doherty, PharmD, MPH[1]
A. J. Day, PharmD
Gus, Bassani, PharmD
Maria Carvalho, PharmD, PhD

PCCA
9901 South Wilcrest Drive
Houston, TX 77099
USA

Background

The utilization of compounded prescription drugs has increased over the years and now represents approximately 1-5% of total prescriptions filled in the United States. Although the trend has remained relatively flat, primarily because of the growth of expensive biologics and other specialty medications in the market, some pharmacy benefits managers (PBMs) and health plans (HPs) have made a myriad of plan design, formulary and clinical decisions to manage the utilization and expenditure of prescription compounds. While some of these decisions are necessary, others have been detrimental to patients' outcomes. One of the most targeted therapeutic options is topical prescription compounds. These products commonly include Amitriptyline 2% -10%, Gabapentin 5%-10%, Imipramine 2% - 10%, Ketamine 5% - 10%, Ketoprofen 10%, and Lidocaine 1% - 10%, amongst others. These agents are typically used for serious pain conditions such as neuropathic, osteoarthritic, oncologic and other types of complex chronic pain syndromes. The clinical basis for using these products as optimal alternatives to systemic therapy for the treatment of pain is predicated on their mechanism of action and the receptors accessible from dermal application of these ingredients. Several studies including anecdotal reports, case reports or case series, cohort analyses and clinical trials have evaluated the efficacy and clinical impact of topical prescription compounds compared to traditional therapy for the treatment of pain. Some PBMs and HPs have based formulary and clinical decisions regarding topical prescription compounds on such studies which concluded that topical prescription compounds show no clinical superiority over manufactured traditional therapies and should, therefore, not be covered.

Objective

To conduct a literature review and appraisal of the key studies on the use of topical prescription compounds versus manufactured products for the treatment of neuropathic, osteoarthritic, oncologic and other complex pain syndromes in order to determine whether they meet the methodological rigor to influence a policy change.

Methods

A comprehensive review and appraisal of the literature on clinical efficacy of topical compounded products versus traditional therapy for the treatment of neuropathic, osteoarthritic, oncologic and other types of complex chronic pain syndromes

For a copy of this poster, please scan the QR code.

[1] Correspondence to: ddoherty@pccarx.com

Figures

Figure 1. Literature Search Process

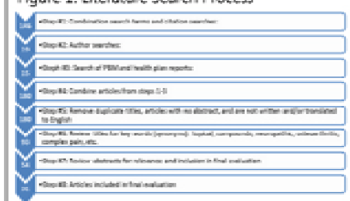

Figure 2. Number of Articles by Design

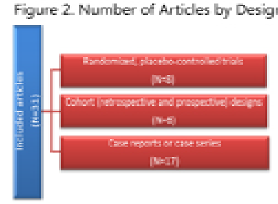

Figure 3. Primary Endpoint and Sample Size by Study Design

	Number of studies with improvement in primary endpoint (n=number of study participants)	Number of studies with no improvement in primary endpoint (n=number of study participants)	Total
Cohort Studies	3 (n=80)	3 (n=63)	6 (n=143)
Randomized Control Trials	3 (n=299)	5 (n=162)	8 (n=460)
Total	6 (n=379)	8 (224)	14 (n=603)

Figure 4. List of Studies

Study	Authors	Objective	Study Design	Sample Size	Citation
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	5	[illegible]
[illegible]	[illegible]	[illegible]	Observational	6	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	20	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	12	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	Prospective trial	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Results and Discussion

After a thorough search process, 31 articles were found that met the search criteria. Of the 31 articles identified, 17 were case reports or case series, 8 were randomized placebo-controlled (2 double blind and cross-over) trials and 6 were cohort (3 retrospective and 3 prospective) studies. Among the 17 case reports or case series identified in this evaluation several hold no predictive value, are anecdotal in nature and could show no potential causal links. The case reports did not provide enough information for a critical appraisal of the evidence presented and were, therefore, excluded from the final analysis. Unlike case reports or case series, cohort studies are longitudinal in nature with a follow up of two or more patient groups in order to observe the outcome of interest. The 6 cohort studies identified in this analysis included a combined 143 participants (averaging 24 per study). In some instances there was no statistical basis for the conclusion, no data was presented to support the conclusion, the sample sizes were too small to produce statistically significant results and, at least in one case, the clinical protocol was questionable since patients were simultaneously receiving other topical products not included in the study. The most significant concern with the cohort studies was a high potential for selection bias which was not addressed by the authors, making the overall conclusion of these cohort studies questionable at best. There were 8 randomized placebo-controlled trials identified in this analysis, including a combined 460 participants (averaging 58 per study). Three of these trials, with an average of 100 participants, showed that patients had a favorable clinical outcome when treated with topical prescription compounds, the remaining five, with an average of 32 participants per trial, showed no improvement in pain outcome. A critical limitation of these trials was the small sample size. To address this, authors used crossover designs with a washout period. In at least one of the trials with a crossover design, the authors themselves question whether the duration of the washout period was adequate. There were also clinical concerns raised by the authors in some of the studies about dose optimization for selected treatments, and whether monotherapy represented optimal treatment in certain cases.

Conclusion

The results of this evaluation demonstrate the lack of evidence or clinical basis to support the decision by some PBMs and HPs to preclude or severely limit the coverage of topical compounds. The majority of the studies included in the final analysis had some methodological challenges and did not have a sample size with the power to show a difference in pain outcome. There is a need for more studies in this area with larger sample sizes, appropriate clinical design, and statistical rigor to address some of the important research questions around the use of topical prescription compounds. However, future studies should not only focus on clinical efficacy, but also on total cost and overall quality of care .

